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General review

## Hajj-associated infections<sup>☆</sup>

### *Infections liées au Hadj*

A. Salmon-Rousseau<sup>a</sup>, E. Piednoir<sup>a</sup>, V. Cattoir<sup>b</sup>, A. de La Blanchardière<sup>a,\*</sup>

<sup>a</sup> Service des maladies infectieuses et tropicales, CHU de Caen, avenue Côte-de-Nacre, 14033 Caen cedex 9, France

<sup>b</sup> Service de microbiologie, CHU de Caen, avenue Côte-de-Nacre, 14033 Caen cedex 9, France

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#### Abstract

**Background.** – The Hajj is the largest annual mass gathering event in the world, thus favoring the transmission of various infections: 183 different nationalities, high temperatures, coincidence with the start of the flu season in the Northern hemisphere, a long barefoot walk, tent-type accommodation, communal toilet facilities, absence of food control, and sharing of razors. Infections are the first cause of hospital admission, which often occurs in the home country of pilgrims.

**Methods.** – Literature review on PubMed from 1952 to November 2015 on the epidemiology and prevention of infections contracted during the Hajj, using the keywords “Hajj” and “infections”.

**Results.** – Respiratory tract infections, ENT infections, influenza, pyogenic pneumonia, whooping cough, and tuberculosis are most frequently observed during the Hajj. Outbreaks of meningococcal meningitis have been reported in pilgrims and their contacts. Waterborne infections such as gastroenteritis and hepatitis A are common, despite the improvement of health conditions. Pyoderma and furuncles are also frequently observed. Recently, dengue fever, Alkhumra hemorrhagic fever, and Rift Valley fever have emerged but no case of MERS-coronavirus, appeared in Saudi Arabia in 2012, have yet been observed during the 2012–2014 Hajj.

**Conclusion.** – Prevention is based on compulsory meningococcal vaccination, vaccination against seasonal influenza and pneumococcal infections for pilgrims at high risk of contracting the infection, and on vaccination against hepatitis A. Updating immunization for diphtheria/tetanus/poliomyelitis/pertussis and measles/mumps is also crucial and pilgrims must comply with hygiene precautions.

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**Keywords:** Hajj; Infections; Mecca; Pilgrimage; Vaccination

#### Résumé

**Contexte.** – Le Hadj, plus grand rassemblement au monde, est propice aux infections : 183 nationalités, température élevée, coïncidence avec la grippe en Occident, longue marche pieds nus, logement en tentes, toilettes collectives, absence de contrôle sanitaire alimentaire, rasoirs à usage multiple. Les infections, qui souvent n'apparaissent qu'après le retour, sont la première cause d'hospitalisation.

**Méthodes.** – Revue systématique de la littérature consacrée à l'épidémiologie et à la prévention des infections contractées lors du Hadj, de 1952 à novembre 2015, en combinant les termes « Hadj » et « infections ».

**Résultats.** – Lors du Hadj, les infections respiratoires dominent, avec les infections ORL, la grippe, les pneumopathies à pyogènes, la coqueluche et la tuberculose. Des épidémies de méningite ont été rapportées chez les pèlerins et leurs contacts. Les infections d'origine hydriques (gastroenterites, hépatites aiguës) demeurent fréquentes malgré l'amélioration des conditions d'hygiène. Les pyodermes et furoncles sont fréquents. Depuis quelques années, la dengue, la fièvre hémorragique Alkhumra et la fièvre de la vallée du Rift émergent. La menace du MERS-coronavirus, apparue en Arabie saoudite en 2012, n'a pas été confirmée au cours des Hadj de 2012 à 2014.

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\* Corresponding author.

E-mail addresses: salmonrousseau@hotmail.fr (A. Salmon-Rousseau), emmanuel.piednoir@ch-avranches-granville.fr (E. Piednoir), cattoir-v@chu-caen.fr (V. Cattoir), delablanchardiere-a@chu-caen.fr (A. de La Blanchardière).

**Conclusion.** – La prévention repose sur la mise à jour du calendrier vaccinal (DTP, coqueluche, rougeole, oreillons, rubéole), la vaccination obligatoire antiméningococcique, mais également sur les vaccinations antigrippale et antipneumococcique pour les personnes à risque, la vaccination contre l'hépatite A, et sur les précautions d'hygiène que les pèlerins, bien que souvent âgés et atteints de comorbidités, adoptent de manière irrégulière.

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**Mots clés :** Hadj ; Infections ; La Mecque ; Pèlerinage ; Vaccination

## 1. Introduction

The origins of the Hajj date back to 2000 B.C. when Ismael, son of the prophet Abraham and Abraham's servant Hager were stranded in the desert. The Angel Gabriel came down to Earth and created a spring of fresh water for the baby. Upon orders from God, Abraham is said to have built a monument on the site of the spring, called the Kaaba. In 630 A.D., the Prophet Muhammad led a group of Muslims there during the first official Hajj.

From the 8th to the 13th day of the 12th month of the Islamic calendar, Mecca, Islam's holiest city, becomes particularly vital; pilgrims making their once-in-a-lifetime 5-day excursion to the site.

Pilgrims have to be in the state of Ihram ("state of purification") before reaching Mecca: they bathe, wear the white Ihram garment, refrain from using scented toilet articles, having sexual intercourse, shaving, cutting their hair and nails. They then begin a long walk barefoot over rough terrain. The climate is extreme, with daytime temperatures that can reach 45 °C in the summer, and night temperatures that occasionally fall to 10 °C (rituals include a night under the stars), and can coincide with the influenza season in the Northern Hemisphere. They typically stay in tent-type accommodation; 50 to 100 pilgrims share the same domestic facilities and move around by buses or on foot. The end of the Hajj is marked by the sacrifice of cattle and by men shaving their hair, using mandatory disposable razors [1,2].

Completion of all of the mandated rituals is believed to guarantee pilgrims a place in heaven as well as the title of Hajji; a coveted and admired title among Muslim communities around the world. Hajj is the fifth pillar of Islam, after the profession of faith, fasting during Ramadan, charitable giving, and ritual prayer.

As there are approximately 1.6 billion Muslims worldwide and that they are all obliged to attend the Hajj at least once in their lifetime, this event has become the largest annually recurring mass gathering event in the world, with an attendance that reached 3 million pilgrims in 2011. Most pilgrims are men (64.3%) coming from over 183 different countries [3,4]: 92% arriving by air, 7% travelling overland, 1% by sea; hence, a huge diversity in terms of ethnic origin and socioeconomic status [1]. Crowd densities can reach 7 individuals per m<sup>2</sup> during the Hajj. Thus, quotas have been set by the Organization of Islamic Cooperation to limit the event to 1000 pilgrims/1 million inhabitants [1]. This figure corresponded, for France, to around 24,000 visas for the 2013 Hajj [5].

Although Muslims are enjoined to undertake the Hajj only when adequately healthy, pilgrims are often middle-aged or

Table 1

Number of deaths and mortality rate during the 2002–2006 Hajj [7].

*Nombre de décès et taux de mortalité au cours du Hadj, de 2002 à 2006 [7].*

	Pilgrims	Deaths	Overall mortality (per 100,000 pilgrims)
February 2002	2,041,129	495	24.2
January 2003	2,012,074	766	38.1
January 2004	2,164,469	651	30.1
January 2005	2,258,050	1084	48.0
December 2006	2,378,636	779	32.7

elderly before they can afford the journey, and they often present with comorbidities [5].

Various epidemics during the 19th and the early 20th centuries (cholera, smallpox, plague, typhus) have led European states and now modern-day Saudi Arabia to an efficient organization of the pilgrimage.

Today, the Saudi state arranges pro bono visas, free health-care services, security services, crowd control, and licensed slaughterhouses and barbers to ensure that all aspects of pilgrimage rituals are safely conducted without any major incident throughout the 5-day Hajj.

Health-related risks during the Hajj are two-fold: non-communicable diseases and infectious diseases. With regard to non-communicable diseases:

- ischemic heart disease is the second cause of hospital admission (12%) during the Hajj after pneumonia [6];
- trauma is the third cause (9%) [6]. The long hours of walking, waiting or travelling, disrupted daily rhythms, pushing and crowd movements, and poor compliance with the use of seatbelts in vehicles may contribute to the physical exhaustion of already weakened people, along with sometimes fatal falls. In 2006, 380 pilgrims died in a stampede [2];
- heat exhaustion and heatstroke are leading causes of morbidity and mortality, particularly in the summer due to the absence of air conditioning, arduous physical rituals, reduced shade, and inadequate fluid intake. Men are more exposed because they do not have the right to cover their heads [2].

According to the ministry of Health of Saudi Arabia, Hajj-related mortality between 2002 and 2006 ranged from 24 to 48 individuals per 100,000 pilgrims (Table 1) [7]. Causes of death in 2006 were reported in a study of 541 pilgrims who died in Mecca and other holy places during the Hajj (Table 2): 56% of documented deaths were of cardiovascular origin and

Table 2

Causes of death listed in the 2006 Hajj (2,378,636 pilgrims) [7].  
*Causes des décès au cours du Hadj de 2006 (2 378 636 pèlerins) [7].*

Causes of death	n (% of deaths)	% of pilgrims
Cardiovascular disease	302 (56%)	0.0126
Cardiac or respiratory failure	111 (21%)	0.0046
Injuries and poisoning	37 (7%)	0.0015
Asthma and bronchial diseases	18 (3%)	0.0007
Diabetes	11 (2%)	0.0004
Renal insufficiency	9 (2%)	0.0003
Infectious diseases	9 (2%)	0.0003
Other respiratory diseases	8 (1%)	0.0003
Undetermined causes	3 (1%)	0.0001
Senility	5 (1%)	0.0002
Other causes	28 (5%)	0.0011
Total	541 (100%)	0.0227

only 2% were caused by infectious diseases [7]. The 2008 mortality among 206,831 Indonesian people who undertook the Hajj reached 216 per 100,000 pilgrims, most often due to cardiovascular (66%) and respiratory (28%) diseases [8].

With regard to infectious diseases and despite a large number of articles devoted to various infectious diseases, there is no recent general review of the epidemiology and prevention of Hajj-associated infectious diseases.

## 2. Methods

We performed a systematic review of English and French articles published from 1952 (first article) to November 2015 via an electronic search on PubMed. We used the keywords “Hajj” AND “infections”. The search was limited to studies conducted in humans. We also retrieved the articles in the reference lists of the selected articles. Meeting abstracts published in supplements of medical journal and information available on official websites were included [3,5,7]. We focused on reviews, updates, outbreaks, emerging infectious diseases, causes of hospitalization, causes of mortality, and prevention. We paid a particular attention to recent studies on MERS-CoV, respiratory tract infections, and vaccinations against respiratory tract infections.

We first identified 281 articles and websites, of which 68 were further selected for extensive analysis mainly based on clinical relevance, study quality and reliability, and date of publication.

## 3. Epidemiology of Hajj-associated infectious diseases

The inevitable overcrowding in a confined area increases the risk of infection. Infections were the leading cause of hospitalization (36%) during the 2003 Hajj (Tables 3 and 4) [6].

The speed of air travel means pilgrims incubating infectious diseases at their time of departure may not experience clinical symptoms until their arrival in another country, thereby facilitating the spread of disease and outbreaks in close contacts who did not travel [9].

Table 3

Causes of hospitalization in 808 patients during the 2003 Hajj (2,012,074 pilgrims) [6].  
*Causes des hospitalisations chez 808 patients au cours du Hadj de 2003 (2 012 074 pèlerins) [9].*

Admitting diagnosis	n (%)	% of pilgrims
Infections	294 (36%)	0.0146
Cardiovascular diseases	201 (25%)	0.0099
Pulmonary diseases	109 (14%)	0.0054
Surgical diseases	98 (12%)	0.0048
Endocrine diseases	75 (9%)	0.0037
Gastrointestinal diseases	34 (5%)	0.0016
Obstetric and gynecological diseases	33 (4%)	0.0016
Heat-related diseases	32 (4%)	0.0015
Renal diseases	19 (2%)	0.0009
Psychiatric diseases	6 (1%)	0.0002
Other diseases	6 (1%)	0.0002

### 3.1. Respiratory tract infections

Infections of the respiratory tract are the most frequently reported complaints among Hajj pilgrims. The severity and clinical spectrum of disease vary from mild inconvenience to severe pneumonia leading to hospitalization and even death.

#### 3.1.1. Acute upper respiratory tract infections (AURI)

Acute upper respiratory tract infections (AURI) are common illnesses during the Hajj. Typical symptoms include coughing, sputum production, sore throat, hoarseness of voice, rhinorrhea, fever, and malaise. AURI may be complicated by exacerbations of asthma, chronic obstructive pulmonary disease, sinusitis, and pneumonia. The estimated incidence of AURI during the Hajj ranges from 20% to 80% depending on the type of method used to confirm the diagnosis [10]. Influenza viruses are the most common cause of AURI, followed by respiratory syncytial viruses, and adenoviruses [11].

#### 3.1.2. Seasonal influenza

Seasonal influenza at Hajj, depending on study designs, ranges from 6% in PCR- or culture-confirmed studies to 38% in serological surveillance [12]. The magnitude of viral

Table 4

Type of infection among 294 hospitalized patients for infection during the 2003 Hajj (2,012,074 pilgrims) [9].

*Type d'infection chez 294 patients hospitalisés pour infection au cours du Hadj de 2003 (2 012 074 pèlerins) [9].*

Admitting diagnosis	n (%)	% of pilgrims
Non-tuberculous pneumonia	159 (55%)	0.0079
Gastroenteritis	27 (9%)	0.0013
Upper respiratory tract infection	27 (9%)	0.0013
Cellulitis	13 (4.5%)	0.0006
Sepsis	11 (4%)	0.0005
Acute bronchitis	10 (3.5%)	0.0004
Pulmonary tuberculosis	10 (3.5%)	0.0004
Meningitis	9 (3%)	0.0004
Urinary tract infection	7 (2%)	0.0003
Diabetic foot infection	6 (2%)	0.0002
Other infections	15 (5%)	0.0007

illnesses occurring during the Hajj has the potential for triggering an influenza pandemic. It appears prudent to consider all Hajj pilgrims as subjects at risk. The 2009 pandemic influenza A (H1N1), which had little impact on pilgrims, led to recommendations for isolation, influenza testing, and definition of criteria for hospital admission [13]. No significant effect of the influenza vaccine or the use of personal protective measures against influenza was established in 2013 from observational studies, but vaccine uptake and adherence to face-masks and hand hygiene were reported as low [12]. Until better evidence is obtained, vaccination coupled with rapid antiviral treatment among symptomatic individuals remains the mainstay of prevention of influenza during the Hajj [12]. Following the official recommendations issued by the Saudi Ministry of Health in 2005, vaccination coverage for influenza increased to 100% by the year 2009, and thereafter remained above 80% in pilgrims from resource-rich countries [14]. A 10-year retrospective analysis of the incidence of influenza-like illness and influenza vaccine uptake among 33,213 pilgrims between 2005 and 2014 suggest that the incidence of influenza-like illness decreased as the vaccine coverage increased (relative risk = 0.2,  $P < 0.01$ ) [15].

### 3.1.3. Pneumonia

Pneumonia was in 2003 the first cause of hospital admission during the Hajj, accounting for 20% of all admissions [6]. A prospective study measured the incidence and type of respiratory tract infections during the 1991 and 1992 pilgrimage seasons: bacterial pathogens were detected in 30% of throat swabs with *Haemophilus influenzae*, *Klebsiella pneumoniae*, and *Streptococcus pneumoniae* being the most common pathogens (10%, 5.2%, and 4.8%, respectively) [16]. Severe (bilateral) community-acquired pneumonia was screened during the 2013 Hajj through sputum samples performed in all pilgrims admitted to 15 healthcare facilities in the cities of Makkah and Medina: respiratory pathogens were detected in 68% of sputum samples; 84% were positive for bacterial pathogens. *H. influenzae* and *S. pneumoniae* were the predominant bacterial species (58% and 54% of positive samples, respectively), followed by *Moraxella catarrhalis* (36%) [17]. At least one third of pilgrims are at risk of pneumococcal disease because of age or pre-existing medical conditions. The pneumococcal carriage during the 2012 Hajj increased from 4.4% before to 7.5%. In 2012, non-susceptible isolates increased from 2.5% to 6.1%. Overall, 90% of infections observed are due to the serotypes covered by the 13-valent pneumococcal conjugate vaccine as well as the 23-valent pneumococcal polysaccharide vaccine. Despite the above knowledge, Saudi Arabia has not yet recommended pneumococcal vaccine for pilgrims, and the vaccination recommendation uptake greatly varies across pilgrims' countries of origin [18,19].

### 3.1.4. *Mycobacterium tuberculosis*

*Mycobacterium tuberculosis*, Gram-negative rods, *S. pneumoniae*, and atypical bacteria were the most common pathogens for patients with no response to first-line therapy and requiring hospital admission during the 1994 pilgrimage (28%,

26%, 10%, and 6%, respectively). Multiple risk factors may explain this high rate of tuberculosis: pilgrims originating from endemic countries, overcrowding and decreased cell-mediated immunity due to old age, exhaustion, and undernourishment [20]. The immune response to tuberculosis antigens evaluated by interferon-gamma release assay (Quanti-FERON TB) had increased three months after the 2002 Hajj in 10% (15/149 pilgrims) of Singaporean pilgrims, confirming that pilgrims were at high risk of acquiring *M. tuberculosis* during the Hajj [21]. Tuberculosis is endemic in Saudi Arabia, with a 2008 incidence rate of 16/100,000 population without taking into consideration incomplete reporting, from which 68% were pulmonary [22]. Multidrug-resistant TB (MDR-TB) between 1979 and 1998 ranged from 1.5% to 44% of isolates depending on regions of Saudi Arabia [22]. The prevalence of resistant tuberculosis is three-fold greater in Mecca and Medina than the Saudi national average [23].

### 3.1.5. Pertussis

Pertussis during the Hajj has only been reported in one prospective seroepidemiological survey which showed a high incidence (1.4%) during the 2002 Hajj among 358 adult pilgrims. This figure should support the administration of acellular pertussis vaccine before pilgrimage [24].

## 3.2. Meningococcal disease

The mass gathering generated by the Hajj has previously resulted in widespread dissemination of meningococcal disease, such as the major serogroup A outbreak in 1987. Bivalent vaccination against groups A and C was subsequently made compulsory in 1988 for Hajj pilgrims, as a requirement for obtaining a Hajj visa, consequently leading to a major reduction in Hajj-associated outbreaks due to these serogroups [2].

A shift from serogroup A disease to serogroup W-135 occurred in 2000 and 2001 when a previously rare meningococcal serogroup W-135 strain caused an outbreak among pilgrims and their contacts, associated with a high attack rate (25/100,000) as well as a high case fatality and sequelae rate (10% and 20%, respectively) despite appropriate antimicrobial therapy [25]. Meningococcal carriers are the primary source of *Neisseria meningitidis* transmission, and the carriage rate of virulent strains may be correlated with the risk of outbreak. A high risk of acquisition of *N. meningitidis* W-135 carriage was documented in Singaporean pilgrims returning from the Hajj in 2001 [26].

In 2001, Saudi Arabia changed the vaccination recommendation from A/C polysaccharide vaccine to compulsory vaccination with a tetravalent A/C/Y/W-135 polysaccharide vaccine for pilgrims entering the country during the Hajj season, following which no further pilgrims developed W-135 disease [25]. Nevertheless, despite this vaccine, the pre-Hajj carriage rate increased from 0.5% to 17% in returning pilgrims. Overall, 23% of them were carrying the W-135 clone and they then transmitted this clone to their household contacts, of whom 13% acquired the clone. Finally, there was a high attack rate of

W-135 disease (28/100,000) amongst contacts in 2001 [26]. Similar results about acquisition of meningococcal serogroup W-135 carriage were observed in vaccinated Turkish Hajj pilgrims during the 2010 Hajj [27]. In 2010, the Ministry of Health of Saudi Arabia introduced the tetravalent meningococcal conjugate vaccine for all children and adults aged 2–65 years living within the Hajj perimeter, pilgrims, all healthcare workers and all government personnel serving the pilgrims in order to achieve a stronger and longer immune response and to reduce the carrier rate [28]. A study performed during the 2012 Hajj showed that 98% of pilgrims arriving through the airport in Jeddah had received meningococcal A/C/Y/W-135 vaccine in the last 3 years and only 0%, 10%, 9%, and 17% had insufficient antibody levels against serogroup A, C, Y, and W, respectively, showing that the vast majority of pilgrims were vaccinated and protected against these four meningococcal serogroups [29].

### 3.3. Waterborne infectious diseases

Various factors contribute to the development of infectious diseases transmitted through water: hygiene, water quality, asymptomatic carriage of pathogenic bacteria, and food storage conditions. Water-associated diseases are less often observed due to improved water supply or disposal of wastewater. Furthermore, Saudi Arabia does not allow pilgrims to bring food and insists that they do not consume food from street vendors who officiate near the holy places.

#### 3.3.1. Gastrointestinal tract infections

Gastrointestinal tract infections were the second cause (6%) of hospitalization for infection in 2003 after pneumonia [6,30]. The mean incidence of diarrhea in pilgrims was 2% despite regular ritual hand washing, but etiological data of diarrheal disease at the Hajj is currently lacking. Such incidence observed despite ritual hand washing should prompt recommendations for a regular use of alcohol-based hand rubs [31]. Cholera reached Hajj areas as far back as 1846. The last cholera epidemic during the Hajj was reported in 1989 and affected 102 pilgrims [2]. With improved water supply and sanitation systems, only sporadic cases have since been reported [32,33].

#### 3.3.2. Hepatitis A

Hepatitis A (HAV) is common during the Hajj for pilgrims under the age of 60 travelling from low endemic areas. Transmission usually occurs through the feco-oral route and spreads from person-to-person because of overcrowding and poor personal hygiene or via ingestion of contaminated water or food. The estimated attack rate among European travelers to the Middle East is 181 per 1000 journeys [34]. Although safe drinking water is supplied during the Hajj, the use of ice from unknown sources carries the risk of contamination. Furthermore, 37% of pilgrims bring foodstuffs from their home countries despite it being banned, 34% buy food from hawkers, and the communal use of toilets without detergents or alcohol increases the risk of HAV infection [35].

### 3.4. Bloodborne infections

Overall, 90% of Muslim men shave their heads at the end of the Hajj [35]; thus increasing the risk of bloodborn infections. Official regulations mandate the testing of barbers for hepatitis B (HBV), C (HCV), and HIV, and the use of disposable razor blades. However, unlicensed barbers operate on the roadside during the Hajj, with non-sterile blades that are re-used on different customers. Data from 1998 showed that 23% of barbers had open hand wounds, 21% used the same blade for more than one shave, and 82% threw at least one used blade to the ground [36]. Data from 1999 obtained from 158 Hajj barbers showed that 4% were positive for HBsAg, 0.6% for HBeAg, and 10% for HCV [37]. Risks related to blood transfusion or blood products and nosocomial infections should not be underestimated as large numbers of Hajjis require admission to hospital.

#### 3.4.1. Hepatitis B

A large number of pilgrims come from the Middle East, where the reported prevalence of HBV infection is 8% [35]. The 2006 prevalence of HBsAg and anti-HBc were 3.0% and 18.7%, respectively, among blood donors in a Saudi tertiary hospital [38].

#### 3.4.2. Hepatitis C

The 2009 reported prevalence of anti-HCV antibodies was 4.3% among blood donors and 2.2% among medical staff from a tertiary hospital close to Mecca [35]. Many pilgrims originate from African and Eastern Mediterranean countries where the prevalence is around 2.5–10% [35,39]. As pilgrims are grouped together in tents, they are also likely to share personal articles such as nail clippers and scissors, hence increasing the risk of HCV transmission [35].

#### 3.4.3. HIV infection

From 1984 to 2003, 7807 HIV case patients were reported in Saudi Arabia, including 1743 nationals and 6064 non-Saudis. Most case patients were concentrated in urban areas and contaminated via heterosexual contact. There has been no reported infection through blood transfusion since 2001 [40]. However, there is no reported data on HIV prevalence in Saudi Arabia and in Hajj pilgrims.

### 3.5. Skin-to-skin transmitted infections

Lengthy rituals of standing and walking, overcrowding, poor hygiene, heat, and humidity promote skin infections which account for 5% of all diseases observed during the Hajj [41]. Pilgrims walk barefoot in certain holy areas. Eczema, intertrigo, and pyoderma are the most common skin diseases [42,43].

### 3.6. Emerging infectious diseases

#### 3.6.1. Dengue fever

Although *Aedes aegypti* is found across the region, the first documented outbreak of dengue fever in Saudi Arabia was observed in 1994, the infection being now endemic. The most

recent outbreak (2010) resulted in 100,000 reported infections and 200 deaths. The potential dissemination into other countries by returning pilgrims who acquire the virus while in Saudi Arabia is a global health issue requiring control measures [44].

### 3.6.2. *Alkhumra hemorrhagic fever (AHF)*

AHF is a tick-borne encephalitis virus, originated from a virus of the *Flavivirus* genus, which usually affects animals (sheep, goats, camels). It is transmitted to humans at night via bites by *Ornithodoros savignyi*, direct contact with the blood of infected animals through a skin wound or consumption of unpasteurized camel milk, but there is no human-to-human transmission [35,45]. A prospective study conducted from 2001 to 2003 reported 20 confirmed cases of AHF in pilgrims who had travelled to or lived in districts around Mecca, where there are livestock markets and slaughterhouses. Acute febrile flu-like illness with hepatitis (100%), hemorrhagic manifestations (55%), and encephalitis (20%) were the main clinical features; the case fatality was 25% [46]. No further case of AHF was published later on.

### 3.6.3. *Rift Valley fever (RVF)*

RVF is due to a virus from the Bunyaviridae family, which predominantly causes necrotic hepatitis, abortion, and death among domestic ruminants (cattle, camels, goats, and especially sheep). The disease is transmitted to humans through *Culex*, *Aedes*, or fly bites, contamination by the raw milk of infected animals, or through traditional slaughtering practices. In November 2000, 165 clinical cases of RVF were laboratory confirmed in Saudi Arabia but not in Mecca [47]. After a 2- to 5-day incubation period, patients may experience flu-like symptoms but fully recover within a week. Major clinical characteristics included hepatocellular failure (75%), acute renal failure (41%), and hemorrhagic manifestations (19%). Case fatality was 34% [48]. However, this threat has not been confirmed, even with serological studies, since the outbreak of 2000 [49].

### 3.6.4. *Middle East Respiratory Syndrome Coronavirus (MERS-CoV)*

In September 2012, the first two cases of acute respiratory infection due to MERS-CoV were reported and originated from Jeddah in Saudi Arabia. The primary source of MERS-CoV remains unknown (bats are suspected) but there is increasing evidence of the presence of MERS antibodies in camels, pointing them as possible intermediate hosts [50,51]. Clinical features of MERS range from asymptomatic or mild disease to acute respiratory distress syndrome and multiple organ failure resulting in death, especially in individuals presenting with underlying comorbidities. No specific drug treatment exists for MERS and infection prevention and control measures are crucial to prevent the infection from spreading in healthcare facilities [51]. On May 31st 2015, 1180 laboratory-confirmed cases (80% from Saudi Arabia) were reported by WHO, with a 40% case fatality [51]. Both community-acquired and hospital-acquired case patients were reported with a low rate of human-to-human transmission in the community. Although most cases of MERS occurred in Saudi Arabia and in the United Arab Emirates, case

patients have been reported in Europe, the USA, and Asia in people who travelled from the Middle East or in their contacts [51]. Saudi Arabia is the only country to report new case patients every week, with 12 new case patients between October 17th and 24th 2015 [52], but no MERS-CoV case patient has been recorded in any of the pilgrimage areas during the Hajj since 2012 [53,54]. Furthermore, if the prevalence of virus and bacteria increased between pre- and post-Hajj nasal specimens during the 2013 Hajj (7% and 15% to 45% and 31%, respectively), no MERS-CoV nasal carriage was observed in a recent prospective study, with similar results, performed in French Hajj pilgrims [55,56]. The estimated epidemic potential of MERS-CoV in Hajj pilgrims seems to be low, with 1 to 7 case patients per Hajj who will develop symptoms [57]. In France, microbiological investigations conducted in 221 individuals, from whom 7 contacts of confirmed cases and 51 individuals meeting the criteria for identifying suspected case patients, led to the confirmation of two case patients in May 2013 (1 death), with a secondary case of nosocomial transmission. No other case patient has since been confirmed [58].

## 4. Health recommendations for travelers to Saudi Arabia for the Hajj

Most infections and outbreaks are avoidable if appropriate awareness and prophylactic measures are implemented. The Ministry of Health of Saudi Arabia publishes health conditions for entry visas for the Hajj every year since 2008 [59]. WHO and the French Institute for Public Health Surveillance (French acronym InVS) annually publish health requirements for pilgrims to Mecca [60,61].

### 4.1. *Mandatory vaccines*

#### 4.1.1. *Meningococcal meningitis*

All travelers aged over 2 years are required to produce a certificate of vaccination with the quadrivalent (A/C/Y/W-135) vaccine against meningitis issued within the past 3 years and not less than 10 days before arrival in Saudi Arabia. In addition, for visitors aged over 12 years arriving from countries in the African meningitis belt, ciprofloxacin chemoprophylaxis (500 mg) is administered at port of entry in order to reduce the rate of carriers [59–61].

#### 4.1.2. *Poliomyelitis*

All travelers arriving from polio-endemic countries and re-established transmission countries, regardless of age and vaccination status, should receive one dose of oral polio vaccine 1 to 12 months prior to departure, and receive another dose on border points on arrival in Saudi Arabia [59–61].

#### 4.1.3. *Yellow fever*

All travelers arriving from countries at risk of yellow fever must present a valid yellow fever certificate showing that they were vaccinated at least 10 days and not more than 10 years before arrival at the border [59–61].

## 4.2. Recommended health measures

### 4.2.1. Vaccines

**4.2.1.1. Seasonal influenza.** Seasonal influenza vaccination is recommended for international pilgrims before arrival and for internal pilgrims, particularly those at increased risk of severe influenza diseases including pregnant women, children aged <5 years, the elderly, and individuals presenting with underlying health conditions such as HIV infection and chronic heart or lung disease. Vaccination is also recommended for all healthcare workers in the Hajj premises [59–61].

**4.2.1.2. Pneumococcal infections.** While there are substantial gaps that need to be addressed regarding our knowledge of the exact burden of these diseases and the effectiveness of pneumococcal vaccination in Hajj pilgrims, it can be assumed that they often have indication for such vaccines [62]. However, only French authorities recommend pneumococcal vaccine for pilgrims with usual indications [61].

**4.2.1.3. Diphtheria/tetanus/poliomyelitis/pertussis and measles/mumps.** Updating immunization is recommended [59–61].

**4.2.1.4. HAV.** French authorities recommend vaccination for pilgrims from developed countries [61].

### 4.2.2. Other recommendations

**4.2.2.1. Concerning the risk of respiratory infectious disease including MERS-coV.** In 2015, the Saudi Ministry of Health recommended to pilgrims aged over 65 years and presenting with chronic diseases, immune deficiency, malignancy or terminal illnesses, pregnant women, and children aged under 12 years to postpone the pilgrimage for their own safety [59]. Moreover, guidance on ensuring effective handwashing, adhering to cough etiquette, wearing facemasks in crowded areas, avoiding contact with sick pilgrims, animals, drinking raw camel milk, and maintaining good personal hygiene were issued [59].

**4.2.2.2. Concerning the risk of waterborne infectious diseases.** Hajj performers are not allowed to bring fresh food into Saudi Arabia, with the exception of canned or sealed food or food stored in containers in small quantities that can easily be inspected [59]. They are also required to have hand hygiene, avoid street vendor food (including ice), and food made with fresh eggs. Water in sealed bottles is recommended for rehydration.

**4.2.2.3. Concerning the risk of bloodborne infections.** Pilgrims are encouraged not to share personal articles such as nail clippers, razors, and scissors.

**4.2.2.4. Concerning the risk of skin-to-skin transmitted infections.** Pilgrims are encouraged to keep their skin dry and to use talcum powder to keep intertriginous areas intact, to use

sunscreens, umbrellas, and protective footwear. They are also encouraged to avoid tick and mosquito bites [2].

## 5. Discussion about limits to health recommendations for Hajj pilgrims

### 5.1. Concerning general advice against MERS-coV

A study conducted through a standardized questionnaire given to 360 French pilgrims showed that 65% were aware of the MERS situation in Saudi Arabia, 35% knew about the Saudi Arabia recommendations for at-risk pilgrims to postpone participation in the 2013 Hajj, and only 50% of them decided to cancel their participation after being advised during consultations. The authors hypothesized that the price of the already paid travel could be the explanation for some of these pilgrims, religious beliefs for others (death during Hajj could have a beneficial outcome during the afterlife) [63].

### 5.2. Concerning non-mandatory vaccines for pilgrims

#### 5.2.1. Influenza vaccination

In 2011 and 2012, only 65% and 89% of 431 Australian pilgrims respectively reported receiving the influenza vaccine. Common reasons for not receiving the vaccine were pilgrims' reliance on their "natural immunity" and believing that the risk to catch influenza or come into contact with influenza patients was low [64].

#### 5.2.2. Pneumococcal vaccination

Only 7% of 101 French 2014 Hajj pilgrims, who had an indication for pneumococcal vaccination, were advised to have the vaccine by their family physician [65].

#### 5.2.3. Diphtheria, tetanus, and poliomyelitis vaccinations

A cross-sectional study conducted in 2006 among French pilgrims showed low vaccination rates for tetanus (18.9%), diphtheria (14.7%), and poliomyelitis (15.0%). French citizenship, higher level of education, better French fluency, and no previous travel to country of origin were the strongest and most significant determinants of DTpolio vaccination status [66]. A questionnaire performed in 2012, in Detroit, for Hajj pilgrims showed a high vaccine awareness for influenza (91%), meningococcal disease (89%), MMR (81%), hepatitis A (79%), hepatitis B (76%), and DTpolio (61%); a low vaccine awareness for typhoid (37%), and the percentage of those receiving a vaccine receipt was high for meningitis (88%), intermediate for influenza (61%), and low for hepatitis A (41%), hepatitis B (41%), DTpolio (38%), and typhoid (9%) [67].

### 5.3. Concerning vaccination coverage among healthcare workers (HCW) in the Hajj

A cross-sectional survey of physicians and nurses in healthcare centers who attended Hajj-medicine training programs immediately before the beginning of the 2003 Hajj showed that 82% of HCWs received the quadrivalent (A/C/Y/W-135)



meningococcal meningitis vaccine, with 84% of them at least 2 weeks before the Hajj, 66% received the three-dose hepatitis B vaccine series, and only 6% received the current year's influenza virus vaccine. There was no statistically significant difference in terms of compliance with the three vaccines between physicians and nurses [68].

## 6. Conclusion

The Hajj presents unique and unprecedented challenges to the management and control of infectious diseases, which involve not only a growing number of often vulnerable Hajj pilgrims but also people who are in contact with them on their return.

All physicians, particularly infectious disease specialists, must be aware of those risks, to prevent, recognize, and cure Hajj-associated infections.

Saudi organization, vaccines, and hygiene advice have certainly reduced the burden of infectious diseases, which were the first cause of hospitalization in 2003.

Nevertheless, preventive measures accepted by pilgrims are too often limited to mandatory vaccines (against meningococcal meningitis and sometimes poliomyelitis and yellow fever). The uptake of seasonal influenza vaccine and pneumococcal vaccines for pilgrims at increased risk, the updating of vaccination for diphtheria/tetanus/poliomyelitis/pertussis and measles/mumps are insufficient. Possible reasons for this low acceptance are that most travelers come to the clinic only for a vaccination that is necessary to obtain a visa; the costs of vaccination, the lack of information on health risks, religious considerations, and language barriers resulting in increasing reluctance or simple negligence with regard to other vaccinations and health advice.

MERS-coV, usually considered as a dramatic potential disaster during such a mass gathering, has not yet been observed during the Hajj and the estimated epidemic potential of MERS-CoV in Hajj pilgrims seems to be low [57]. However, actions taken by health services, public health experts, and Hajj pilgrims must not be delayed if such cases were to emerge.

## Authors' contribution

A.S and A.D.L.B. designed and wrote the article.

A.S., E.P., V.C., and A.D.L.B amended and approved the article.

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The authors declare that they have no competing interest.

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