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CIRCULATION OF RESPIRATORY PATHOGENS AT MASS GATHERINGS, WITH SPECIAL FOCUS ON THE HAJJ PILGRIMAGE

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1 INTRODUCTION

Mass gathering (MG) medicine is a new field that includes risk assessment, surveillance, and early response to health threats associated with MGs.¹ A MG is usually defined as more than a specified number of persons at a specific location, for a specific purpose, for a defined period of time, and which may greatly vary between different MGs.² The number of participants that classifies an event as a MG is arbitrary. Some guidelines specify any gathering to be a MG when more than 1000 attendees are present. Others require the attendance of as many as 25,000 attendees to qualify. However, outbreaks occur irrespective of the size of a gathering. Outbreaks have been reported in settings such as weddings, private parties, and other events involving fewer than 1000 people, but also in large religious MGs attended by millions of pilgrims or sport, sociocultural, political, or commercial large events.³ According to the World Health Organization, a MG should be defined as "any occasion that attracts sufficient numbers of people to strain the planning and response resources of the community, city or nation hosting the event."² These MGs can be planned or not, and they may be sporadic or recurrent. A major public health concern in relation to MGs is the international circulation of infectious diseases, and the spread between participants and to the population of the nation hosting the event.^{2,4} A number of infectious diseases have been caused or have the potential to cause illnesses and deaths at MGs. The risk and pattern of diseases at MGs are influenced by the features of the event, notably its duration and location, particular activities, and also the participants' characteristics, including their immunity to infectious agents. The first recognition of the consequences of the unique nature of infectious disease for MGs was for food-borne illness arising from person-to-person transmission, with historical reports of cholera outbreaks in the context of the Hajj Muslim pilgrimage and in the Kumb Mela Hindu pilgrimage.⁴ By contrast, the majority of outbreaks occurring at MG events reported over the last few decades resulted from respiratory transmission. Respiratory transmission generally requires close contact and is thus more common in MGs with overcrowded living conditions. Intercontinental outbreaks of Neisseria meningitidis have been described in the context of various MGs, notably at the Hajj between 1987 and 2001.⁴ Over the last 15 years, the rapid international spread of influenza and other respiratory

pathogens in association with MGs have been reported on many occasions. It is now clear that one of the major health risks at modern international MGs is the acquisition of respiratory pathogens, with further spread to origin countries through returning attendees.

In this chapter, we review the available data about the circulation of respiratory pathogens at MGs, with a special focus on the Hajj Muslim pilgrimage which has been better studied.

2 RESPIRATORY TRACT INFECTIONS AT THE HAJJ

The annual Hajj pilgrimage to Mecca in the Kingdom of Saudi Arabia (KSA) is the fifth pillar of Islam. The pilgrimage is mandatory for all adult Muslims with physical and financial capacity, at least once in their lifetime. Therefore, 2–3 million Muslims from over 180 countries across the globe gather each year in Mecca for the Hajj. The Hajj and its rituals are physically demanding. Although the Hajj rituals only take 1 week, many pilgrims gather in the KSA for the month-long Hajj season. Upon arrival in Mecca, the holiest city in Islam, most Hajj pilgrims begin their visit by performing the "Umrah" (also known as the minor pilgrimage). The Umrah is not compulsory but is highly recommended. It can be undertaken at any time of the year and include the "Tawaf" (circumambulation seven times in an anticlockwise direction) of the "Kaaba," known as "Tawaf al-Umrah," and "Sa'I" (seven trips between two small mountains, "Al-Safa" and "Al-Marwah") inside "Al-Masjid al Haram" (ie, "The Sacred Mosque"). The Hajj, which retraces the footsteps of the Prophet Mohammed over approximately 1 week, is performed continuously from the 8th to the 13th of "Dhul Hijja" (ie, "the month of Hajj"), the last month of the Islamic lunar calendar. As this Islamic lunar calendar is 11 days shorter than the Gregorian calendar, the exact dates of Hajj vary from year to year. As part of the Hajj rituals, pilgrims have to visit different sacred places located outside the city of Mecca, including Mina, where they spend the night from 8th to 9th *Dhul Hijja*; the plain of Arafat for the "standing ceremony", the culminating experience of the Hajj, which lasts on 9th Dhul Hijja from after dawn to slightly after sunset; and Muzdalifah where they stay from after sunset on 9th Dhul Hijja to after dawn on 10th Dhul Hijja. Back at Mina, on 10th Dhul Hijja, the pilgrims perform the ritual of "Jamarat" (stoning the columns symbolizing the Devil) by throwing seven stones at only the largest of the three pillars in the four-level Jamarat Bridge. After the ritual of Jamarat, animals are slaughtered in slaughterhouses at Mina, marking the first day of "Eid al-Adha" (ie, "Festival of the Sacrifice"). On the same or the following day, the pilgrims return to Mecca for a second circumambulation of the Kaaba, known as "Tawaf al-Hajj" or "Tawaf al-Ifadah", and the "Sa'l," and then hasten back to Mina to again perform the stoning of the Devil ritual (but this time by throwing seven stones at each of the three pillars) on the 11th and 12th Dhul Hijja. The pilgrims are then allowed to return to Mecca after this storing, but they can also prolong their stay in Mina for another day (the 13th Dhul Hijja) to perform the same process of stoning of the pillars as of 11th and 12th Dhul Hijja. Finally, pilgrims can leave Mecca after a final circumambulation of the Kaaba, known as "Tawaf al-Wada" (ie, "the farewell circumambulation"). However, while not required as part of the Hajj, most pilgrims extend their trips to the city of Medina to visit Islam's second holiest site, "Al-Masjid Al-Nabawi" (ie, "the Mosque of the Prophet"), which contains Muhammad's tomb.

The Hajj presents a major public health and infection control challenges, both for the Saudi authorities, as well as for the national authorities of the countries of origin of the Hajj pilgrims.⁵ In addition to physical exhaustion, sleep deprivation, and extreme heat (in Mecca during October, the average temperature is greater than 38°C during the day and greater than 25°C at night), which increase the susceptibility of pilgrims to airborne infections, inevitable overcrowding for a short period in housing and ritual sites, especially when performing the circumambulation of the *Kaaba* inside the Sacred Mosque in Mecca, with up to eight pilgrims per square meter near the *Kaaba*,⁶ when using the pedestrian tunnels leading to the *Jamarat* Bridge in Mina, and in the Mina camp, this is approximately a 3-km² area where pilgrims are accommodated in tents, some with up to 50–100 people,⁷ greatly increases the risk of acquiring and spreading infectious diseases during the pilgrims' stay, especially airborne diseases. Moreover, returning Hajj pilgrims may contribute to the international spreading of these diseases.

2.1 SYNDROMIC SURVEILLANCE DATA

The "Hajj cough" is considered by pilgrims almost de rigueur.⁸ Early reports from the 1978 Hajj season indicated that upper tract respiratory infections formed the bulk of the workload of medical teams attending pilgrims.⁹ Recent data indicated that 61% of 4136 ill pilgrims consulting at Mina primary health structures suffered respiratory tract infections.¹⁰ Respiratory tract infection was the leading cause of medical admissions in Saudi hospitals during the Hajj, accounting for 57% in a study, among 160 patients in various hospitals in Mina and Arafat and for 74% in another study, among 16,232 outpatients at an hospital in Medina.^{11,12} During the Hajj, pneumonia accounted for 22–39% of 1268 medical admissions in tertiary care structures in Mecca, Mina and Arafat and for 46% of 16,232 medical admissions in a tertiary care hospital in Medina.^{11–14} Pneumonia accounted for 22–27% of 505 admissions in intensive care units where they were responsible for 55% of sepsis.^{15–17} The incidence of pneumonia evaluated in cohorts of Iranian pilgrims was 3.4 per 100,000 pilgrims in 2005.¹⁸

Results of cohort surveys evidenced attack rates of respiratory symptoms of 53% among domestic Saudi pilgrims and of, respectively, 71% and 92% among foreign pilgrims from Iran and Indonesia.¹⁹⁻²¹ In a survey conducted among French pilgrims participating to the Hajj in 2012–2014, the prevalence of cough was 81% and a high proportion presented with associated sore throat (91%), rhinitis (79%), and hoarseness (63%). Myalgia was reported in 48% of cases and subjective fever in 47%. The incubation time of respiratory symptoms was about 8 days and 52% of pilgrims presenting with a cough during their stay were still symptomatic on return. Among pilgrims with a cough, 69% took antibiotics.²² Consumption of antibiotics by Hajj pilgrims suffering mild respiratory symptoms is frequent including 54% of patients consulting at various primary health care centers in Mina,¹⁰ 95–99% patients consulting at the Ear, Nose, and Throat clinic of a Hospital in Mecca,^{23,24} 72% of a cohort of Iranian pilgrims and 94% of in cohort of Indonesian pilgrims.¹⁹⁻²⁵

2.2 ISOLATION OF RESPIRATORY PATHOGENS IN ILL HAJJ PILGRIMS

2.2.1 Viruses

Recent studies using PCR tools were conducted from 2005 through 2014 among a total of 1784 pilgrims who were suffering from upper respiratory tract infections, influenza like illness, lower tract respiratory infection, or pneumonia. Definition of syndromes differed according to authors. Sample size varied from 7 to 555 individuals. These surveys were conducted in ill pilgrims from various nationalities recruited at tertiary care hospitals and primary health care centers in Saudi Arabia or at Mina encampment or when returning in home country. The types of samples included were throat swabs, nasal swabs, nasopharyngeal swabs, sputum, bronchoalveolar, and nasopharyngeal aspirates, depending on the studies.^{7,26-33} The viruses most commonly isolated from symptomatic patients during the Hajj are rhinovirus (3 out of 10 ill pilgrims), followed by influenza virus (1 out of 10) and coronaviruses (1 out of 10); other viruses (1 out of 10, grouped) being less frequently isolated, including adenovirus, parainfluenza virus, respiratory syncitial virus, and enterovirus by decreasing frequency. The ongoing Middle East Syndrome Coronavirus (MERS-CoV) epidemic in Saudi Arabia has prompted several countries to establish an enhanced surveillance system to rapidly detect and investigate possible cases of MERS-CoV infection among travelers to from the Middle East, including Hajj and Umrah pilgrims. Results from England, France, Canada, and US revealed that influenza A and B were the viruses most frequently isolated.^{34–37} From 2012 through 2014, the surveillance data failed to evidence any case of MERS among Hajj pilgrims and only eight Umrah-associated MERS cases where identified over an estimated 20 million pilgrims who visited Mecca during this period.³⁸

2.2.2 Bacteria

There are a few available recent studies addressing the role of bacteria in respiratory tract infections at the Hajj. Data gathered from 1983 pilgrims suffering pneumonia or lower tract respiratory infections between 1991 through 2013. Definition of syndromes differed according to authors. Sample size varied from 38 to 713 individuals. These surveys were conducted in ill pilgrims from various nationalities recruited at hospitals in Saudi Arabia; one was conducted among ill pilgrims arriving at an airport in Saudi Arabia. Types of samples included were serum, sputum and bronchoalveolar and nasopharyngeal aspirates, depending on the studies. Pathogens were identified by conventional culture methods, serology or PCR in one study. The bacteria most commonly isolated from symptomatic patients during the Hajj are *Haemophilus influenzae* (2 out of 10 ill pilgrims), followed by *Streptococcus pneumoniae* (1–2 out of 10), *Mycobacterium tuberculosis* (1 out of 10), *Pseudomonas aeruginosa* (1 out of 10), *Klebsiella pneumoniae* (1 out of 10), and *Chlamydophila pneumoniae* (1 out of 10). Other bacteria were less frequently isolated or investigated including by decreasing frequency *Moraxella catarrhalis, Enterecoccus sp., Legionella pneumophila, Acinetobacter baumannii, Staphylococcus aureus, Mycoplasma pneumoniae, Bordettela pertussis, Escherichia coli, and Stenotrophomonas maltophilia.*^{17,21,32,39–42}

2.3 SYSTEMATIC SCREENING OF RESPIRATORY PATHOGENS IN HAJJ PILGRIMS BEFORE AND AFTER THE PILGRIMAGE

2.3.1 Viruses

From 2003 to 2013, the prevalence of respiratory viruses in cohorts of Hajj pilgrims was systematically investigated independently on the presence of respiratory symptoms in 11 epidemiological studies. ^{25,35,43–53} However, the design of these studies was also diverse, and included cohorts and longitudinal studies of national pilgrims recruited before they departed from or after they return to their home country, or international pilgrims arriving to and departing from the King Abdulaziz International Airport in Jeddah or at Mina encampment. In these studies, pilgrims were tested using different samples, including throat swabs, nasal swabs, nasopharyngeal swabs, or serum.

A range of respiratory viruses have been detected among pilgrims attending the Hajj pilgrimage. Influenza was the most frequently investigated. The mean prevalence of influenza (detected by PCR methods) was 2.1% among arriving pilgrims and 3.6% among departing pilgrims, with most strains

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identified as influenza A. In one UK study, a 38.3% seroconversion rate (mostly due to influenza H3N2) was observed in pilgrims returning from Hajj. However, in an Iranian study, the seroconversion rate was 3.6%. A difference in vaccination coverage may explain in part the difference in the reported seroconversion rates between the two studies. Respiratory syncytial virus prevalence was investigated in seven studies, six of which were PCR-based. In PCR-based studies, the mean prevalence of respiratory syncytial virus among pilgrims was 0.5% before and 1.2% after the Hajj. The prevalence of rhinovirus and adenovirus were investigated in six studies. For rhinovirus, the mean prevalence increased from 6.9% before to 19.7% after the Hajj. For adenovirus, the mean prevalence was 0.5% before and 0.6% after the Hajj. Coronaviruses prevalence were also investigated in seven studies, with the mean prevalence rising markedly from 1.2% before to 13.8% after the Hajj, with most infections due to coronavirus 229-E. MERS coronavirus was never isolated. Metapneumovirus and parainfluenza virus carriage were investigated by PCR methods in five studies. The mean prevalence of metapneumovirus was 0.4%before and 0.3% after the Hajj, and that of parainfluenza virus was 1% before and 1.6% after the Hajj. Bocavirus was investigated in four PCR-based studies and detected in only a few arriving pilgrims. Enterovirus was investigated in three PCR-based studies, and the mean prevalence was 0.7% among arriving and 1.1% among departing pilgrims. As far as is known, cytomegalovirus and parechovirus were investigated in only two studies, and were never isolated.

2.3.2 Bacteria

Unfortunately, while numerous studies investigating the carriage of numerous viral pathogens in healthy pilgrims and in pilgrims suffering from respiratory symptoms have been conducted in the past, most of the studies addressing bacterial carriage in Hajj pilgrims have been limited to *N. meningitidis* because of the international *N. meningitidis* serogroup W135 outbreak that occurred in 2001 and 2002.⁵⁴

During the 2013 Hajj season, nasal specimens were prospectively collected from a large multinational cohort of pilgrims from 13 countries and tested for *S. pneumoniae*, *H. influenzae*, *K. pneumoniae*, *S. aureus*, *Coxiella burnetii*, *B. pertussis*, *M. pneumoniae*, *L. pneumophila*, *S. pyogenes*, *Salmonella* spp., *Pneumocystis jirovecii*, and *C. pneumoniae*.⁵³ In this study, the overall prevalence of bacteria increased from 15.4% before the Hajj to 31% after the Hajj, due to the significant acquisition of *S. pneumoniae*, *H. influenzae*, and *S. aureus*. The overall acquisition rate of bacteria was 28.3% (12.0%, 11.4% and 7.5%, respectively, for *S. pneumoniae*, *H. influenzae*, and *S. aureus*). *K. pneumoniae* and *C. burnetii* were also acquired during the stay in KSA by a low proportion of the pilgrims (0.1–3.9%). None of the pilgrims tested positive for *B. pertussis*, *M. pneumoniae*, *S. pyogenes*, *L. pneumophila*, *Salmonella* spp., *C. pneumoniae*, or *P. jirovecii* at any point during the study period.

Nasopharyngeal pneumococcal carriage prevalence was investigated during the 2011 and 2012 Hajj seasons with four large cross-sectional studies conducted among a cohort of pilgrims sampled using nasopharyngeal swabs at the beginning of Hajj in Mecca (within 2 days of arrival in Mecca) and a cohort of pilgrims sampled at the end of the Hajj in Mina (at any time after arrival in Mina).⁵⁵ This study showed an overall pneumococcal carriage prevalence of 6.0% among pilgrims and an increase in pneumococcal carriage from the beginning of Hajj to the end of the Hajj (4.4% versus 7.5%, respectively), particularly of conjugate vaccine serotypes and antibiotic nonsusceptible strains. During the 2012 Hajj season, nasal specimens were collected from a French cohort of pilgrims before departing from France and before leaving the KSA after the 2012 Hajj season. The results from this study demonstrated the acquisition of *S. pneumoniae* nasal carriage in returning Hajj pilgrims, with a prevalence of 7.3% before departing for the KSA and 19.5% before leaving the KSA. None of the participants tested

positive for *B. pertussis* or *M. pneumoniae* at any point during the study period.⁵⁶ These results were confirmed the following year in another study conducted among a second French cohort of pilgrims departing from France for the 2013 Hajj season, which have reported a *S. pneumoniae* pharyngeal carriage of 50% before departing for the KSA and 62% before leaving the KSA.⁵⁰ As part of this second study, nasal samples were also tested for *S. aureus*, thus demonstrating a high rate (22.8%) of nasal carriage of *S. aureus* among pilgrims on return from the Hajj, with a significant increase of the emerging clonal complex 398.⁵⁷ In an earlier study, a low rate of methicillin resistant *S. aureus* (MRSA) carriage was noticed among pilgrims attending the 2004 Hajj pilgrimage. In fact, of pilgrims screened, 20.6% were positive for *S. aureus* of which only 1.5% were MRSA.⁵⁸

In a 2005 study, the increased risk of acquiring *M. tuberculosis* infection during the 2002 Hajj season was shown by measuring the immune response to TB antigens, prior to departure and 3 months after return from the Hajj pilgrimage, using a whole-blood assay (Quanti-FERON TB assay) among a cohort of Singaporean pilgrims, who attended a pre-Hajj meningococcal vaccination campaign.⁵⁹ Thus, among those pilgrims who were negative prior to the Hajj, 10% had a significant rise in immune response to TB antigens. In a previous prospective seroepidemiological study, 1.4% of adult Singaporean pilgrims were found to have acquired pertussis (defined as prolonged cough and a 14-fold increase in the level of immunoglobulin G to whole-cell pertussis antigen) during their pilgrimage.⁶⁰

3 RESPIRATORY TRACT INFECTIONS AT OTHER MASS GATHERINGS

A number of outbreaks of respiratory tract infections have been reported in various other MG settings.

3.1 RELIGIOUS MASS GATHERINGS

In 2010, in Pakpattan, Pakistan, during the annual celebration of the Urs of Baba Farid, attended by an estimated 500,000 people, the prevalence of acute respiratory illness showed a 25-fold increase while the population increased by a factor of 3.⁶¹ Respiratory tract infections due to influenza (100 cases) were recorded during World Youth Day 2008 in Australia (500,000 participants).⁶² Another influenza outbreak (38 cases) was recorded during the Itzapalapa Passion Play celebration in Mexico, 2009 (>2 million participants).^{63,64} A measles outbreak (34 cases) occurred at a church gathering in the US, 2005 (500 participants) among unvaccinated participants and another was recorded during the 2010 Taizé festival in France (3500 participants), affecting 27 individuals mainly unvaccinated subjects including secondary and tertiary cases mainly in Germany.^{65,66} In 2006, an outbreak of mumps with 214 identified patients occurred after an Easter festival in Austria.⁶⁷ A syndromic survey conducted during the 2013 Kumb Mela pilgrimage in India (estimated 100 million participants), evidenced a peak in upper respiratory tract infection symptoms just after the bathing day.⁶⁸ Of 412,703 patients who attended to outpatient departments of the hospitals, respiratory infections accounted for 70% of illnesses.⁶⁹

3.2 SPORT MASS GATHERINGS

We found some examples of outbreak at sport events. One involved 36 individuals participating in the Winter Olympiad in Salt Lake City (2002) (1.5 million participants) who tested positive for influenza among 188 individuals presenting with influenza like illness.⁷⁰ Special Olympic World Games are

reserved for athletes with disabilities; after the Minneapolis gathering in 1991 (20000 participants) a small outbreak of measles (25 cases) was recorded involving not only athletes but also volunteers and a few spectators, most of whom had not been previously vaccinated.⁷¹ Another small measles outbreak (7 cases) occurred subsequent to an international youth sport event in Pennsylvania in 2007 (265,000 participants), and again the majority had previously received no or one dose of vaccine.⁷²

3.3 FESTIVALS AND PRIVATE MASS GATHERINGS

Person-to-person transmission of influenza, measles, and mumps viruses has been recorded in the context of large scale open air festivals. Outbreaks of respiratory tract infections due to influenza A(H1N1) pdm09 (totalizing 71 cases) were recorded during the year 2009 at various music festivals in Belgium, Hungary, and Serbia (100,000–4,000,000 participants each).^{73–75} Outbreaks of measles occurred at various MGs (totalizing 281 cases), including a large wedding in Spain (2010),⁷⁶ a music festival in Germany in 2011 (50,000 participants),⁷⁷ an international dog show in Slovenia in 2014 (11,000 participants) resulting in a chain of transmission in Italia,^{78,79} and at the Disney theme parks in California in 2014–2015 (24 million annual attendance) resulting in a multistate outbreak.^{80,81} Finally, an outbreak of mumps (77 cases) was recorded at an annual village festival in Spain in 2006 (>4500 participants).⁸²

4 CONCLUSIONS

The Hajj cough is very common, probably resulting of crowded conditions during ritual performance. It affects all individuals whatever their comorbidities, age, and adherence to preventive measures against respiratory infections including use of face mask, hand hygiene, social distancing, and vaccination.²² Vaccination against influenza may be considered, although contradictive results have been obtained.⁸³ A metaanalysis of observational studies demonstrated a significant effect of vaccination on laboratory-proven influenza although the overall effect of the vaccine on disease is yet to be seen and controlled studies exploring the efficacy of influenza vaccine among attendees of MGs are not available.⁸⁴ Studies are necessary to evaluate knowledge, attitudes, and practices of Hajj pilgrims regarding vaccination. Randomized controlled trials are needed to assess the efficacy of vaccines and improve the vaccination coverage in this vulnerable population.⁸³

Nonpharmaceutical methods, such as face mask use, hand washing or use of hand gel, cough etiquette, social distancing, can be theoretically effective to mitigate the interhuman transmission of respiratory viruses⁸⁵ and are consequently recommended to Hajj pilgrims by national public health agencies⁸⁶ However, given the limited and inconclusive evidence of their effectiveness at the Hajj, prospective cohort studies are required to confirm whether or not such interventions are effective in interrupting or reducing the spread of respiratory pathogens at the Hajj.⁸⁷ A trial is being conducted to provide evidence on the efficacy of face masks in preventing viral respiratory tract infections among pilgrims. However, the adherence to face mask use by Hajj pilgrims remains a challenge.⁸⁷ By contrast, and despite their poor knowledge of the usefulness of hand hygiene in preventing respiratory tract infections, hand washing compliance of pilgrims is quite good.⁸⁷ Pending further rigorous studies on their effectiveness, we recommend effective hand hygiene practices, notably the use of alcoholbased hand gel, since it requires less time than classical hand washing, and act more rapidly. Social distancing measures are not realistic given the high density to which pilgrims are exposed at holy sites.⁸⁷ Transmission of respiratory pathogens at the Hajj Muslim pilgrimage in the Kingdom of Saudi Arabia is highly frequent, resulting in high acquisition rates of virus and bacteria carriage. The Hajj may, therefore, contribute to the globalization of common respiratory pathogens resulting from the cross-contamination of participants harboring pathogens that easily spread among pilgrims. Numerous viral and bacterial clinical infections of the upper and lower respiratory tract do occur during the pilgrimage leading to a high number of in- and outpatients in Saudi medical structures. Over the past 10 years, the emergence of several viruses including influenza AH1N1, severe acute respiratory syndrome (SARS)-CoV, and MERS-CoV have been a great concern for the international medical community.⁵ However, no major outbreaks have occurred at the Hajj, up to now. We must remember that aside from the highly publicized exotic and emerging pathogens, we must be alert to the circulation of common pathogens, which silently cause much more casualties than the exotic newcomers which occupy the forefront of the stage and get all the headlines.⁸⁸

Although outbreaks are less frequently reported in or after MGs outside the Hajj and Umrah pilgrimages, they do sometimes occur. Most common were vaccine preventable diseases, mainly measles and influenza, while outbreaks of mumps have rarely been recorded. Almost all measles outbreaks at MGs have occurred among unvaccinated or incompletely vaccinated individuals.⁸⁴ However, the effectiveness of vaccination in this context remains to be evaluated. It is also noticeable that many outbreaks occurring at MGs result in international spread of communicable diseases.

Despite extensive surveillance, reports of outbreaks of respiratory tract infections at large sport events including the Olympics, the FIFA, and EURO football cups are scant. This is likely because the crowd density is much lower and because collective housing is not common at these events. Large music festivals, by contrast, share some characteristics with the Hajj regarding crowd density and housing conditions in tent camps. The younger age of the participants at music festivals likely account for the distinct pattern of pathogens responsible for outbreaks in this context, compared to that of the Hajj.⁸⁹ Other large religious MGs, like the Kumb Mela, have been poorly studied and the data concerning the health status of the pilgrims and potential health risks are scarce.⁹⁰

Hopefully, public health research projects, developed in the context of international scientific collaboration, will elucidate the dynamics of communicable diseases transmission during the MGs and the consequence for their international spread. Large multinational cohort surveys are needed to better assess the risk of respiratory pathogens acquisition at MGs. The role of host factor including vaccination status, underlying chronic diseases age, and so on, and the role of environmental factors on the transmission of viruses and bacteria also warrant investigation. Interventional studies addressing the effectiveness of preventive measures are needed. The results of these studies will allow the implementation of evidencebased recommendations on prevention strategy including notably vaccination, hand hygiene, and face mask use. Investigations are also needed to evaluate the relationship link between communication and behavior in order to better adapt preventive message according to needs of specific communities.

REFERENCES

Memish ZA, Stephens GM, Steffen R, Ahmed QA. Emergence of medicine for mass gatherings: lessons from the Hajj. *Lancet Infect Dis.* 2012;12:56–65.

World Health Organization. Communicable disease alert and response for mass gatherings. Technical workshop. Geneva, Switzerland, April 29–30, 2008. www.who.int/csr/resources/publications/WHO_HSE_ EPR_2008_8c.pdf.

- 3. Kok J, Blyth CC, Dwyer DE. Mass gatherings and the implications for the spread of infectious diseases. *Future Microbiol.* 2012;7:551–3.
- 4. Abubakar I, Gautret P, Brunette GW, Blumberg L, Johnson D, Poumerol G, et al. Global perspectives for prevention of infectious diseases associated with mass gatherings. *Lancet Infect Dis.* 2012;**12**:66–74.
- Memish ZA, Zumla A, Alhakeem RF, Assiri A, Turkestani A, Al Harby KD, et al. Hajj: infectious disease surveillance and control. *Lancet* 2014;383:2073–82.
- 6. Alnabulsi H, Drury J. Social identification moderates the effect of crowd density on safety at the Hajj. *Proc Natl Acad Sci USA* 2014;**111**:9091–6.
- Barasheed O, Almasri N, Badahdah AM, Heron L, Taylor J, McPhee K, et al. Pilot randomised controlled trial to test effectiveness of facemasks in preventing influenza-like illness transmission among Australian Hajj Pilgrims in 2011. *Infect Disord Drug Targets* 2014;14:110–6.
- 8. Shafi S, Booy R, Haworth E, Rashid H, Memish ZA. Hajj: health lessons for mass gatherings. *J Infect Public Health* 2008;1:27–32.
- 9. Paterson FW. Letter from abu dhabi: welfare of the Hajj. Br Med J 1980;280:1261-2.
- Al-Zahrani AG, Choudhry AJ, Al-Mazroa MA, Turkistani AH, Nouman GS, Memish ZA. Pattern of diseases among visitors to Mina health centers during the Hajj season, 1429 H (2008 G). J Infect Public Health 2012;5:22–34.
- 11. Al-Ghamdi SM, Akbar HO, Qari YA, Fathaldin OA, Al-Rashed RS. Pattern of admission to hospitals during muslim pilgrimage (Hajj). *Saudi Med J* 2003;**24**:1073–6.
- 12. Yousuf M, Al-Saudi DA, Sheikh RA, Lone MS. Pattern of medical problems among Haj pilgrims admitted to King Abdul Aziz hospital, Madinah Al-Munawarah. *Ann Saudi Med.* 1995;**15**:619–21.
- 13. Al-Harbi MA. Pattern of surgical and medical diseases among pilgrims attending Al-Noor Hospital, Makkah. *J Famy Commun Med* 2000;7:21–4.
- Madani TA, Ghabrah TM, Al-Hedaithy MA, Alhazmi MA, Alazraqi TA, Albarrak AM, et al. Causes of hospitalization of pilgrims in the Hajj season of the Islamic year 1423 (2003). *Ann Saudi Med* 2006;26:346–51.
- 15. Madani TA, Ghabrah TM, Albarrak AM, Alhazmi MA, Alazraqi TA, Althaqafi AO, et al. Causes of admission to intensive care units in the Hajj period of the Islamic year 1424 (2004). *Ann Saudi Med* 2007;**27**:101–5.
- Baharoon S, Al-Jahdali H, Al Hashmi J, Memish ZA, Ahmed QA. Severe sepsis and septic shock at the Hajj: etiologies and outcomes. *Travel Med Infect Dis* 2009;7:247–52.
- 17. Mandourah Y, Al-Radi A, Ocheltree AH, Ocheltree SR, Fowler RA. Clinical and temporal patterns of severe pneumonia causing critical illness during Hajj. *BMC Infect Dis* 2012;**12**:117.
- Meysamie A1, Ardakani HZ, Razavi SM, Doroodi T. Comparison of mortality and morbidity rates among Iranian pilgrims in Hajj 2004 and 2005. *Saudi Med J* 2006;27:1049–53.
- 19. Deris ZZ, Hasan H, Sulaiman SA, Wahab MS, Naing NN, Othman NH. The prevalence of acute respiratory symptoms and role of protective measures among Malaysian Hajj pilgrims. *J Travel Med* 2010;**17**:82–8.
- Al-Jasser FS, Kabbash IA, Al-Mazroa MA, Memish ZA. Patterns of diseases and preventive measures among domestic hajjis from Central, Saudi Arabia. *Saudi Med J* 2012;33:879–86.
- Razavi SM, Sabouri-Kashani A, Ziaee-Ardakani H, Tabatabaei A, Karbakhsh M, Sadeghipour H, et al. Trend of diseases among Iranian pilgrims during five consecutive years based on a Syndromic Surveillance System in Hajj. *Med J Islam Repub Iran* 2014;27:179–85.
- 22. Gautret P, Benkouiten S, Griffiths K, Sridhar S. The inevitable Hajj cough: surveillance data in French pilgrims, 2012–2014. *Travel Med Infect Dis* 2015;**13**(6):485–9.
- Al-Herabi AZ. Road map of an ear, nose, and throat clinic during the 2008 Hajj in Makkah, Saudi Arabia. Saudi Med J 2009;30:1584–9.
- 24. Al-Herabi AZ. Impact of pH1N1 influenza A infections on the otolaryngology, head and neck Clinic during Hajj, 2009. *Saudi Med J* 2011;**32**:933–8.
- 25. Imani R, Karimi A, Habibian R. Acute respiratory viral infections among Tamattu' Hajj pilgrims in Iran. *Life Sci J* 2013;**10**:449–53.

90 CHAPTER 6 CIRCULATION OF RESPIRATORY PATHOGENS

- Rashid H, Shafi S, Haworth E, El Bashir H, Ali KA, Memish ZA, et al. Value of rapid testing for influenza among Hajj pilgrims. *Travel Med Infect Dis* 2007;5:310–313.
- 27. Rashid H, Shafi S, Booy R, El Bashir H, Ali K, Zambon M, et al. Influenza and respiratory syncytial virus infections in British Hajj pilgrims. *Emerg Health Threats J* 2008;1:e2.
- 28. Rashid H, Shafi S, Haworth E, El Bashir H, Memish ZA, Sudhanva M, et al. Viral respiratory infections at the Hajj: comparison between UK and Saudi pilgrims. *Clin Microbiol Infect* 2008;**14**:569–74.
- 29. Alborzi A, Aelami MH, Ziyaeyan M, Jamalidoust M, Moeini M, Pourabbas B, et al. Viral etiology of acute respiratory infections among Iranian Hajj pilgrims, 2006. *J Travel Med* 2009;**16**:239–42.
- **30.** Moattari A1, Emami A, Moghadami M, Honarvar B. Influenza viral infections among the Iranian Hajj pilgrims returning to Shiraz, Fars province. *Iran. Influenza Other Respir Viruses* 2012;**6**:e77–9.
- Barasheed O, Rashid H, Alfelali M, Tashani M, Azeem M, Bokhary H, et al. Viral respiratory infections among Hajj pilgrims in 2013. Virol Sin 2014;29:364–71.
- Memish ZA, Almasri M, Turkestani A, Al-Shangiti AM, Yezli S. Etiology of severe communityacquired pneumonia during the 2013 Hajj-part of the MERS-CoV surveillance program. *Int J Infect Dis* 2014;25:186–90.
- Aberle JH, Popow-Kraupp T, Kreidl P, Laferl H, Heinz FX, Aberle SW. Influenza A and B Viruses but Not MERS-CoV in Hajj Pilgrims, Austria, 2014. *Emerg Infect Dis* 2015;21:726–7.
- 34. German M, Olsha R, Kristjanson E, Marchand-Austin A, Peci A, Winter AL, Gubbay JB. Acute respiratory infections in travelers returning from MERS-CoV-affected areas. *Emerg Infect Dis* 2015;**21**(9):1654–6.
- Gautret P, Charrel R, Benkouiten S, Belhouchat K, Nougairede A, Drali T, et al. Lack of MERS coronavirus but prevalence of influenza virus in French pilgrims after 2013 Hajj. *Emerg Infect Dis* 2014;20:728–30.
- **36.** Thomas HL, Zhao H, Green HK, Boddington NL, Carvalho CF, Osman HK, et al. Enhanced MERS coronavirus surveillance of travelers from the Middle East to England. *Emerg Infect Dis* 2014;**20**:1562–4.
- Shahkarami M, Yen C, Glaser C, Xia D, Watt J, Wadford DA. Laboratory testing for Middle East respiratory syndrome coronavirus, California, USA, 2013–2014. *Emerg Infect Dis* 2015;21:1664–6.
- Sridhar S, Brouqui P, Parola P, Gautret P. Imported cases of Middle East respiratory syndrome: an update. *Travel Med Infect Dis* 2015;13:106–9.
- 39. El-Sheikh SM1, El-Assouli SM, Mohammed KA, Albar M. Bacteria and viruses that cause respiratory tract infections during the pilgrimage (Haj) season in Makkah, Saudi Arabia. *Trop Med Int Health* 1998;3:205–9.
- 40. Alzeer A, Mashlah A, Fakim N, Al-Sugair N, Al-Hedaithy M, Al-Majed S, et al. Tuberculosis is the commonest cause of pneumonia requiring hospitalization during Hajj (pilgrimage to Makkah). *J Infect* 1998;**36**:303–6.
- Asghar AH, Ashshi AM, Azhar EI, Bukhari SZ, Zafar TA, Momenah AM. Profile of bacterial pneumonia during Hajj. *Indian J Med Res* 2011;133:510–3.
- 42. Abdulrahman NK, Chaudhry AJ, Al Mazroa M. Etiology of upper respiratory tract infection among international pilgrims arriving for Hajj 2010 G. *Saudi Epidemiol Bull* 2011;19:14–5.
- El Bashir H, Haworth E, Zambon M, Shafi S, Zuckerman J, Booy R. Influenza among UK pilgrims to Hajj, 2003. Emerg Infect Dis 2004;10:1882–3.
- 44. Kandeel A1, Deming M, Elkreem EA, El-Refay S, Afifi S, Abukela M, et al. Pandemic (H1N1) 2009 and Hajj Pilgrims who received Predeparture Vaccination, Egypt. *Emerg Infect Dis* 2011;17:1266–8.
- 45. Memish ZA, Assiri AM, Hussain R, Alomar I, Stephens G. Detection of respiratory viruses among pilgrims in Saudi Arabia during the time of a declared influenza A(H1N1) pandemic. *J Travel Med* 2012;**19**:15–21.
- 46. Gautret P, Charrel R, Belhouchat K, Drali T, Benkouiten S, Nougairede A, et al. Lack of nasal carriage of novel corona virus (HCoV-EMC) in French Hajj pilgrims returning from the Hajj 2012, despite a high rate of respiratory symptoms. *Clin Microbiol Infect* 2013;19:e315–7.
- 47. Ziyaeyan M, Alborzi A, Jamalidoust M, Moeini M, Pouladfar GR, Pourabbas B, et al. Pandemic 2009 influenza A (H1N1) infection among 2009 Hajj Pilgrims from Southern Iran: a real-time RT-PCR-based study. *Influenza Other Respir Viruses* 2012;6:e80–4.

- Benkouiten S, Charrel R, Belhouchat K, Drali T, Salez N, Nougairede A, et al. Circulation of respiratory viruses among pilgrims during the 2012 Hajj pilgrimage. *Clin Infect Dis* 2013;57:992–1000.
- **49.** Ashshi A, Azhar E, Ayman Johargy A, Asghar A, Momenah A, Turkestani A, et al. Demographic distribution and transmission potential of influenza A and 2009 pandemic influenza A H1N1 in pilgrims. *J Infect Dev Ctries* 2014;**8**:1169–75.
- Benkouiten S, Charrel R, Belhouchat K, Drali T, Nougairede A, Salez N, et al. Respiratory viruses and bacteria among pilgrims during the 2013 Hajj. *Emerg Infect Dis* 2014;20:1821–7.
- Memish ZA, Assiri A, Almasri M, Alhakeem RF, Turkestani A, Al Rabeeah AA, et al. Prevalence of MERS-CoV nasal carriage and compliance with the Saudi health recommendations among pilgrims attending the 2013 Hajj. J Infect Dis 2014;210:1067–72.
- Annan A, Owusu M, Marfo KS, Larbi R, Sarpong FN, Adu-Sarkodie Y, et al. High prevalence of common respiratory viruses and no evidence of Middle East Respiratory Syndrome Coronavirus in Hajj pilgrims returning to Ghana, 2013. *Trop Med Int Health* 2015;20:807–12.
- Memish ZA, Assiri A, Turkestani A, Yezli S, Al Masri M, Charrel R, et al. Mass gathering and globalization of respiratory pathogens during the 2013 Hajj. *Clin Microbiol Infect* 2015;21:e571–9.
- Al-Tawfiq JA, Zumla A, Memish ZA. Respiratory tract infections during the annual Hajj: potential risks and mitigation strategies. *Curr Opin Pulm Med* 2013;19:192–7.
- Memish ZA, Assiri A, Almasri M, Alhakeem RF, Turkestani A, Al Rabeeah AA, Akkad N, Yezli S, Klugman KP, O'Brien KL, van der Linden M, Gessner BD. Impact of the Hajj on pneumococcal transmission. *Clin Microbiol Infect* 2015;21:77e8–77e11.
- Benkouiten S, Gautret P, Belhouchat K, Drali T, Salez N, Memish ZA, et al. Acquisition of *Streptococcus pneumoniae* carriage in pilgrims during the 2012 Hajj. *Clin Infect Dis* 2014;58:e106–9.
- 57. Verhoeven PO, Gautret P, Haddar CH, Benkouiten S, Gagnaire J, Belhouchat K, et al. Molecular dynamics of *Staphylococcus aureus* nasal carriage in Hajj pilgrims. *Clin Microbiol Infect* 2015;**21**:650e5–8.
- Memish ZA, Balkhy HH, Almuneef MA, Al-Haj-Hussein BT, Bukhari AI, Osoba AO. Carriage of Staphylococcus aureus among Hajj pilgrims. Saudi Med J 2006;27:1367–72.
- 59. Wilder-Smith A, Foo W, Earnest A, Paton NI. High risk of *Mycobacterium tuberculosis* infection during the Hajj pilgrimage. *Trop Med Int Health* 2005;10:336–9.
- Wilder-Smith A, Earnest A, Ravindran S, Paton NI. High incidence of pertussis among Hajj pilgrims. *Clin Infect Dis* 2003;**37**:1270–2.
- 61. Hassan S, Imtiaz R, Ikram N, Baig MA, Safdar R, Salman M, et al. Public health surveillance at a mass gathering: urs of Baba Farid, Pakpattan district, Punjab, Pakistan, December 2010. *East Mediterr Health J* 2013;**19**(Suppl. 2):S24–8.
- 62. Blyth CC, Foo H, van Hal SJ, Hurt AC, Barr IG, McPhie K, et al. Influenza outbreaks during World Youth Day 2008 mass gathering. *Emerg Infect Dis* 2010;**16**:809–15.
- 63. Zepeda HM, Perea-Araujo L, Zarate-Segura PB, Vázquez-Pérez JA, Miliar-García A, Garibay-Orijel C, et al. Identification of influenza A pandemic (H1N1) 2009 variants during the first 2009 influenza outbreak in Mexico City. J Clin Virol 2010;48:36–9.
- 64. Zepeda-Lopez HM, Perea-Araujo L, Miliar-García A, Dominguez-López A, Xoconostle-Cázarez B, Lara-Padilla E, et al. Inside the outbreak of the 2009 influenza A (H1N1)v virus in Mexico. *PLoS One* 2010;**5**:e13256.
- 65. Parker AA, Staggs W, Dayan GH, Ortega-Sánchez IR, Rota PA, Lowe L, et al. Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. *N Engl J Med* 2006;**355**:447–55.
- 66. Pfaff G, Lohr D, Santibanez S, Mankertz A, van Treeck U, Schonberger K, Hautmann W. Spotlight on measles 2010: measles outbreak among travellers returning from a mass gatering, Germany, September to October 2010. *Euro Surveill* 2010;15(50.) pii: 19750.

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- **67.** Schmid D, Holzmann H, Alfery C, Wallenko H, Popow-Kraupp TH, Allerberger F. Mumps outbreak in young adults following a festival in Austria, 2006. *Euro Surveill* 2008;13 pii: 8042.
- 68. Singh BP, Mudera CP. Mass gathering health care. *Popul Health Manag* 2014;17:316–7.
- 69. Cariappa MP, Singh BP, Mahen A, Bansal AS. Kumbh Mela 2013: healthcare for the millions. *Med J Armed Forces India* 2015;**71**:278–81.
- 70. Gundlapalli AV, Rubin MA, Samore MH, Lopansri B, Lahey T, McGuire HL, et al. Influenza, Winter Olympiad, 2002. *Emerg Infect Dis* 2006;**12**:144–6.
- Ehresmann KR, Hedberg CW, Grimm MB, Norton CA, MacDonald KL, Osterholm MT. An outbreak of measles at an international sporting event with airborne transmission in a domed stadium. *J Infect Dis* 1995;**171**:679–83.
- Centers for Disease Control, Prevention (CDC). Multistate measles outbreak associated with an international youth sporting event—Pennsylvania, Michigan, and Texas, August–September 2007. *MMWR Morb Mortal Wkly Rep* 2008;57:169–73.
- 73. Gutiérrez I, Litzroth A, Hammadi S, Van Oyen H, Gérard C, Robesyn E, et al. Community transmission of influenza A (H1N1)v virus at a rock festival in Belgium, 2–5 July 2009. *Euro Surveill* 2009;14 pii = 19294.
- 74. Botelho-Nevers E, Gautret P, Benarous L, Charrel R, Felkai P, Parola P. Travel-related influenza A/H1N1 infection at a rock festival in Hungary: one virus may hide another one. *J Travel Med* 2010;**17**:197–8.
- 75. Ristic M, Seguljev Z, Nedeljkovic J, Ilic S, Injac D, Dekic J. Importation and spread of pandemic influenza virus A(H1N1) in autonomous province of Vojvodina in preepidemic period. *Med Pregl* 2010;**63**:502–5.
- 76. Lopez HB, Laguna SJ, Marin R, I, Gallardo G, V, Perez ME, Mayoral Cortes JM. Spotlight on measles 2010 An ongoing outbreak of measles in an unvaccinated population in Granada, Spain, October to November 2010 an ongoing outbreak of measles in an unvaccinated population in Granada, Spain, October to November 2010. *Euro Surveill* 2010; 15, pii: 19746.
- 77. Santibanez S, Prosenc K, Lohr D, Pfaff G, Jordan Markocic O, Mankertz A. Measles virus spread initiated at international mass gatherings in Europe, 2011. *Euro Surveill* 2014;19 pii: 20891.
- Grgič-Vitek M, Frelih T, Ucakar V, Fafangel M, Jordan Markocic O, Prosenc K, et al. An outbreak of measles associated with an international dog show in Slovenia, November 2014. *Euro Surveill* 2015;20:pii:21012.
- 79. Filia A, Riccardo F, Del Manso M, D'Agaro P, Magurano F, Bella A. Regional contact points for measles surveillance. Measles outbreak linked to an international dog show in Slovenia primary cases and chains of transmission identified in Italy, November to December 2014. *Euro Surveill* 2015;20:pii: 21050.
- 80. McCarthy M. Measles outbreak linked to Disney theme parks reaches five states and Mexico. *BMJ* 2015;**350**:h436.
- Zipprich J, Winter K, Hacker J, Xia D, Watt J, Harriman K. Centers for Disease Control and Prevention (CDC). Measles outbreak—California, December 2014–February 2015. *MMWR Morb Mortal Wkly Rep* 2015;64:153–4.
- 82. Gerstel L, Lenglet A, Garcia CM. Mumps outbreak in young adults following a village festival in the Navarra region, Spain, August 2006. *Euro Surveill* 2006;11 pii 3078.
- Alqahtani AS, Rashid H, Heywood AE. Vaccinations against respiratory tract infections at Hajj. *Clin Microbiol Infect* 2015;21:115–27.
- Alqahtani AS, Alfelali M, Arbon P, Booy R, Rashid H. Burden of vaccine preventable diseases at large events. *Vaccine* 2015;33(48):6552–63.
- 85. Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database Syst Rev* 2011;7 CD006207.
- Alqarni H, Memish ZA, Assiri AM. Health conditions for travellers to Saudi Arabia for the pilgrimage to Mecca (Hajj)—2015. *J Epidemiol Glob Health* 2015;6(1):7–9.
- 87. Benkouiten S, Brouqui P, Gautret P. Non-pharmaceutical interventions for the prevention of respiratory tract infections during Hajj pilgrimage. *Travel Med Infect Dis* 2014;**12**:429–42.

- 88. Charrel RN, Hajj. Umrah, and other mass gatherings: which pathogens do you expect? Beware of the tree that hides the forest! *Travel Med Infect Dis* 2014;**12**:418–9.
- 89. Botelho-Nevers E, Gautret P. Outbreaks associated to large open air festivals, including music festivals, 1980 to 2012. *Euro Surveill* 2013;**18**:20426.
- 90. Sridhar S, Gautret P, Brouqui P. A comprehensive review of the Kumbh Mela: identifying risks for spread of infectious diseases. *Clin Microbiol Infect* 2015;**21**:128–33.