

# The Traveller's Guide to Vaccines, Part 1: The Hajj

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An estimated 3.3 billion travellers took to the sky in 2014, with about 1.3 billion of them crossing international boundaries.<sup>1</sup> Larger aircrafts such as the Airbus A380 can be configured to carry over 800 passengers and fly more than 15000 km. The advent of commercial aviation and the current exponential explosion in information technology has truly created a global village. It has also minimised the time taken to traverse previously incomprehensible vast distances. Other factors have been brought to the forefront though, with the spread of infectious disease being one of them. Joshua Lederberg, the Nobel Laureate, famously remarked that: 'The microbe that felled one child in a distant continent yesterday can reach yours today, and seed a global pandemic tomorrow.'<sup>2</sup>

## Travel and disease spread

This scenario was vividly illustrated by the 2003 Severe Acute Respiratory Syndrome (SARS) outbreak.<sup>3</sup> A symptomatic Chinese physician checked into the 9th floor of a Hong Kong hotel and within 24 hours infected 16 others on the same floor. Over the next few days infected guests departed for countries which included Vietnam, Singapore and Canada and by the time the outbreak was contained, over 8000 infections were documented with close to a 10% mortality in 26 countries. Despite effective HEPA filters on modern aircrafts with efficient laminar flow that minimises the spread of pathogens, the SARS virus was spread up to 8 rows away from index patients. Rapid control measures were effective in curbing the spread of the disease. Other viruses such as the 2009 pandemic influenza, which spread from Mexico to the rest of the world within a few months, are far more difficult to control. Decreasing air traffic from Mexico City<sup>4</sup> by 40% would have slowed the spread by two days and decreasing the air traffic by 90% would have slowed it by only two weeks.

## The Hajj

The Hajj is the largest annual mass gathering (MG) on earth, with between 3-5 million Muslims converging on the Saudi Arabian city of Mecca from more than 180 different countries.<sup>5</sup> Though the pilgrimage known as the Hajj takes place over a period of five days, most pilgrims stay for a few weeks. The Hajj is a set of rituals that takes place in a prescribed sequence at specified sites in a relatively confined area. This leads to intense congestion and crowding, with sharing of ablution facilities, adverse climatic conditions, dust and air pollution, inadequate ventilation and the exposure to the ritual slaughtering of sacrificial animals all increasing the chances for the spread of infectious diseases. Conditions at the Hajj have aptly been described as 'a disease amplifying chamber.' It has also been described as a 'moving target'<sup>6</sup> as it follows the lunar calendar, resulting in it moving



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10 days earlier every year. Most countries have a set quota of pilgrims that they are allowed to send annually and many countries have a waiting list that stretches for years. South Africa does not permit those younger than 18 to perform the Hajj. This currently results in older people travelling, with 25% of pilgrims being over 60. A significant number of them have underlying comorbidities<sup>5</sup> such as diabetes, hypertension and respiratory afflictions, greatly enhancing the acquisition of infectious diseases with more serious resultant consequences.

The Hajj has been associated with outbreaks of infectious diseases throughout the ages. The transmission of typhoid, cholera, polio, tuberculosis, pertussis, hepatitis B has been addressed by routine vaccination, booster doses and increased levels in sanitation. Extensive spraying programmes attempt to control vector borne diseases such as yellow fever (vaccine preventable) and dengue (no current vaccine), transmitted by locally occurring *Aedes* mosquito species. Respiratory tract infections (RTI) have been the most frequently documented diseases at the Hajj, with attack rates of up to 80%.<sup>7</sup> In a large 2005 analysis, of 75,676 Iranian pilgrims,<sup>8</sup> 70% presented with RTI, which was twice that recorded for the year before (35% in 2004). Most presented with the common cold, but close to 20% presented with influenza-like illness (ILI). Returning pilgrims had influenza viruses (H1N1, H3N2, and Influenza B) isolated in France<sup>9</sup> and South Africa. Influenza vaccination recommendations are not easy to carry out due to antigenic drift and shift, the fact that the southern hemisphere influenza season lags behind the northern one, and that the recommended vaccine might not be available worldwide before the Hajj commences. The potential spread of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) from the Hajj is a current concern. This follows the South Korean May/June 2015 outbreak<sup>10</sup> caused by a single traveller returning from the Middle East (not Hajj travel related) and resulting in 186 laboratory-confirmed cases of MERS-CoV infection, including 36 deaths. A total of 16 693 contacts had to be quarantined before the outbreak was brought under control. The September 2015 Hajj had no MERS-CoV related incidents.

### Meningococcal Disease and the Hajj

Outbreaks of meningococcal disease occurred during 1987, 2000 and 2001, and indicate the potential of the Hajj as a nidus for disease as well as its potential worldwide spread.<sup>11</sup> Six of the 13 known serogroups of *Neisseria meningitidis*, (classified according to capsular polysaccharides) are clinically important, namely A, B, C, Y, W, and X. The overall risk for the general traveller of contracting meningococcal disease is 0.4/100,000 travellers per month, and it increases to 200/100,000 travellers during the Hajj.<sup>12</sup> Nasopharyngeal colonisation rates of this Gram-negative diplococcus for whom humans are the only known carriers, has been reported in up to 80% of pilgrims in Mecca.<sup>13</sup> The modes of transmission are aerosol secretions and droplets spread and there is a frequent but as yet unverified report of upper respiratory tract infections prior to invasive disease.

A virulent serogroup A meningococcus that originated in China spread via Nepal in 1984 to Saudi Arabia by 1987. From the Hajj it was carried by returning pilgrims to sub-Saharan Africa where it subsequently caused epidemics in the late 1980s and 1990. It also was associated with isolated cases in Muslim communities in other countries globally and linked to returning pilgrims.<sup>14</sup> This led, in 1987, to the compulsory introduction of the bivalent meningococcal A and C vaccine for all pilgrims. The administration of ciprofloxacin to all sub-Saharan pilgrims was introduced in order to eliminate

nasopharyngeal carriage. These requirements were lifted in 1999. In the subsequent Hajj seasons, 1,300 and 1,109 cases of meningitis were recorded in 2000 and 2001, respectively. A virulent clone of the W135 serotype<sup>15</sup> was implicated in a large number of cases. In 2000, over 300 secondary cases, in close contact with returning pilgrims, were documented in 14 countries.

This led to the introduction of the quadrivalent polysaccharide ACWY vaccine (which does not eliminate nasopharyngeal carriage or induce herd immunity) as a visa requirement, with Sub-Saharan pilgrims from the 'meningitis belt' (Senegal in the west to Ethiopia in the east) also given oral ciprofloxacin for nasopharyngeal elimination. All pilgrims were advised to repeat oral prophylaxis on returning to their home countries to eliminate possible nasopharyngeal acquisition. In one study in 2001, 1.3% of vaccinated American pilgrims returning home had W135 isolated<sup>16</sup> and in another study, 4.7% of hospital employees examined in Mecca in 2001 had meningococcus isolated, 40% of these being W135.<sup>17</sup> Ciprofloxacin has been shown to reduce carriage rate significantly. The measures resulted in a significant reduction in carriage rates during 2003. Since 2001 there have been no further outbreaks of epidemic meningitis, and Saudi Arabia stopped issuing ciprofloxacin to its local pilgrims in 2006. The shift to conjugate quadrivalent ACWY vaccines, which eliminated nasopharyngeal carriage, will also greatly reduce the transport back of the organism by pilgrims to their home countries.

### Pneumococcal disease at the Hajj

Respiratory infections accounted in one instance for 57% of hospital admissions with pneumonia being identified in 39% of all such cases.<sup>18</sup> Pneumonia was diagnosed in 24/10 000 Iranian pilgrims in 2004 and 34/10 000 in 2005,<sup>8</sup> though causative organisms were not documented. Pneumococcus was the cause of 6/9 cases of meningitis in a 2003 study, and pneumococcus was isolated in 5% of hospital admissions<sup>18</sup> in another investigation. Amongst 38 patients admitted with bilateral pneumonia in 2013, a microbiological aetiology was established in 26 (68.4%) cases, and *S. pneumoniae* was identified in 14 (53.8%) of positive samples.<sup>19</sup> The acquisition of different serotypes of *Strep pneumoniae* has recently been demonstrated during the Hajj, and was 12% of pilgrims in one study.<sup>20</sup> Pneumococcus currently is estimated to lead to 1.6 million deaths annually. The Hajj has the potential to lead to the virulent expansion of virulent clones of pneumococci and its spread worldwide as with meningococcus. Currently there is a debate about whether the indirect benefits of pneumococcal conjugate vaccination (PCV) before the Hajj through reduced transmission and carriage outweighs individual protective effects.

Antibiotic resistance is also a concern and PCV has been shown to reduce it in certain serotypes. An association between influenza and subsequent pneumococcal infection has been established. The high incidence of influenza and the difficulty of obtaining appropriate

vaccines for the Hajj put the importance of pneumococcal vaccination into the spotlight. An Iranian study concluded that, administration of influenza vaccine solely or accompanied by polysaccharide pneumococcal 23 vaccine (PPV23), decrease the mean of duration of the fever, cough, post nasal discharge, dirty sputum, bed rest, number of visits by physicians and total period of the disease.

The 'PREVENT' (The PReventive Vaccination for pneumococcal disease in mass gatherings) expert opinion panel concluded that: 'The advisory board members feel that while there are limited data on the burden of pneumococcal disease at Hajj, the available data as well as the circumstances of Hajj (vulnerability of large proportion of pilgrims due to their age and pre-existing illnesses, intense crowding and air pollution) warrant pneumococcal vaccination. 'Conjugate vaccines may become the vaccines of choice for Hajj pilgrims if supported by the local epidemiology.'<sup>18</sup>

More studies are currently under way; one recently published<sup>22</sup> showed 38% of serotypes carriage by pilgrims to be contained in PCV whilst the figure was 53% for PPV.<sup>23</sup> Although the effectiveness of pneumococcal vaccination for the prevention of *S. pneumoniae* infections in elderly pilgrims is yet to be ascertained, these individuals might benefit from vaccination with the polyvalent pneumococcal vaccine for the common pneumococcal serotypes that are circulating during Hajj.

The advantage of the conjugate vaccine is that it induces long term immunological memory, reduces herd carriage, is effective in infants, gives prolonged protection and can be boosted. A currently employed strategy as recommended by the Advisory Committee on Immunization Practices (ACIP) is to first give the conjugate one in vaccine naive adults over 65 years of age, followed a year later by the polysaccharide vaccine, with a minimum interval of at least eight weeks. Those who had the polysaccharide vaccine before should wait a year before taking the conjugate vaccine. Those over the age of 50 but under 65 with comorbidities should also be considered for the PCV13.

## Keypoints

1. Number of travellers, distances covered and new destinations are rising exponentially.
2. Diseases have the potential to rapidly spread along travel routes, as highlighted by the 2003 SARS epidemic and the 2009 influenza pandemic.
3. The Hajj is the largest annual mass gathering on earth attracting pilgrims from more than 180 countries.
4. These pilgrims can potentially facilitate the carriage of pathogens resulting in epidemics during the Hajj and disseminating them worldwide upon the return of the pilgrims to their home countries.
5. Meningococcal meningitis outbreaks have been effectively halted by the introduction of compulsory polysaccharide vaccination. This did not prevent carriage back to home countries by pilgrims.

6. Pneumococcal infection is a well-recognised cause of hospitalisation during the Hajj and vaccination should be encouraged in susceptible pilgrims.

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