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Pandemic influenza: mass gatherings and mass infection

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Mass gatherings, such as this year's Beijing Olympic Games, typically involve travel and extended close contact among participants and spectators. Influenza is one of the most frequently identified respiratory viruses in travellers,¹ and the high density of people at mass events further increases the risk of transmission. Despite this, the epidemiology of influenza outbreaks in large congregations is poorly understood. Variability of venues and the infrequency of mass events may have been barriers for systematic study of communicable diseases in these situations. However, because the venue does not change and the event occurs every year, the Islamic Hajj pilgrimage to Mecca, Saudi Arabia, does provide an excellent opportunity to research infectious diseases that not only affect a mass event but also have the potential for pandemic spread.

Infectious diseases at the Hajj have been reported for centuries. During the first Hajj in 632AD, the pilgrims had febrile illness known locally as "Yethrib fever", which is now believed to be malaria.² Subsequently, major epidemics such as plague and cholera have been reported. Over the past decades there have been several intercontinental outbreaks of meningococcal disease, first caused by serogroup A and later by W135.³

Currently, respiratory infections are the commonest illnesses encountered at the Hajj and include, among others, influenza, pertussis, and tuberculosis.³ Depending on study design, the occurrence of seasonal influenza at the Hajj ranges from 6% to 38%, affecting both domestic and overseas pilgrims.⁴⁻⁶ So far, no human case of avian influenza A (H5N1) has been reported at the Hajj or in

Saudi Arabia, but cases of H5N1 in human beings (table) have been reported in Indonesia, Pakistan, and Turkey, countries from which many people make the annual pilgrimage to Mecca. Counting Bangladesh, Iraq, Egypt, Azerbaijan, Nigeria, and Djibouti, a total of nine countries with predominantly Muslim populations have already been affected by the virus. As of July 25, 2008, over half (214/385) of the reported number of H5N1 influenza cases have been in Muslims.⁷ Furthermore, there was an outbreak of H5N1 influenza in Saudi poultry earlier last year.

The recent account of likely human-to-human transmission of H5N1 influenza in China, reported by Wang and colleagues,⁸ alerts us to the possibility of a pandemic arising from mass events such as the Hajj pilgrimage. In Wang and colleagues' report the index case was a young salesman whose source of exposure could not be ascertained; for the second case, which concerned his retired father, the infected son was the only apparent source of exposure. Genomic sequencing showed that the viruses from both patients were essentially homologous. This is the third example of potential person-to-person transmission of H5N1 influenza after the Thai and Indonesian family clusters.⁸

What can be done to prevent an influenza outbreak during the Hajj? An awareness campaign and better surveillance can have an important role. Severe acute respiratory syndrome (SARS) is a good example of the success of this approach. During the 2003 episode, of 8000 cases of SARS reported worldwide at least 142 were travel-associated.⁹ However, tight measures taken by Saudi authorities, which included applying a ban on visitors from SARS-hit countries, home quarantine for domestic travellers, installation of thermal cameras in major airports, and ensuring facilities for rapid detection of SARS virus, prevented establishment of the virus in the country.¹⁰

Initial results from studies of prototype vaccines against H5N1 influenza were disappointing, with two or more doses, of high antigenic content, being necessary to induce protective immunity.¹¹ Also, from our experience with seasonal influenza, we can assume that the H5N1 vaccine could be ineffective despite good immunogenicity if the pandemic strain does not match with the vaccine strain(s). Three studies from Pakistan, Malaysia, and Iran have so far

	Population (millions)	Proportion of population who are Muslim	Number of pilgrims per year	Number of cases of H5N1 influenza ⁷	H5N1 case fatality (%) ⁷
Indonesia	237.5	86.1%	200 000	135	110 (81%)
Pakistan	167.8	97%	150 000	3	1 (33%)
Turkey	71.9	99.8%	120 000	12	4 (33%)
Nigeria	138.3	50%	90 000	1	1 (100%)
Egypt	81.7	90%	75 000	50	22 (44%)
Bangladesh	153.6	83%	65 000	1	0 (0%)
Iraq	28.2	97%	30 000	3	2 (67%)
Azerbaijan	8.2	93.4%	4000	8	5 (63%)
Djibouti	0.5	94%	2000	1	0 (0%)
Total	736 000	214	145 (68%)

Table: Muslim countries with H5N1 influenza that send pilgrims on Hajj

assessed the effectiveness of seasonal influenza vaccine against influenza-like illness among Hajj pilgrims. The Pakistani and Malaysian studies reported the vaccine to be effective; however, the Iranian study, which was done over two consecutive influenza seasons, reported that the vaccine was effective during the 2003 Hajj but not during the 2004 Hajj.¹²⁻¹⁴ Virological surveillance reports suggest that the rate of influenza in vaccinated pilgrims might not significantly differ from that in unvaccinated pilgrims.^{5,6}

Stockpiling antiviral drugs is another important control strategy but resistance can be a problem. Therefore, a multi-pronged approach will be required to prevent pandemic influenza at mass gatherings such as the Hajj. Key elements of this approach include education and awareness, improved surveillance, rapid diagnosis, and containment with antiviral treatment of cases and close contacts, non-pharmacological interventions including surgical masks, and, above all, coordinated global research with viral typing in countries of origin and sharing of these data.

Because the recent report of probable inter-human transmission of H5N1 occurred in China,⁸ the host of this year's Olympic Games, we believe that pandemic influenza should be an important consideration in public-health planning for the event. With data from other mass sporting events, we can postulate that respiratory and gastrointestinal infections will predominate during this year's Olympic season. Respiratory illnesses were the leading medical encounters during the 2002 Winter Olympics in Salt Lake City, USA; a hospital electronic medical record-based public-health surveillance system deployed during the event suggested a substantial increase in influenza during the games.¹⁵

For the past few years the Hajj has been a winter event. At this time of year, there is increased risk of human influenza and also the possibility of dual infection with human and avian viruses, potentially leading to a genetically altered influenza virus of high virulence and transmissibility. The latest report of likely inter-human transmission of H5N1 influenza suggests that the virus is slowly becoming more adapted to human beings.⁸ If the transmission among human beings becomes sustained, mass gatherings could help spread the virus all over the world at a very rapid pace. Therefore, coordinated global response and research is a high priority.

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