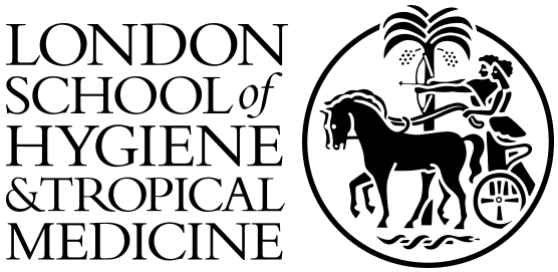

Influenza on cruise ships

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Key words: Influenza; cruise ships; older persons; frailty; influenza vaccines; immunosenescence; traveler.

Highlights:

Influenza outbreaks on cruise ships are of concern. Many cruise ship passengers are of older age, and have chronic medical conditions. The response to influenza vaccine declines with older age due to changes in the immune system termed immunosenescence. New strategies are needed.

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Influenza is a common vaccine-preventable infection among travelers.[1] All modes of travel play a major role in influenza acquisition and the global seeding of new outbreaks to home and host countries.[2] Cruise ships passengers spend prolonged periods in close quarters, facilitating the rapid spread of highly infectious agents such as influenza.

Rogers et al in a recent issue of the Journal of Travel Medicine described two large influenza outbreaks among cruise ship passengers and crew.[3] On one ship, 3.7% of passengers and 3.1% of crew had medically attended acute respiratory illness, and on the second ship 6.2% of passengers and 4.7% of crew reported a respiratory illness. While influenza activity was low at both ships' ports of call, a number of passengers reported recent respiratory illness prior to first boarding, suggesting that this was the source of the outbreak.[3] Following introduction, influenza rapidly spread among crew members and passengers. Similarly, in 2012, a wave of influenza B swept a cruise ship sailing off the coast of Sao Paulo, Brazil, and 104 persons needed to be hospitalized for acute respiratory illness (ARI), of which 52% were crew members and 49% passengers. One mortality among these patients was caused by post-influenza *Staphylococcus aureus* pneumonia.[4] Another outbreak of the 2009 pandemic A/H1N1 strain and influenza A/H3N2 occurred on a cruise ship in May 2009. Of 1,970 passengers and 734 crew members, 82 (3.0%) were infected with A/H1N1, 98 (3.6%) with

A/H3N2, and 2 (0.1%) with both. Among the 45 children who visited the ship's childcare center, the incidence of A/H1N1 infection was even higher.

Influenza infections can become widespread during cruise ship outbreaks and can occur outside of traditional temperate-climate influenza seasons. It often leads to an increased use of health care services including hospitalization, discontinuation of original travel itineraries and incapacitation of essential crew members with interruption in services. The events around the 2009 A/H1N1 influenza pandemic highlight the need for careful planning to ensure protection of those on vessels, at ports of call, and for business continuity. The variety of stakeholders involved in the management of a pandemic, and the speed at which it can emerge, hamper establishing a cohesive plan during the event itself.

Influenza is preventable with vaccination. Vaccination programs can help to ensure staff have received timely vaccines, and pre-cruise advice for passengers should address influenza and its prevention, whenever appropriate on the basis of the epidemiological situation concerned. Vaccination against influenza should be strongly recommended for travelers at high-risk for developing complications, particularly when there has been a recent change in vaccine strain composition. The majority of cruise ship tourists are older adults above the age of 55 where influenza vaccination should be routinely recommended. In addition, seasonal influenza vaccination should be considered for any traveler, regardless of age, wishing to reduce the risk of incapacitation.

Several issues need to be addressed with regards to influenza vaccination in cruise ship passengers.

Availability of vaccines

Travelers from temperate regions to the tropics often depart outside of the influenza season. As cruise ship vacations are often taken in opposite hemispheres, influenza vaccines covering the strains circulating in the opposite hemispheres are needed. However, most Western countries often only offer the vaccine strain that was predicted for their hemisphere. Outside of the Northern influenza season, influenza vaccines are not available for the Southern Hemisphere, and vice versa. Alternate hemisphere and out-of-season influenza vaccine availability needs to be enhanced.[5]

Vaccine refusal

Vaccine refusal is not infrequent. Refusal of recommended travel-related vaccines among U.S. international travelers in Global TravEpiNet showed that of 23 768 eligible travelers,

6573 (25%) refused one or more recommended vaccine(s). Influenza vaccination was refused in 3527 (33%) of 10 539 travelers.[6] A lack of concern about the associated illness was the most commonly cited reason for all refused vaccines. More effective education about disease risk is needed for international travelers, even those who seek pre-travel advice.

Duration of protection after influenza vaccination

Vaccine effectiveness peaks 2-4 weeks after vaccination, but then declines significantly.[7] This waning is a concern when timing routine vaccination prior to the annual onset of the 'flu season in temperate climates, but also has important implications for vaccination of travelers to tropical countries where influenza circulates throughout the year, or to opposite hemispheres when vaccination may have been more than six months prior. Biannual vaccination has been suggested to be necessary to provide year-round protection.[8] We conducted the TROPICS1 study, a randomised clinical trial of six-monthly versus annual influenza vaccination. This study aimed to determine if a repeat influenza vaccine at six months improves year-round serological measures of protection against influenza in older adults.[8] Results suggest six-monthly vaccination may be able to overcome issues with variation in the timing of epidemics in tropical countries, new vaccine strains between hemisphere winters, and waning titres/vaccine effectiveness. An observational study of antibody persistence conducted over 2016-17 among older adults in Hong Kong also showed that six-monthly vaccination improved protection against circulating seasonal influenza strains.[9]

Older and frail travelers

Many cruise ship passengers are of older age, and have chronic medical conditions. The response to influenza vaccine declines with older age due to changes in the immune system termed immunosenescence. This results in both lower antibody titres immediately after vaccination, and a significant fall in antibody titres in older adults within six months[10], and hence accine effectiveness is affected. Adults at more advanced age, frailty, or health-limiting co-morbidities are more likely to benefit from six-monthly vaccination.[11] Newer vaccines are available which improve protection in older adults. This includes vaccines with an immune adjuvant (MF-59), a higher dose of virus antigen, or a recombinant antigen which avoids some of the issues with viral culture in eggs.[12] However, while these vaccines offer improved short-term immunogenicity and modest reduction in influenza infection rates, it is not known if they will also extend protection beyond a temperate climate winter (eg extend over more than 6 months), notwithstanding protection when new antigenic variants emerge between hemisphere winters.

Concluding remarks

Besides advice concerning vaccination, the use of antivirals to interrupt influenza transmission needs to be be considered.[5] In the report by Rogers et al[3], both ships voluntarily reported the outbreaks to the CDC and implemented outbreak response plans including isolation of sick individuals, early antiviral treatment and prophylaxis. Effective control measures to limit influenza transmission on cruise ships are needed to reduce morbidity and mortality. New strategies are required to increase uptake of pre-travel influenza vaccination. As many cruise ship travelers are old, often also frail, immune responses to influenza vaccination decline, necessitating novel approaches to overcome immunsenescence. Repeat influenza vaccination may be required, possibly with better adjuvants, however, potential interference in vaccine response with sequential years` vaccination need to be addressed before routinely offering 6 monthly re-vaccination.

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