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REVIEW

Avian influenza — A review for doctors in travel medicine

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Summary First identified in humans in Hong Kong, influenza A/H5N1, known commonly as avian influenza, has caused human disease in 15 countries around the world. Although the current number of confirmed patients is tiny compared to seasonal and the recently emerged H1N1 'swine' influenza, H5N1 remains a candidate for the next highly pathogenic influenza pandemic. Currently, H5N1 has very limited ability to spread from person-to-person but this may change because of mutation or reassortment with other influenza viruses leading to an influenza pandemic with high mortality. If this occurs travellers are likely to be affected and travel medicine doctors will need to consider avian influenza in returning febrile travellers. The early clinical features may be dismissed easily as 'the flu' resulting in delayed treatment. Treatment options are limited. Oral oseltamivir alone has been the most commonly used drug but mortality remains substantial, up to 80% in Indonesia. Intravenous peramivir has been filed for registration and IV zanamivir is being developed. This review will focus on the epidemiological and clinical features of influenza A/H5N1 avian influenza and will highlight aspects relevant to travel medicine doctors.

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Introduction

Avian influenza due to the influenza A/H5N1 virus has emerged as a potential global threat.[1] The H5N1 virus joins a list of other respiratory pathogens that have emerged in the past 40 years and which often cause severe clinical disease like *Legionella pneumophila*, SARS coronavirus and Hanta virus pulmonary syndrome.[2–4]

When a new pathogen emerges and causes a high mortality, much angst is generated globally. The main question is whether there is potential for efficient spread from person-to-person and, therefore, the risk of an epidemic or pandemic. To date, person-to-person transmission of H5N1 has been very rare and associated with close human contact.[5] Never the less, the threat remains that H5N1 may cause the next pandemic with substantial mortality.

The global spread of avian influenza has been through the poultry trade and infected birds and many countries have experienced poultry outbreaks (Fig. 1). By contrast, the SARS epidemic and the current (2009) pandemic of H1N1 swine influenza are good examples of how global travel played an important role in the spread of these two viruses.[3,6] If H5N1 acquired the ability to spread easily, then air travel would be a very efficient way to transport infected passengers and cause outbreaks far from their original source.

H5N1 infection of humans was first reported in Hong Kong in 1997, causing 6 deaths in 18 confirmed patients. Infected poultry in Hong Kong's wet markets were the likely source.[7,8] Mass culling of chickens was necessary to curtail this small epidemic. As of September 2009, H5N1 has been documented and reported to the WHO in 442 patients in 15 countries of which 6 are in SE Asia (www.who.int/csr/disease/avianinfluenza/country/casestable200809_10/en/index.htm, accessed November, 2009). H5N1 infections in wild birds, chickens and other poultry have been reported in 61 countries in Africa, Asia and Europe (Fig. 1).

The history of influenza pandemics explains the anxiety regarding H5N1. There have been three pandemics of influenza in the past 100 years and the one upper most in our minds is the 1918 pandemic because of its size and high, total mortality of some 40 million people.[9] Patients of all ages died, including young adults aged 20—40 years. This was a distinct difference from the usual pattern of mortality of seasonal influenza epidemics in which patients at the extremes of age suffer the greatest mortality. A lack of influenza immunity was an important reason for its easy spread and high mortality which has also been attributed to viral genes that facilitate high viral loads, excessive innate inflammatory response and fatal primary viral pneumonia.[10–13] A recent re-examination of microbiological data and lung tissue from 1918 has suggested strongly that secondary bacterial pneumonia also played a key role in the high mortality.[14] In 2009, the world is experiencing a fourth pandemic of a novel influenza A/H1N1 virus. Our knowledge of this infection is increasing and important lessons learnt may impact our thinking regarding H5N1.[15,16]

One theme is common to the three major influenza pandemics and the 'swine' flu pandemic; the viruses responsible had an avian link. The H1N1 1918 pandemic is thought to have arisen through the adaptation of an avian like influenza virus that allowed for easy human to human transmission whereas the H2N2 (1957 pandemic) and H3N2 (1968 pandemic) influenza viruses acquired new genes from Eurasian avian viruses by genetic reassortment with the circulating human H1N1 virus.[9] The 2009 'swine' H1N1 influenza virus is an assortment of avian, human and swine influenza viruses.[17] Currently, highly pathogenic H5N1 avian

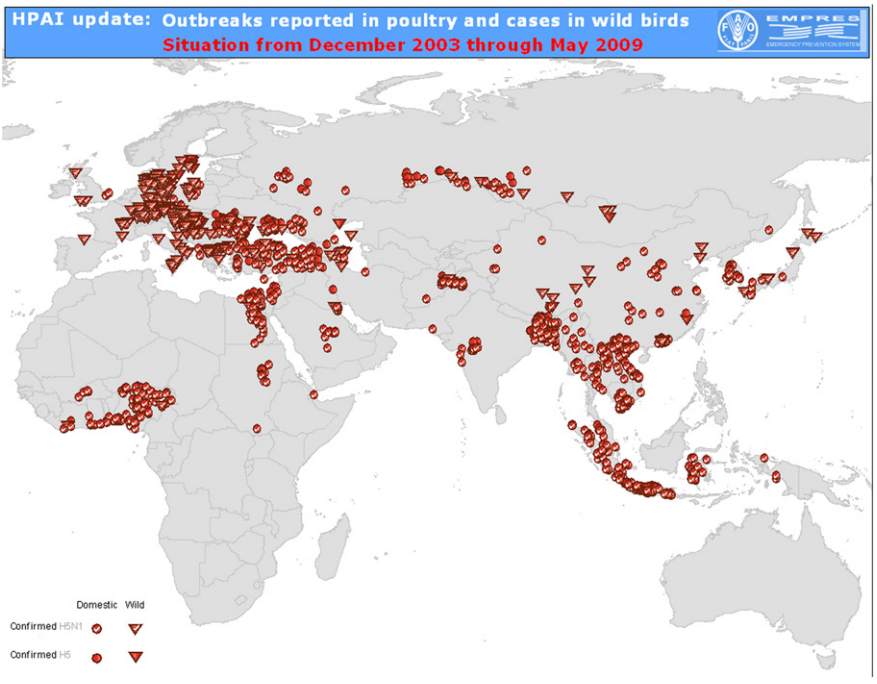

Figure 1 Map of the global distribution of poultry outbreaks since the first detection of H5N1 in 2003 to June 2009.