Title: Human exposures to H5N6 Avian influenza , England, 2018

Authors: Alicia C Thornton, Frances Parry-Ford, Elise Tessier, Nisha Oppilamany, Hongxin Zhao, Jake Dunning, Richard Pebody & Gavin Dabrera

Corresponding Author: Alicia C Thornton. Tel: +44 20 8327 6977. Email: Alicia.Thornton@PHE.gov.uk

Author Affiliations:

Alicia C Thornton. National Infection Service, Public Health England, London, UK NW9 5EQ

Frances Parry-Ford. Immunisations and Countermeasures Division, National Infection Service, Public Health England, London, UK NW9 5EQ

Elise Tessier. Immunisations and Countermeasures Division, National Infection Service, Public Health England, London, UK NW9 5EQ

Nisha Oppilamany. Respiratory Diseases Department, National Infection Service, Public Health England, London, UK NW9 5EQ

Hongxin Zhao. Immunisations and Countermeasures Division, National Infection Service, Public Health England, London, UK NW9 5EQ

Jake Dunning. Virus Reference Department, National Infection Service, Public Health England, London, UK NW9 5EQ

Richard Pebody. National Infection Service, Public Health England, London, UK NW9 5EQ

Gavin Dabrera. National Infection Service, Public Health England, London, UK NW9 5EQ

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Abstract

The human risk following exposure to the European reassortant avian influenza A (H5N6) is unknown. We used routine data collected as part of public health follow-up to assess outcomes of individuals exposed to H5N6 infected wild birds in England. There were 19 separate incidents of confirmed H5N6 among wild birds in the first quarter of 2018 in England and 69 individuals exposed to infected birds during these incidents. Five exposed individuals developed respiratory symptoms. However, no H5N6 infection was detected among those individuals with respiratory symptoms who underwent diagnostic testing, indicating that the human risk from this strain remains low.

Key words: Avian influenza; public health; prophylaxis; follow-up

Background

New strains of Avian Influenza (AI) result from the reassortment of genetic material during viral replication and can lead to new outbreaks in avian species with uncertainties about the related risk for humans. Currently, influenza A (H5NX) viruses are known to be circulating among birds in Africa, Europe and Asia with some subtypes, such as H5N1 and H5N6, known to cause disease in humans [1, 2] . Some influenza A (H5N6) viruses have caused severe disease in humans in China [3-7]. In Europe, influenza A (H5N6) was initially reported among wild birds and poultry in the Netherlands, in December 2017. Phylogenetic analysis of the Dutch virus showed that it was not related to the Chinese viruses the same subtype and instead was a distinct clade formed as a result of the reassortment of an influenza A (H5N8) subtype [8]. The reassortant influenza A (H5N6) viruses which have caused outbreaks among birds in Europe have all clustered within clade 2.3.4.4b. This clade has caused one single human case in China [9]. However, the assignment to clade is based on the H5 sequence only. Additional viral characteristics relevant to human transmission and pathogenicity are not included in this classification Beerens et al also analysed the genome of the

novel H5N6 virus for signatures associated with risk of human disease and found that the virus has a specific avian receptor and no sequences associated with increased airborne transmission. The overall composition of the European viruses detected in birds so far differs from the human case detected in China. [8].

In England AI infections among wild birds are monitored through a routine surveillance system. The system consists of regular patrols conducted by wardens within bird reserves and collections of dead birds made by members of the public and submitted to the Animal and Plant Health Authority (APHA). When AI is suspected or confirmed by laboratory testing Public Health England (PHE) is notified in order to assess the risk to human health.

Since there was a lack of evidence regarding the new H5N6 European reassortant virus and its ability to cause disease in humans following an exposure to an infected bird, a precautionary approach to human exposures was adopted. In England, persons exposed to avian influenza A (H5N6) detected in wild birds were followed up by local Health Protection Teams following notification by animal health counterparts. All exposed individuals were risk assessed with regard the nature of their contact; receipt of prophylactic antivirals; and whether they had experienced acute respiratory symptoms (such as cough, coryza, and/or fever) and/or conjunctivitis in the 10 days following their exposure [10]. Any individuals reporting symptoms had respiratory or conjunctival swabs tested by RT-PCR for Influenza A and H5. Individuals with direct exposure to wild birds with laboratory confirmed H5N6 virus infection were offered post-exposure oseltamivir prophylaxis if within 7 days of exposure and health surveillance (daily telephone contact to check on health status) for 10 days after their last exposure. If they became symptomatic within the 10 days after their last exposure they were offered a treatment dose of antivirals.

We aimed to use the routine surveillance data collected on individuals exposed to wild birds infected with influenza A (H5N6) to assess the public health management of these incidents and determine the risk of these types of exposure to human health.

Methods

All individuals identified as having had field exposures to influenza A (H5N6) in wild birds in England, during the first three months of 2018, were included. Field exposures were defined as all individuals who came into contact with the infected bird/contaminated objects in any situation outside of an APHA laboratory.

A standardised report form collected information gathered during the risk assessment and follow-up of exposed persons; this was collated nationally by the PHE National Infection Service. Risk assessment for all exposed individuals included whether there was handling or contact with the bird, bird faeces, litter or other fomites which may have been contaminated by infected birds; whether the person was exposed while using personal protective equipment (PPE); and whether the person have received any antiviral prophylaxis either prior to or after the exposure. Appropriate PPE for use where avian influenza is suspected includes use of disposable overalls, gloves, boots goggles and an FFP3 respirator [11]. However, for the purposes of this analysis any use of PPE when the exposure occurred was included. Descriptive analysis of the types of exposures, the actions taken and the outcomes of exposed individuals was conducted.

Results

In England from 1st January 2018-31st March 2018, there were 19 reported incidents of confirmed influenza A (H5N6) in wild birds. No AI incidents in poultry or farmed birds were reported during this time. These incidents resulted in a total of 69 human field exposures: 15 nature reserve workers; 13 veterinary staff; 11 members of the public; 9 staff members involved in wild bird surveillance collection; 8 staff working at other sites where birds were found; 6 bird volunteers/bird workers; 4 staff involved in post mortems of birds; and 3 other individuals. The median follow up period for exposures was 10 days (range 1-42 days). Shorter follow up resulted from time intervals required for avian testing to be completed. Longer follow-up was conducted where exposures were ongoing in localised settings.

Information on the use of any PPE at the time of exposure was available for 65 exposures of which 72% (47/65) had been exposed without PPE. No pre-exposure antiviral prophylaxis was reported. Post exposure antiviral prophylaxis was provided for 35 (51%) exposures in total: 6/18 exposures with PPE and 29/47 exposures without PPE (**Error! Reference source not found.**). For the majority of occasions where antivirals were not prescribed, this was because the notification of AI was received outside of the 7 day window or because the offer was declined.

Table 1: Use of Personal protective equipment and antiviral prophylaxis during AI incidents, 2018

Received antiviral prophylaxis	Nature of exposure			
	With PPE	Without PPE	Use of PPE unknown	Total
Yes	6 (33%)	29 (62%)	0 (0%)	35 (51%)
No	12 (66%)	18 (38%)	4 (100%)	34 (49%)
Total	18 (100%)	47 (100%)	4 (100%)	69 (100%)

Five individuals developed symptoms within 10 days of exposure; no conjunctivitis reported. No symptomatic individuals had used PPE at the time of exposure or pre-exposure prophylaxis and all received oseltamivir post-exposure prophylaxis. Of the five individuals who experienced symptoms, four underwent diagnostic sampling (one did not undergo sampling as symptoms resolved within a day). No influenza virus or other respiratory viruses were identified from any of these samples.

Discussion

England has experienced a large number of laboratory-confirmed H5N6 AI incidents in wild birds in the early part of 2018. This provided a unique opportunity to examine the outcomes of human exposure to this reassortant influenza A (H5N6) as, unlike incidents on poultry farms, wild bird incidents often result in unplanned exposures of individuals to AI without the use of PPE or pre-exposure antiviral prophylaxis. In addition, as any of use of PPE was considered within the analysis, the range of PPE used may have varied from full PPE, as recommended by Health and Safety Executive guidelines, to simple use of gloves to handle dead birds.

A previous study has reported no transmission to poultry farm workers during H5N6 outbreaks in Korea, however all exposed individuals in that study were exposed while wearing appropriate PPE [12] and these outbreaks were caused by a different H5N6 clade to that observed in this report. To our knowledge, this is the first report of individuals followed up after exposure to the recently identified reassortant influenza A (H5N6) virus in wild birds.

The reporting of acute respiratory symptoms by exposed persons by exposed individuals in this cohort may be explained by the circulation of seasonal respiratory viruses during winter months in England and is in keeping with findings from individuals exposed to influenza A (H5N8) AI in Europe

[13]. Our analysis was not able to identify asymptomatic infection in humans, and is not directly comparable to poultry farm incidents. In addition symptomatic individuals were tested using RT-PCR and no serological testing was conducted. This represents a limitation as RT-PCR does not detect low levels of virus however RT-PCT was chosen due to its rapid nature which would allow swift public health action in the event of any positive results. Despite these limitations, our study does provide additional information that human exposure to infected wild birds, even without the consistent use of antivirals and PPE, did not result in significant human disease.

Our experience suggests that exposures to this reassortant H5N6 AI does not appear to lead to symptomatic infection in humans and, although there were only 69 exposures, provides reassurance that the risk to public health from this virus is likely to be very low. As no human cases occurred, we are not able to comment on the infection severity. As shown by the earlier analysis by Adlhoch et al, for avian H5N8 [13], this analysis demonstrates how outcome data on contacts collected as part of the routine public health response to exposures could be applied in the future to inform public health risk assessments of impact on the human population for emerging strains of avian influenza.

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Conflicts of Interest

None declared

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