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Advisory Committee on Dangerous Pathogens

Risks to human health from non H5/7 Avian Influenza serotypes

Risk Assessment of Low Pathogenicity H6 Avian Influenza to Humans in the UK

This document is based upon an HPA teleconference '*Risk assessment of low pathogenicity H6 avian influenza to humans in the UK*', 27 March 2008. The participants were Nick Phin, Nigel Lightfoot, John Watson, Maria Zambon, Alison Bermingham and Nick Gent. European and UK virological data and commentary were supplied by Ian Brown, Richard Irvine and Bhudipa Choudhury of the VLA.

This report represents our current understanding of the risks associated with Low Pathogenicity H6 avian influenza.

Issue

Following reports by two farms in the east of England of low level die-offs of turkeys and a drop in egg production, veterinary investigations have been confirmed as a low path H6 avian influenza in the birds. The farms are owned by the same company, are 50 miles apart, and each farm has approximately 10,000 birds. There are believed to be 10 staff at each of the sites. The turkeys in one farm are nearing the end of their productive life and it is proposed to slaughter them and put them in the food chain. The turkeys in the other farm are much younger and, given that the birds are showing some clinical improvement, it is proposed to keep the birds alive and that normal production should continue. The HPA has been asked for a public health risk assessment of the impact of these courses of action.

Background to H6

The H6 influenza virus subtype was first identified in turkeys in 1965. Since then it has been detected with increasing frequency in wild and domestic birds. In Southern China the H6 virus is prevalent in poultry all the year round[1]. Wild bird surveillance over eight years in Europe and America found that the H6 subtype was the most frequently detected influenza subtype and had the broadest host range of any other subtype[2]. All of the H6 isolates that have been examined have been of low pathogenicity. The virus normally causes asymptomatic infections in waterfowl but infection in chickens has been associated with reduced egg production, upper respiratory tract infection, and increased mortality.

Human infection with H6

No natural human infections have been reported with the H6 subtype, however, serological studies of American vets in contact with birds and poultry workers in China have detected low levels of H6 specific antibodies[3],[4] and volunteers experimentally inoculated with the H6 virus developed mild upper respiratory infection and shed virus[5],[6]. However, the virus could mutate to become more virulent to humans, and at present the receptor binding characteristics of these viruses is unknown making an assessment of their potential for transmission to humans extremely difficult as this is a key biological determinant. At present there have been no recorded instances of human to human transmission from either naturally or experimentally infected people [6].

Pandemic potential of H6

During the H5N1 outbreak in Hong Kong in 1997 an H6 influenza subtype isolated from a teal was found to have seven of the eight genes present in the H5N1 strain at that time. This linked to the prevalence of the virus and the possibility of re-assortment with H5N1 and H9N2 viruses in the southern China region could lead to increased diversity of the H6 subtype and the possibility of that the virus might evolve to infect humans.

The World Health Organization has listed H6 as one the avian influenza subtypes with pandemic potential. The list, in priority order, is H5, H7, H9, H2, H6, and H4.

European situation

Table 1 below shows that incursions of H6 viruses into the domestic poultry compartment occur sporadically but regularly in the EU. Detections are most frequent in turkeys (presumably as a result of increased susceptibility to AI viruses and clinical presentation) and ducks (possibly due to frequent contact with wild waterfowl).

Table 1

Year	Country	Virus subtype	Poultry host
2001	France	H6N2	Turkeys and ducks
	Italy	H6N1	Partridges
2002	Germany	H6N2	Turkeys (x19)
	France	H6Nx	Turkeys
	Denmark	H6N8	Ducks
2003	UK	H6N2	Ducks
	France	H6N2	Turkeys and ducks
	Germany	H6N1	Ducks
	Germany	H6N2	Geese
2004	France	H6N2	Turkeys (x5)
	Germany	H6N2	Turkeys (x3)
2005	France	H6N1	Ducks
	France	H6N2	Ducks
	France	H6N8	Ducks
2006	Germany	H6Nx	Ostriches
	Germany	H6Nx	Ducks
	Netherlands	H6N5	Turkeys (x31)
2007	France	H6N2	Turkeys
	France	H6N2	Ducks
	Germany	H6N2	Turkeys
	Germany	H6N1	Ducks (x6)
	Germany	H6N2	Ducks (x6)
	Germany	H6N8	Geese
	Belgium	H6N8	Turkeys
	Ireland	H6N2	Chickens

Source of information: Proceedings of the annual meetings of the national Newcastle Disease and Avian Influenza laboratories of countries of the European Union
http://ec.europa.eu/food/animal/diseases/controlmeasures/avian/crls_proceedings_en.htm

Within Europe, culling is not always undertaken in an economically viable flock if a low pathogenicity avian influenza virus is identified. The disease may be allowed to run its course within a flock. This is because in most instances the birds do recover and egg production can return to normal.

Wild bird surveillance in Great Britain – detections of H6 viruses
Table 2

Year	AIWBS activity & Positive H6 result and species of bird			Total number H6 positive wild birds
	Trapped	**Shot**	**Found dead**	
2008	H6N2 Teal x1 (*Anas crecca*)	-	-	1
2007	-	H6N2 Mallard duck x1 (*Anas platyrhynchos*)	H6N5 Mute swan x1 (*Cygnus olor)*	2
2006	H6N1 Teal x1 H6N2 Teal x1	H6N8 Pink-footed goose *(Anser brachyrhynchus)*	H6N8 Greylag goose (*Anser anser*)	4
2005	-	H6N2 Mallard x1	-	1
2004	-	-	-	0
2003	-	-	-	0
Total	*3*	*3*	*2*	*8*

Number of wild birds positive for H6 subtype Avian Influenza (AI) virus infection in Great Britain AI Wild Bird Surveillance (AIWBS) activity over the period 2003 to 2008

The results are typical of the EU wild bird surveillance programme as a whole demonstrating the relatively common occurrence/circulation of H6 viruses especially in wild waterfowl.

Virus characteristics of H6

There are very limited genetic data available on European H6 viruses, especially recent strains. However analysis of the haemagglutinin gene (only data for this gene on European strains available) reveals significant divergence from North American and Asian viruses. The constellation of genes encoding internal viral proteins are shared between H9N2, H5N1 (HPAI) and H6N1 co-circulating in Asia. There is no information on these genes for European strains but given the divergence in HA it is quite possible they may be distinct. Currently VLA-Weybridge (CRL for AI) is sequencing the whole genome of H6N1 viruses associated with the AI outbreaks in two UK poultry farms. Further analysis will be conducted and shared once the data are available.

Confusion exists about the designation of high or low pathogenicity in birds and the clinical implications of infection in humans. No assumption can be made about the clinical significance in humans based on the designation in birds.

Defra position

The H6 subtype is not governed by European legislation and therefore Defra are not required to take action on control, however, they have reserved powers to take action where an unusual risk to

public or veterinary health may be present. As already discussed, in certain European countries a flock will be allowed to continue to the end of its economic life. There would therefore need to be a compelling public health issue for them to take action.

Occupational risk to poultry handlers and veterinary staff

The highest risk factor for catching avian influenza is exposure to infected poultry. People closely associated with poultry (ie poultry industry workers and vets) will be more at risk than the general population. Apart from the information from serological studies there have been no reported cases of illness related to H6 among these occupational groups. In addition, the receptor binding characteristics of these viruses is a key biological determinant; this is unknown for this subtype making any risk assessment of their potential for transmission to humans extremely difficult. Nevertheless the risk of re-assortment with this subtype exists and therefore there is the potential either for human disease or evolution into a pandemic strain.

Shedding of H6 virus is believed to continue for 7-10 days after the birds have recovered and it is therefore recommended that poultry workers or veterinary staff in contact with infected birds, their waste or bedding material should wear personal protective equipment (PPE) and their health should be monitored. Health monitoring should continue for up to seven days after last contact with infected birds.

Occupational risk in catching and killing

This group of workers would have similar exposures to those above and the same recommendations would apply.

Occupational risk during slaughter, gutting and de-feathering

The slaughtering and evisceration processes have the potential for the release of large amounts of virus. There have been reports of infection with H5N1 either in the preparation of infected meat or de-feathering of infected birds.

It is therefore recommended that workers involved in the slaughtering and evisceration processes should wear appropriate PPE while handling infected birds.

Occupational exposure in the further stages of meat processing

If the birds were still shedding virus at slaughter it is likely that virus may still be present on the meat and present a potential means of environmental contamination or route of infection.

It is therefore recommended that workers involved in the meat processing should wear appropriate PPE while handling infected birds.

Public exposure due to handling or consumption of meat.

The Food Standards Agency, who has the statutory responsibility for food safety, has advised that “avian flu does not pose a food safety risk for UK consumers. For people the risk of catching the disease comes from being in close contact with live poultry that have the disease and not through eating cooked poultry or eggs”.

Summary: Preliminary risk assessment and advice based on current knowledge

The research literature on the human health risks of H6 avian influenza is very limited and there are a number of unknowns. What limited data is available suggests that this subtype causes asymptomatic or mild infection in humans and has not so far shown any tendency to be transmitted from person to person. Nevertheless its close association with the H5N1 and H9N2 subtypes in southern China and its diversity suggest that it has the potential to infect humans. It is also considered by the WHO to be one of six influenza subtypes that have the potential to contribute to the development of a strain of influenza with pandemic potential. On balance, the risk to humans is considered low but the necessity to keep any such event, and associated human illness, under close scrutiny is recognised. In view of the low clinical risk, it is not considered necessary to offer prophylaxis, either post exposure or for those in contact with infected birds and wearing PPE.

Those with contact with infected birds should undergo health monitoring until the completion of a full incubation period after their last exposure.

Recommendation

In order to minimise the risk of exposure of humans, the HPA would prefer that the turkeys were culled. Recognising, however, the limited information available, the high probability of low risk of human infection and standard practice for the management of these incidents elsewhere in Europe, the HPA would be content that the incident be managed by slaughter of the older turkeys and maintaining alive the younger turkeys (followed by later slaughter) provided that:

- full PPE be maintained for all workers having occupational exposure to potentially infected turkeys
- health surveillance be maintained on all those already exposed, and those subsequently exposed, including the reporting of symptomatic illness and that this should continue for seven day after last exposure to the birds, their waste or bedding.
- the collection of paired blood specimens (>14 days apart) for serology is undertaken

The HPA should work with Defra and other relevant agencies to review the approach that should be adopted generally to the risk assessment of exposure of humans in low pathogenicity avian flu incidents of any relevant subtype.

Actions/ Work required (not necessarily by participants of the teleconference)

- The provisional conclusions of the risk assessment group to be relayed to the chair of the IMT immediately by telephone
- The provisional conclusions of risk assessment group to be relayed to the chair of the Defra meeting
- Ensure the HPA CEO is briefed
- The report to be finalised, circulated amongst teleconference members for comment and then forwarded to the IMT
- Virus exchange with the VLA will need to be undertaken in order to develop the necessary serological tests (underway)

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[1] Cheung et al Establisment of influenza A virsu (H6N1) in minor poultry species in southern China Journal of Virology 2007 81: 10402-10412

[2] Munster et al Spatial, temporal and species variation in prevalence of influenza A viruses in wild migratory birds 2007 PloS Pathology 3 630-638

[3] Myers FP Setterquist SF Capuano AW Gray GC Infection due to 3 avian influenza subtypes in United States Veterinarians CID 2007 45 4-9

[4] Shortridge KF Pandemic Influenza a zoonosis? Semin Resp Infect 1992 7 11-25

[5] Beare AS, Webster RG Replication of avian influenza viruses in humans. Archives of Virology 1919 119 37-42

[6] Subbarao, K. And Katz, J., Avian influenza viruses infecting humans Cell. Mol. Life Sci. (2000) 57 1770-1784