RAPID RISK ASSESSMENT

Human infection by low pathogenic avian influenza A(H7) viruses

11 February 2015

Main conclusions and recommendations

On 2 February 2015, British authorities reported an outbreak of low pathogenic avian influenza virus A(H7N7) on a chicken farm in Hampshire in the United Kingdom. Culling of the birds in the affected holding has started, with a restriction zone established, and investigations into how the birds became infected have been initiated. The virus has been analysed genetically and does not contain key mutations associated with increased risk for zoonotic infection.

Outbreaks in poultry holdings caused by low pathogenic or high pathogenic avian influenza A(H7N7) viruses have been reported previously in Europe, as well as human infections with low pathogenic avian influenza virus A(H7N7). Such infections generally cause mild disease with influenza-like symptoms or conjunctivitis.

The group at risk for infection includes people with occupational exposure to poultry. This group should be made aware of the clinical features of infection, and advised to alert authorities and healthcare providers about any relevant exposure if they develop influenza-like illness or other symptoms.

There is a low risk of zoonotic transmission to people who are directly exposed to infected birds during the culling and destruction process when there are outbreaks in poultry farms. The risk can be minimised if the exercise is performed under the safety measures recommended in Directive 2005/94/EC. Persons with direct contact to infected poultry before or during culling and disposal should be monitored for symptoms, and post-exposure antiviral prophylaxis should be considered.

The risk for zoonotic transmission to the general public in EU/EEA countries is considered to be extremely low.

Source and date of request

By request of the European Commission, 6 February 2015.

Public health issue

This document summarises the epidemiological and virological information about human infections with low pathogenic avian influenza A(H7N7) viruses and assesses the risk to public health in the EU/EEA, in response to an outbreak on a poultry farm in the United Kingdom in February 2015.

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Event background information

On Monday 2 February, the Department for the Environment and Rural Affairs (DEFRA) declared an outbreak of low pathogenic[i] avian influenza (LPAI) virus of type H7 in Hampshire, England [1]. Initial laboratory testing indicated a low pathogenic A(H7N7) virus. Results from N-subtyping and pathogenicity testing (intravenous pathogenicity index, IPIV) have yet to be confirmed.

On 3 February, the World Organisation for Animal Health (OIE) was officially notified [2] that 52 birds had died in a flock of approximately 10 000 forty-week-old housed broiler breeder chickens. An H7 virus was isolated and early serology results suggested that the outbreak had already passed its peak and was resolving by the time it was detected. The preliminary analysis conducted by the AI EU Reference Laboratory (APHA-Weybridge, UK) on the full genome of virus isolated suggests that five genes, PA, HA, M, NP and NS are of avian origin. Three other genes, NA, PB1 and PB2 are also likely to be of avian origin. However, these genes also have a close homology with genes from influenza H10N7 viruses isolated from seals in Sweden, Denmark and Germany in 2014 that are most likely derived from an avian progenitor strain. There are no strong correlates for increased human affinity. Phylogenetic analysis of the HA gene places this isolate in a cluster with contemporary European H7 sequences from poultry from Germany (2013) and Italy (2011). These viruses group closely with contemporary strains from wild ducks. The presence of a full 'stalk' in the neuraminidase supports a recent introduction of virus from a wild bird source or contaminated environment.

An epidemiological investigation has started. Culling and disinfection measures have been initiated on site and restriction and surveillance zones have been established according to EU regulation Directive 2005/94/EC [2,3].

Three persons who had been exposed to the flock reported an influenza-like illness or conjunctivitis. Nose, throat and eye samples were collected, and treatment with oseltamivir was given. No human infections with H7N7 or other respiratory viruses were identified. Persons performing the culling and clean-up operations were wearing appropriate personal protective equipment. Those exposed to the flock prior to or during the culling and clean-up operations will be monitored for symptoms and those involved in the culling of the flock and disposal of the carcasses have been offered antiviral chemoprophylaxis for up to 10 days following their last exposure.

Public Health England assesses the risk to public health as very low and the Food Standards Agency in the UK stated that there is no food safety risk for consumers [4,5].

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[i] According to Council Directive 2005/94/EC: 'highly pathogenic avian influenza (HPAI)' means an infection of poultry or other captive birds caused by:

(a) avian influenza viruses of the subtypes H5 or H7 with genome sequences codifying for multiple basic amino acids at the cleavage site of the haemagglutinin molecule similar to that observed for other HPAI viruses, indicating that the haemagglutinin molecule can be cleaved by a host ubiquitous protease; or

(b) avian influenza viruses with an intravenous pathogenicity index in six-week old chickens greater than 1.2;2.

Disease background information

Low pathogenic avian influenza viruses A(H7N7)

Low pathogenic avian influenza (LPAI) viruses are commonly found in the wild bird reservoir and normally cause mild clinical symptoms or no apparent disease [6]. Wild birds shed LPAI viruses in their droppings which can result in transmission to susceptible poultry and other birds via the faecal-oral route [7].

The H7 type of avian influenza identified in this outbreak is classified as low pathogenic in birds. The classification of avian influenza viruses as low pathogenic or high pathogenic is defined either by the composition of the cleavage site in the haemagglutinin (HA) gene, or by the intravenous pathogenicity index in six-week old chickens, according to Council Directive 2005/94/EC. The fact that an avian influenza strain is highly pathogenic for birds does not necessarily mean that it is pathogenic for humans. In addition, it is likely that there are asymptomatic infections and infections with mild symptoms that are never diagnosed because LPAI is not suspected and tested for.

Outbreaks of low pathogenic avian influenza virus A(H7N7) have been detected in poultry holdings in the EU in Denmark, 2013, [8] Germany in 2009 [9], 2011 [10] and 2013, [11] as well as in the Netherlands, 2011, [12] 2012 [13] and 2013 [14]. To our knowledge, no human cases were associated with these outbreaks.

Figure 1. Outbreaks of low pathogenic avian influenza virus A(H7N7) in poultry, Europe 2011–2015

Source: EMPRES-i database (http://empres-i.fao.org/eipws3g/) and OIE notifications (http://www.oie.int/alerts-disease-information/)

Highly pathogenic avian influenza viruses A(H7N7)

Conversion from LPAI to HPAI is correlated with the acquisition of multiple basic amino acids (arginine and lysine) at the cleavage site of HA [15]. This enables highly pathogenic viruses to replicate in many tissues causing systemic infection in birds [16].

A limited number of human cases associated with highly pathogenic avian influenza (HPAI) virus outbreaks in poultry have been reported since 1959 (the date of first recognition). There have been reports of single cases of people infected from their domestic poultry which mixed with wild birds [17,18]. Outbreaks related to HPAI of the H7-type have occurred in densely populated commercial bird populations such as in Italy in 1999 (H7N1), the Netherlands, Belgium and Germany in 2003 (H7N7), and Canada in 2004 (H7N3) [19]. HPAI A(H7N7) was detected in Oxfordshire, England in 2008 [20]. An outbreak of HPAI A(H7N7) in birds, which began in the Netherlands in February 2003, caused the death of one veterinarian (from an acute respiratory illness). It also caused 89 human cases showing some mild illness (mostly eye infections) in poultry workers and members of their families indicating limited human-to-human transmission [21-24]. Outbreaks of HPAI A(H7N7) virus were reported from Italy in 2013 and caused three human cases showing conjunctivitis and influenza-like illness [23,25,26].

Other low pathogenic avian influenza H7 viruses

Human infections with LPAIs and particular of H7-type seen in Europe have only been associated with mild to moderate self-limiting disease, primarily conjunctivitis or flu-like illness [27-30], and only a limited number of cases have required hospitalisation. In addition, it is likely that there are asymptomatic infections and infections with mild symptoms that are never diagnosed because LPAI is not suspected and tested for. Serologic studies performed in Northern Italy 2008–2010 showed that 6 out of 188 (3.2%) poultry workers exposed during low and high H5 and H7 avian influenza virus outbreaks were H7-seropositive, and none of the 379 non-exposed controls were positive [31].

Other low pathogenic avian influenza viruses of the H7-type have been shown to transmit to humans causing mild to severe diseases. A(H7N3) caused conjunctivitis and influenza-like illness to exposed persons and poultry workers in England [28]. In 2007 in Wales, United Kingdom, several cases of influenza-like illness, of which three required hospitalisation, were linked to a laboratory confirmed poultry outbreak caused by avian influenza A(H7N2) virus [32]. A(H7N9) viruses circulating in poultry in China have also raised attention over the past years, as they are the first low pathogenicity avian viruses that have been documented to cause severe human disease and fatalities [33-35]. The major source of infection with influenza A(H7N9) for humans is likely to be poultry or birds handled in live bird markets or slaughtered at home. While wild birds are the reservoir for H7 and N9 genes of influenza viruses [36,37], live bird markets seem to serve as amplifiers [38]. No A(H7N9) viruses circulating in China have so far been detected in Europe [33].

Human surveillance of avian influenza viruses in Europe

All novel influenza strains are notifiable diseases in the EU according to Commission Decisions and the International Health Regulations (IHR) through the Early Warning and Response System and IHR, respectively [39]. Infectious disease protocols for case investigations are available from the Consortium for the Standardization of Influenza Seroepidemiology (CONSISE) [40] and national authorities.

Evidence of the effectiveness of contact tracing on board airlines in limiting spread of infection is limited and should only be considered upon a risk assessment on a case-by-case basis [41].

Bird surveillance of avian influenza viruses in Europe

The establishment and implementation of surveillance systems, diagnostic tools for early detection of highly and low pathogenicity avian influenza viruses, and harmonised restriction and control measures, are laid-down in EU legislation for surveillance and control of highly pathogenic avian influenza viruses in bird species [3,42]. This included introducing programmes of passive surveillance of wild bird populations as an early warning system. This is complemented by active monitoring of poultry in the EU for all strains of H5 and H7 irrespective of pathogenic type and control measures provided in legislation.

All infections in poultry caused by avian influenza virus of any subtype fulfilling the *in vivo* criteria for high virulence laid down in the Terrestrial Animal Health Code of the World Organisation for Animal Health (OIE), and also all H5 and H7 avian influenza virus, irrespective of virulence, are reported to animal health authorities as notifiable avian influenza [42].

Diagnostics of avian influenza infections in humans

With routine diagnostic laboratory assays, A(H7N7) viruses should be detected as positive for influenza A virus, and negative for influenza B, A(H1), A(H1)pdm09, A(H3) and A(H5) viruses. Hence, influenza A(H7N7) viruses are expected to be classified as un-subtypeable influenza A if no specific A(H7) diagnostic test is performed. It is standard procedure in diagnostic laboratories to send influenza A virus isolates or clinical samples that cannot be subtyped to the national reference laboratory (National Influenza Centres; NICs), and further to a WHO Collaborating Centre for characterisation.

Vaccination

Vaccination of poultry has been successful in controlling subtype H7 influenza [43]. The World Health Organization recommended avian influenza viruses of the H7-type as candidate viruses for pandemic preparedness [44], and vaccine candidates against avian H7N7 or H7-type influenza viruses are under development [45-49].

ECDC threat assessment for the EU

The risk of infection with LPAIs is almost entirely confined to people who have close contact with domestic poultry (chickens, ducks, etc.) or their droppings. Human cases have almost entirely been in this category. People with small domestic and pet flocks are probably most at risk, as they are less likely to be able to take precautions than those working in industry and may be less aware of the risks. Other groups that have occasionally been infected are veterinarians, people involved in controlling outbreaks in birds (culling) and people who work on industrial poultry farms. Most EU Member States have standard occupational guidance for the latter group. For the vast majority of people, who have no direct contact with domestic birds or their droppings, the risk of acquiring LPAIs and the risk to health is almost non-existent.

There is no evidence of human infection through consumption of contaminated food [50].

The affected poultry in the UK were housed in a closed farm. After detection of the virus all birds were immediately culled and the farm disinfected to prevent any further spread. A control zone was established to control the disease and identify related outbreaks in close proximity.

Low pathogenicity A(H7) outbreaks have generally been associated with limited transmission causing small numbers of human infections with mild influenza-like respiratory illnesses and conjunctivitis. Persons at risk are mainly people with occupational exposure and direct contact/handling of diseased chickens or their carcasses e.g. farmers, veterinarians and those labourers involved in the culling. This group should be made aware of the clinical features of infection, and advised to take precautions. There is only a very low theoretical risk for persons without direct occupational exposure, especially for family members and healthcare workers providing care for the patients.

All people living in the affected farms as well as exposed workers and their cohabiting contacts with direct contact to sick animals should be actively monitored up to 10 days after the last exposure by the local health authorities. Human infections need to be monitored very closely regarding potential human-to-human transmission. Pre- or post-expositional prophylaxis using antiviral treatment for people at risk needs to be considered by the respective authorities based on a situational risk assessment.

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