RAPID RISK ASSESSMENT

Outbreaks of highly pathogenic avian influenza A(H5N8) in Europe

Updated 18 November 2016

Main conclusions and recommendations

On 27 October 2016, the Hungarian authorities reported the detection of highly pathogenic avian influenza (HPAI) virus A(H5N8) in a wild swan. Further notifications of HPAI A(H5N8) viruses detected in wild birds and poultry holdings have been made recently by seven additional European countries. Austria, Hungary and Germany reported outbreaks in poultry and detections in wild birds. Croatia, Denmark, Poland and Switzerland reported infection in wild birds only, while the Netherlands detected HPAI A(H5N8) in wild birds and birds in a zoo. Outside of Europe, India and Israel are currently reporting outbreaks in birds while South Korea, Taiwan and the Russian Federation reported outbreaks earlier this year. Culling of the affected poultry in European countries is ongoing or completed. Protection zones and surveillance zones have also been established.

Influenza A(H5N8) viruses have been continuously detected among wild birds in Asia since 2010 where it has caused several outbreaks on commercial poultry farms in China, Japan and South Korea. This is the second time this virus has been introduced into Europe via the autumn migration of wild birds, with an increased mortality in wild birds being observed in 2016 compared with 2014/2015. Preliminary genetic analyses indicates that these viruses associated with the recent incursions are closely related to those that previously appeared in 2014/2015 but form a distinct genetic cluster.

Ongoing monitoring and testing of wild birds and domestic poultry in the EU plays an important role in the detection and protection against exposure, and subsequent spread of the virus in poultry across Europe. This may equally minimise the human risk via exposure to infected birds. To date, no human infections with this virus have ever been reported world-wide and the risk of zoonotic transmission to the general public in EU/EEA countries is considered to be very low. The full genome sequences of several recent HPAI A(H5N8) viruses showed that these viruses to date are still essentially bird viruses without any specific increased affinity for humans.

However, given that the virus with the HA gene has evolved from the widely circulating A(H5N1) viruses, people in direct contact with or handling diseased birds or poultry and their carcasses (e.g. hunters, farmers, veterinarians and labourers involved in the culling and rendering) might be at risk of infection. Given this potential zoonotic risk, contingency plans for the control of avian influenza in poultry and birds are being implemented in collaboration with public health and occupational health authorities, to ensure that persons at risk are sufficiently protected from infection. Appropriate personal protective equipment, including respiratory protection, should be made available and used.

People exposed at affected holdings or having direct contact with infected wild birds should be monitored for ten days in order to identify possible related symptoms. Local health authorities may consider actively monitoring these groups and administering antiviral prophylaxis as recommended for persons with exposure to A(H5N1), dependent on the local risk assessment (i.e. intensity of exposure). Many EU Member States offer vaccination against seasonal influenza to persons exposed to poultry as a result of their occupation.

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Source and date of request

Internal decision to update the rapid risk assessment on highly pathogenic avian influenza A(H5N8) dated 14 November 2016.

Public health issue

This Rapid Risk Assessment (RRA) summarises the epidemiological, virological and environmental information relating to outbreaks of highly pathogenic avian influenza A virus subtype A(H5N8) in Europe up to 18 November 2016, and assesses the risk to public health in EU/EEA countries associated with the outbreak. It builds on the Rapid risk assessment on an outbreak of highly pathogenic avian influenza A(H5N8) in Germany, Rapid risk assessment on outbreaks of highly pathogenic avian influenza A(H5N8) in Europe and the Rapid risk assessment on human infections with avian influenza A viruses, China, which relates to A(H7N9) and A(H5N1).

Consulted experts

Internal ECDC staff (in alphabetical order): Kaja Kaasik Aaslav, Cornelia Adlhoch, Denis Coulombier, Lara Payne Hallström, Angeliki Melidou, Pasi Penttinen.

External reviewers and contributors: John McCauley, Rod Daniels (WHO Collaborating Centre for Reference and Research on Influenza, Crick Worldwide Influenza Centre, London, UK); Diane Gross (WHO Regional Office for Europe, Copenhagen, Denmark); Frank Verdonck (European Food Safety Authority, Parma, Italy) and Ian Brown (EU/World Organisation for Animal Health (OIE) /Food and Agriculture Organization of the United Nations International Reference Laboratory for Avian Influenza and Newcastle Disease; World Organisation for Animal Health (OIE) Reference Laboratory for Swine Influenza, Animal and Plant Health Agency (APHA), Weybridge, UK).

Disease background information

Outbreaks caused by highly pathogenic avian influenza* (HPAI) A(H5N8) viruses have been reported from Asia since 2010. In 2014/2015, outbreaks in HPAI A(H5N8) were reported in Germany, Hungary, Italy, the Netherlands, Sweden and the United Kingdom as well as in the US and Canada [1-3]. In the sequence database, Thailand has provided the sequence of a A(H5N8) virus detected in a duck in 2012 [4].

No human cases of avian influenza A(H5N8) have been reported in relation to the current circulating virus or other viruses of this subtype.

The influenza A(H5N8) virus was first detected in domestic ducks in China during routine surveillance activities at a live poultry market [5]. Since the beginning of 2014, several outbreaks involving novel reassortant HPAI A(H5N8) viruses have been detected in poultry and wild bird species in South Korea [6-8] as well as in China [5,9,10] and Japan [11]. The viruses have been detected in captured and apparently healthy wild migratory birds and dead wild birds as well as in domestic chickens, geese and ducks [8,9]. To date HPAI A(H5N8) viruses have been detected in 30 wild bird species [12]. While ducks are generally resistant to the pathogenic effects of influenza viruses and severe illness or death in wild mallard ducks has not been seen, HPAI A(H5N8) viruses have shown moderate pathogenicity in domestic ducks in South Korea (0–20% mortality rate). As clinical signs and deaths are rare in ducks, except for a drop in egg production at duck breeder farms, domestic ducks may be silent carriers of the reassortant HPAI A(H5N8) viruses, making it difficult to detect them in farms and live bird markets, while mallards may be long distance vectors of these viruses, shedding the virus for long periods [13,14]. During the 2014 epizootic, HPAI A(H5N8) viruses were isolated from free-living wild birds of the orders *Accipitriforme*, *Anseriforme*, *Charadriiforme*, *Falconiforme* and *Gruiforme*. In live wild birds, HPAI A(H5N8) virus detections were limited to ducks (order: Anseriformes) of the species common teal (*Anas crecca*), mallard (*Anas platyrhynchos*), spot-billed duck (*Anas poecilorhyncha*), Eurasian wigeon (*Anas Penelope*), American wigeon (*Anas americana*) and gadwall (*Anas strepera*) [15].

*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.

Importation of live poultry and live captive birds from the East Asian region into the EU is not authorised. Imports of fresh meat are authorised from Thailand and treated egg products and eggs for processing may be imported from Thailand, South Korea and China. Heat-treated poultry meat products are authorised for import into the EU from South Korea and from the Shandong province of China. No imports of any poultry commodities are permitted from Japan, where outbreaks caused by the HPAI A(H5N8) virus have also occurred. Given the heat-labile nature of all influenza viruses, these commodities are not considered to pose a risk of influenza virus transmission to consumers [16].

Virus characteristics

HPAI A(H5N8) viruses cluster in the haemagglutinin (HA) clade 2.3.4.4. as is the case for A(H5N6) and A(H5N1) viruses from Asia [5].

Avian influenza A(H5N8) viruses from South Korea were shown to bind preferentially to alpha 2-3 sialic receptors and, to a lesser degree, to alpha 2-6 sialic acid receptors [17]. However, analyses of the 2014/2015 viruses did not show increased affinity for humans [18]. They were also not able to directly transmit between ferrets although they were able to replicate in human bronchial epithelial cells [19,20]. Viruses of this clade were therefore assessed to have low to moderate virulence in mammals, although mammals such as ferrets, dogs and cats were able to be infected experimentally [17].

The virus lacks cross-reaction with antisera raised against many pre-pandemic H5 vaccine strains, but an influenza A(H5N8) virus, A/gyrfalcon/Washington/41088-6/2014, has been developed as a candidate vaccine virus for use in humans. It is available via the World Health Organization Global Influenza Surveillance and Response System (GISRS) for pilot lot vaccine production, clinical trials or other pandemic preparedness purposes [21]. The precise antigenic relationship between the newly circulating A(H5N8) viruses and A/gyrfalcon/Washington/41088-6/2014 remains to be firmly established.

A high degree of evolution among these viruses, particularly so within this clade, has been observed for A(H5N8) viruses [22]. More information is needed about the genetic composition of these currently circulating viruses to better understand their relationship to previously circulating viruses and evolutionary processes.

Event background information

During October and November 2016, Austria, Germany and Hungary reported detections of HPAI A(H5N8) in wild birds and poultry holdings, while Croatia, Denmark, the Netherlands, Poland and Switzerland reported detections in wild birds. The Netherlands also reported sick birds in an animal park (Figure 1).

Outside of Europe, India and Israel are currently also reporting outbreaks in birds while South Korea, Taiwan and the Russian Federation reported outbreaks earlier this year [2].

Up to 15 November 2016, eight outbreaks in poultry holdings have been reported from Austria, Germany and Hungary affecting nearly 100 000 birds of different species (ducks, turkeys, chicken, doves, and geese) [11]. Dead wild birds have been discovered around lakes across the affected countries with a high mortality in a moderately small group of water-associated wild bird species to date, but there is uncertainty on susceptibility, and carriage by other species is unknown at present.

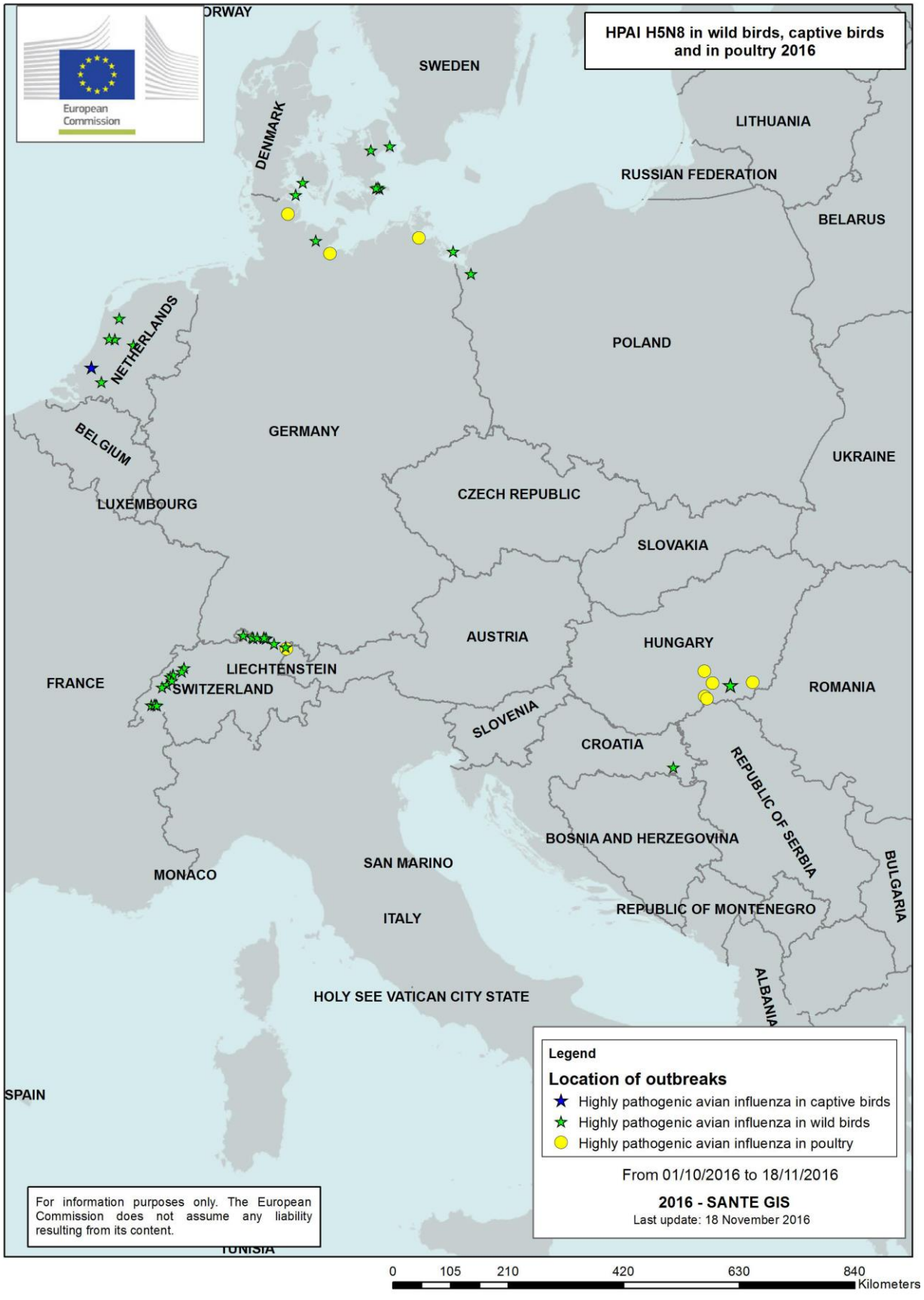
Culling of the affected poultry is ongoing or completed, and protection and surveillance zones have been established according to the EU-legislation Directive 2005/94/EC [23]. Infected dead wild birds are being destroyed.

Preliminary genetic analyses indicates that these viruses associated with the recent incursions are closely related to those that previously appeared in 2014/15 but form a distinct genetic cluster.

The European reference laboratory for avian influenza viruses has analysed the full genome sequences of several recent HPAI A(H5N8) viruses with the key focus on the first poultry outbreak in the EU (Turkeys in Hungary), and has assessed this virus as representative. The algorithm followed checks for specified mutations that have been associated with possible increased tropism/virulence for mammalian species including humans (listed via CDC Atlanta website).

According to the analysis of the EU reference laboratory, these viruses to date are still essentially bird viruses without any specific increased affinity for humans.

Figure 1. Regions in Europe with confirmed detections of highly pathogenic avian influenza virus A(H5N8) in wild birds, captive birds or poultry, 2016 (until 18 November 2016)



Source: Directorate General for Health and Food Safety – European Commission

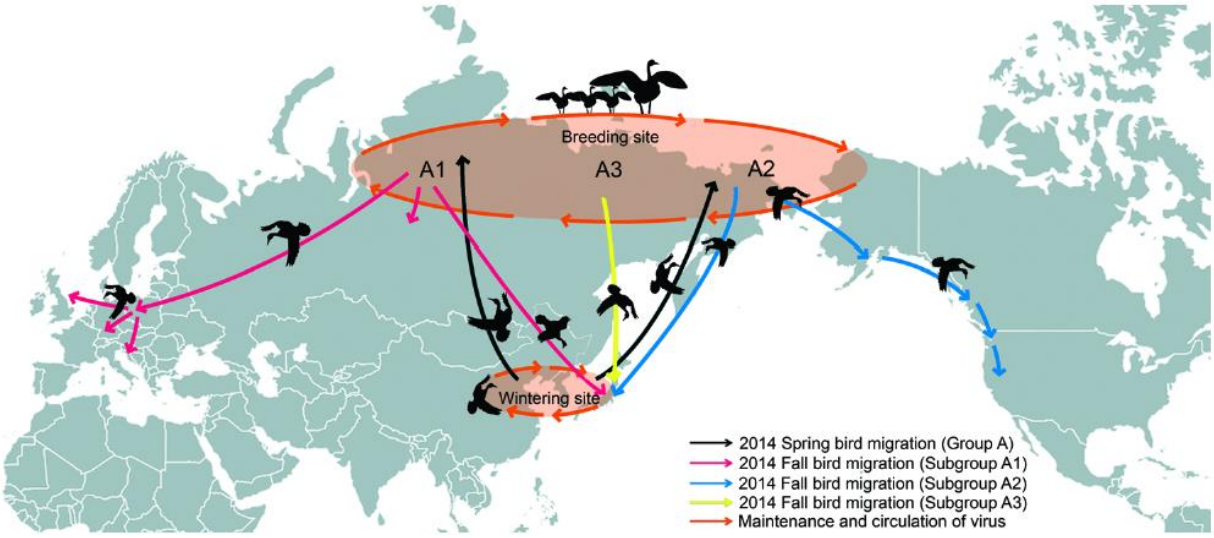
Introduction into Europe

Available information identifies wild migratory birds as a possible source of virus introduction due to infected wild birds returning from Russia and Asia during the autumn migration with routes going from northeast to southwest (Figure 2) [9,13,24]. HPAI A(H5N8) virus was detected in Russia in May 2016 in a wild swan on the migratory route between east Asia and Europe [25,26]. The Food and Agriculture Organization of the United Nations (FAO) suggests that wild birds may play a role in the long-distance spread of the virus from Asia to Europe [26].

Transmission of viruses between migratory birds and domestic poultry could occur through direct or indirect contact, as HPAI A(H5N8) is shed in the faeces of wild birds [8]. The affected poultry holdings in Europe are in close proximity to water habitat sites where dead infected wild birds have been discovered. The virus might have been introduced into farms via direct or indirect contact with wild birds or their droppings as well as through contaminated material brought into the facilities.

In the past, HPAI A(H5N8) has not been associated with high mortality in ducks. In 2016 however, a higher mortality in wild birds was observed. The virus is virulent for poultry as well as for several bird species. It is not known which wild birds might also carry the virus without showing any symptoms. Preventing contact of poultry with wild birds and increasing biosecurity are the most important preventive measures for the introduction into poultry holdings. Close observation of poultry for clinical signs or changes in productions data and fast reaction to virus detection in wild birds and poultry populations is important to avoid further virus spread and introduction into poultry farms. At this stage, further virus transmission to domestic poultry from wild migratory birds cannot be excluded. It is not known yet whether the virus has already spread to the local wild bird reservoir. The Commission has urged Member Sates' authorities to increase their awareness and preventive measures. Most wild birds usually migrate in the early autumn, but there are still significant migration movements of geese at this time of the year and of Whooper and Bewick's swans even later. Some movements at this season are influenced by cold weather. The regions currently affected by HPAI A(H5N8) were previously identified in a study of HPAI A(H5N1) spread in Europe to be areas at high risk for the spread of avian influenza viruses in wild bird populations [27]. It is important that bird watchers, hunters and others report mortalities in wild birds during outdoor activities.

Figure 2. Indicative transmission routes of HPAI A(H5N8) through birds migrating into Europe



Journal of Virology, 2015, Jun;89(12):6521-4, doi 10.1128/JVI.00728-15. Reproduced with permission from the American Society for Microbiology

Group A: *comprises Chinese, Russian, South Korean, Japanese, European and North American A(H5N8) 2.3.4.4 viruses representing intercontinental group A;* ***Subgroup A1:*** *composed of A(H5N8) viruses from Europe and Russia from late 2014 and three viruses detected in Japan in December 2014;* ***Subgroup A2:*** *composed of A(H5N8), as well as H5 clade 2.3.4.4 North American HPAIV reassortants (A(H5N2) and A(H5N1))detected in North America starting in late 2014 and a Japanese virus, A/crane/Kagoshima/KU1/2014(H5N8), detected in November 2014;* ***Subgroup A3:*** *composed of A(H5N8) viruses isolated in Japan in December 2014 and Korea in January 2015 [28].*

ECDC threat assessment for the EU

To date, no human infections with this virus have been reported and the risk of zoonotic transmission to the general public in EU/EEA countries is considered to be very low.

However, this second HPAI A(H5N8) introduction event is another indication of the widespread circulation and continuous re-assortment of avian influenza viruses, notably for H5 viruses in animal populations, which continues to pose a long-term risk of human influenza pandemics. The recent emergence of A(H5N6) viruses in China that have caused severe disease in humans highlights the possibility of transmission from birds to humans of reassorted viruses from clade 2.3.4.4 [21]. The full genome sequences of several recent HPAI A(H5N8) viruses showed that these viruses to date are still essentially bird viruses without any specific increased affinity for humans.

Strict food safety and veterinary measures are in place in the EU/EEA Member States to prevent meat or eggs from unhealthy animals entering the food chain. Even in the unlikely event of the virus being present in meat or eggs sold in the EU, thorough cooking destroys the virus, so well-cooked meat and eggs pose no risk. A(H5N8) viruses are reliably detectable using EU-recommended avian influenza laboratory methods (M 1.2 and H5), which are continuously reviewed by the Avian influenza EU Reference Laboratory as being fit for purpose to support outbreak and surveillance investigations. Any modifications to existing assays must be balanced against broad sensitivity of such assays for application in wider passive and active surveillance programmes where the virus subtype(s) is unknown. It is suggested that laboratory methods in human national influenza reference laboratories be evaluated for their suitability to detect A(H5N8) viruses.

As a precautionary principle and based on experience and the risk posed by A(H5N1) viruses, several countries in the EU apply preventative measures to lower the possible risk of human exposure and any subsequent infection due to exposure to avian influenza viruses.

In order to prevent spread of avian influenza viruses, Directive 2005/94/EC [23] requires that Member States have contingency plans detailing measures for the killing and safe disposal of infected poultry, feed and contaminated equipment as well as procedures and methods for cleaning and disinfection. Reinforcing biosecurity measures to prevent contact between domestic poultry and wild birds is expected to reduce the risk of infection if wild birds are identified as a source of infection.

The Directive also requires the development of contingency plans for the control of avian influenza in poultry in collaboration with public health and occupational health authorities to ensure that persons at risk are sufficiently protected from infection. Personal protective equipment, and in particular respiratory protection, should be considered. Persons at risk of exposure to the virus are mainly those in direct contact with or handling diseased birds and poultry, or their carcasses (e.g. farmers, hunters, veterinarians and labourers involved in the culling).

Protective measures have been recommended in accordance with national guidelines for HPAI, including personal protection equipment and oseltamivir prophylaxis for up to 10 days after the last contact [29]. Persons exposed to the virus are asked to report any symptoms to the municipal health service and in the event that they develop conjunctivitis or influenza-like-illness, sampling material will be obtained for diagnostic testing. These measures have also been recommended by the US Centers for Disease Control and Prevention (CDC) during HPAI A(H5N1), A(H5N2) and A(H5N8) outbreaks in the US in 2015 [30]. The FAO also raised awareness regarding HPAI A(H5N8) providing general recommendations as well as those pertaining to poultry producers, hunters and national authorities [31].

Routine vaccination with seasonal influenza vaccine is recommended in most countries for workers having contact with birds and poultry to minimise the possibility of co-infection with human and avian influenza viruses thereby reducing the risk of reassortment.

Persons in direct contact with infected poultry before or during culling and disposal, including poultry workers, should be monitored for 10 days, in order to identify possible related influenza-like symptoms, fever or conjunctivitis. Local health authorities may consider actively monitoring these groups. Administration of antiviral prophylaxis for exposed persons (as recommended for A(H5N1)) can be considered as a precautionary measure depending on the local risk assessment (i.e. intensity of exposure) and in the context of the start of seasonal influenza in the EU to minimise the likelihood of reassortment events [32]. Healthcare workers managing symptomatic exposed (or possible) cases should follow standard, contact and respiratory precautions, depending on the local risk assessment.

Conclusions

The risk of zoonotic transmission to the general public in EU/EEA countries is considered to be very low. Monitoring and testing of wild birds and domestic poultry in the EU plays an important role in the detection of further virus spread among birds and consequently reduce the possible risk for exposure of humans to infected birds.

It is important to remain vigilant, identify any possible early transmission events to humans and ensure active surveillance of exposed workers at the affected holdings for human health complaints, particularly during and after culling operations. Additionally, persons with direct exposure to wild birds should be monitored and as a minimum, exposed persons should be instructed to report health complaints (passive monitoring).

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