Situation overview: highly pathogenic avian influenza virus A of H5 type

4 December 2015

Main conclusions and options for response

- Highly pathogenic avian influenza (HPAI) of the subtypes A(H5N1) and A(H5N2) have been detected in birds in a backyard and in two poultry farms in the Dordogne region of France.
- The HPAI A(H5N1) virus detected in France is not related to the A(H5N1) viruses circulating in other parts of the world, but appears to have evolved from a low pathogenic avian influenza virus circulating in Europe.
- No human case has been reported related to the HPAI A(H5N1) virus detected in France.
- No human case has been reported related to any HPAI A(H5N2) virus worldwide.
- When avian influenza viruses circulate in poultry, sporadic infections or small clusters of human cases are possible in people exposed to infected poultry or contaminated environments, especially in households and at live bird markets in areas where the viruses are circulating. Sustained human-to-human transmission of influenza A(H5N1) virus and its highly pathogenic reassortants have never been observed.
- The risk of foodborne transmission, e.g. through the consumption of eggs or meat is considered extremely low.
- People having direct contact with diseased birds or poultry, or their carcasses (e.g. farmers, veterinarians and labourers involved in the culling and rendering) are at a potential risk of infection. Persons at risk of exposure should therefore wear personal protective equipment.
- People who have been exposed to the HPAI A(H5N1) or A(H5N2) virus should be monitored for at least 10 days.
- Animal and public health authorities should be prepared for a possible introduction of HPAI A(H5N1) or A(H5N2) virus into other European countries, although the risk is considered low.

Source and date of request

Request by the Directorate-General for Health and Food Safety – C3 Health Threats on 25 November 2015 to produce a rapid risk assessment on the current situation in relation to H5N1 human infection.
Public health issue

Highly pathogenic avian influenza (HPAI) of the subtype A(H5N1) and A(H5N2) have been detected in birds at a backyard farm in France.

Human cases due to A(H5N1) have been reported since 1997 [1]. An increasing number of outbreaks due to A(H5N1) in poultry have recently been observed in several Asian and African countries.

The risk to humans of developing the disease needs to be assessed in the light of the most recent advancements in the knowledge of the human infection.

Consulted experts

ECDC internal response team: Kaja Kaasik-Aaslav, Cornelia Adlhoch, Pasi Penttinen, Emmanuel Robesyn, Wim Van Bortel

External experts: Timm Harder, Friedrich-Loeffler-Institut, Germany; Isabelle Bonmarin, Institut de Veille Sanitaire, France; Frank Berthe and Frank Verdonck, European Food Safety Authority (EFSA).

ECDC acknowledges the valuable contributions of all experts. All experts have submitted declarations of interest. ECDC has reviewed these and finds that none of them present a conflict of interest with the comments and suggestions the experts have made. It should be noted that opinions expressed by individual experts do not necessarily represent the opinion of their institutions.

Disease background information

The highly pathogenic avian influenza (HPAI) A(H5N1) virus was first observed in China in 1996. It affected poultry initially in the Far East and later in Europe, the Middle East and Africa [2].

Highly pathogenic avian influenza virus A(H5N1) of Asian origin and all its highly pathogenic reassortants (e.g. H5N6, H5N8, and H5N2) are highly infectious for most bird species, including poultry. Unlike most other avian influenza viruses, some lineages of this virus type (H5N1, H5N6) are also pathogenic for humans. However, the viruses remain poorly adapted to humans:

- Transmission from birds to humans is infrequent.
- Only limited clusters of human cases have been reported since the first human epidemics of A(H5N1).
- No sustained human-to-human transmission has been observed.

Zoonotic transmission to humans from infected birds occurs either directly or through environmental contamination. Hence, almost all human infections have been related to close contact with infected or sick birds or their faecal products in domestic settings – for example at ‘wet markets’ in Asia.

During 2015, outbreaks caused by HPAI A(H5N1) and its descendants have been reported from an increasing number of countries in Asia, Africa and Europe. Since 2014, Asian-origin highly pathogenic A(H5N8) viruses and their reassortants (H5N1, H5N2) have also caused widespread infection in wild birds and poultry in North America, but no human cases have been reported so far.

Human and avian surveillance of A(H5N1) in Europe

All novel influenza strains and human infections with A(H5N1) are notifiable diseases under EU legislation and the International Health Regulations* (IHR), through, respectively, the Early Warning and Response System (EWRS) and IHR notification system [3, 4].

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1. ‘Avian influenza’ means an infection of poultry or other captive birds caused by any influenza A virus:
   a) of the subtypes H5 or H7; or
   b) with an intravenous pathogenicity index (IVPI) in six-week old chickens greater than 1.2.
2. ‘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
3. ‘Low pathogenic avian influenza (LPAI)’ means an infection of poultry or other captive birds caused by avian influenza viruses of subtypes H5 or H7 that do not come within the definition in paragraph 2.

**Human cases due to avian influenza A viruses of H5 type**

No human cases related to HPAI A(H5N1) have ever been reported from EU/EEA countries.

No cases related to A(H5N2) have been identified in humans.

Between 2003 and 26 November 2015, 844 laboratory-confirmed human cases of avian influenza A(H5N1) virus infection, including 449 deaths, were reported to WHO from 16 countries (Table 1, Figure 1). No human cases were reported in the EU. The number of human cases in the winter 2014/15 was the highest number of cases reported in any given year, and even more than 2007, when A(H5N1) was affecting nine different countries. Overall, the most affected countries are Egypt and Indonesia. In 2014 and 2015, Egypt reported most cases and has become the most affected country with the highest number of human cases (Table 1, Figure 1).

According to WHO, despite the recent increase in human cases, the demographic and epidemiological characteristics of the recently reported cases do not significantly differ from previous periods. However, WHO concedes that there is a need for increased vigilance in the animal and public health sectors [7].

ECDC has published rapid risk assessments on 23 December 2014 and 13 March 2015, followed by an epidemiological update summarising the situation of A(H5N1) in Egypt on 10 April 2015.

The only human infections caused by influenza A(H5) viruses have been influenza A(H5N1) viruses and three human infections with influenza A(H5N6) virus detected in China [5, 6]. No human cases caused by the remaining A(H5) viruses have been reported, although they might have the potential to also cause disease in humans.

The last human case due to A(H5N1) was reported from Egypt in July 2015 (Figure 2).

**Figure 1. Cumulative number of confirmed human cases of avian influenza A(H5N1) reported to WHO, 2003–2015, as of 13 November 2015**

![Cumulative number of confirmed human cases of avian influenza A(H5N1) reported to WHO, 2003–2015, as of 13 November 2015](image)

*Source: WHO/GIP [7]*

* Case definitions for the four diseases requiring notification in all circumstances under the International Health Regulations (2005) are available at [http://www.who.int/ihr/Case_Definitions.pdf](http://www.who.int/ihr/Case_Definitions.pdf) [17]
Avian influenza in birds

Avian influenza viruses can cause infection in birds and humans. ‘Highly pathogenic’ avian influenza viruses cause high mortality in poultry, while ‘low pathogenic’ viruses result in mild disease. The classification of avian influenza viruses as ‘low pathogenic’ or ‘highly 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 in accordance with the criteria listed in Council Directive 2005/94/EC and the OIE International Health Standards [21].

Avian influenza viruses have the ability to evolve from low pathogenic precursors into highly pathogenic forms in the absence of reassortment, acquiring mutations responsible for highly pathogenicity [9].

Virus characteristics of highly pathogenic avian influenza A viruses of the H5 type

Since their first detection, HPAI A(H5) viruses have evolved, resulting in multiple genetic lineages (‘clades’) across the world, based on the H5 HA gene [10] (see Map 1).

HPAI A(H5N1) strains found in Asia are different from strains currently circulating in Egypt, the United States and Canada, as well as from the strain identified in France. A summary of the viruses circulating worldwide by H5 HA clades, providing information on their distribution and endemicity, is shown below (Map 1).

The HPAI A(H5N1) viruses detected recently in Israel and Palestine* belong to the same clade as those which are endemic in Egypt, namely clade 2.2.1.2.

In Asia, viruses from different clades are currently circulating among wild birds and sporadically causing outbreaks in poultry. In 2015, Asian clade 2.3.2.1a was detected in birds in Bangladesh, Bhutan and Indonesia, while clade 2.3.2.1c affected birds and poultry in Cambodia, China, India, Indonesia, and Vietnam; clade 2.3.4.2 was detected in Myanmar/Burma.

* This designation shall not be construed as recognition of a State of Palestine and is without prejudice to the individual positions of the Member States on this issue.
Viruses of clade 2.3.2.1c were also imported to Africa, causing large outbreaks in poultry in Burkina Faso, Côte d’Ivoire, Ghana, Niger, and Nigeria. These viruses were also detected in early 2015 in pelicans, a dove and a backyard poultry flock in Bulgaria and Romania, as well as in wild birds in Iran, Kazakhstan, Russia, and Turkey on the westward flyway between Asia and Europe.

In 2015, viruses with the H5 HA gene from clade 2.3.4.4 [A(H5N1), A(H5N2), AH5N3), A(H5N8)] were circulating in China, South Korea and Vietnam, the United States and parts of Europe. The HPAI A(H5N1) virus reported in the United States is a reassortant virus of avian influenza viruses circulating in birds in Asia (HA) and northern America (NA) and is genetically different from the other A(H5N1) viruses.

Further information on characteristics is available in the WHO summary of the antigenic and genetic characteristics of zoonotic influenza viruses from September 2015 [22].

**Map 1.** Distribution of H5 clades, 2014–2015, as of 26 November 2015

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**Detection of highly pathogenic avian influenza A viruses of H5 type**

According to reports received by OIE, various influenza A(H5) subtypes, such as influenza A(H5N1), A(H5N2), A(H5N3), A(H5N6) and A(H5N8) have been detected since January 2015 in birds in Europe, North America, Asia and Africa.

The viruses HPAI A(H5N2), A(H5N8) and A(H5N1) of clade 2.3.4.4 have been reported from Canada and the United States in 2014 and 2015, in wild birds as well as large outbreaks in poultry farms.,

In 2015, outbreaks or detections of highly pathogenic avian influenza virus A(H5N1) in birds were reported from countries and regions in different parts of the world, e.g. Northern America, Europe, Africa and Asia (Tables 1 and 2, Map 2) [5].
Map 2. Countries reporting highly pathogenic avian influenza A(H5N1) in poultry or wild birds, 2014–2015, as of 26 November 2015

Table 1. Countries reporting avian influenza A viruses of H5 type in wild birds in 2015, as of 26 November 2015

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Table 2. Countries reporting avian influenza A of H5 type in domestic birds in 2015, as of 26 November 2015

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### Region and Country Summary

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Source: EMPRES-i; available from: [http://empres-i.fao.org/eipws3g](http://empres-i.fao.org/eipws3g); accessed 26 November 2015 [8]

### Low pathogenic avian influenza A(H5N1) and A(H5N2) detections

According to the European reference laboratory annual report on surveillance for avian influenza viruses (EURL) in the EU, low pathogenic avian influenza (LPAI) viruses of A(H5N1) were detected in 2009 in the Calvados département, northern France on decoy ducks used by hunters [23]. In 2014, LPAI was detected in chickens in Germany and the Netherlands as well as in ducks in Italy. LPAI A(H5N1) viruses of the ‘classic’ European lineage have been sporadically isolated from both poultry and wild birds in Europe, but mutation of these strains to high pathogenicity is a rare event. The last known occurrence of such an event was in 1991 in the United Kingdom when mutation occurred in a single commercial flock, according to a recent report from the UK Animal & Plant Health Agency [24].

In January 2015, low pathogenic A(H5N2) virus was detected in a hobby duck holding in Arezzo, Italy and in April the Netherlands reported A(H5N2) in a bird holding in Noord-Brabant.

On 11 November and 1 December 2015, Italy reported to the European Commission the detection of low pathogenic avian influenza A(H5N2) virus in one farm with ducks and another with turkeys in the Region of Emilia-Romagna, respectively.

According to the UN Food and Agriculture Organization (FAO), detections of low pathogenic A(H5N2) viruses have been reported from Taiwan, South Africa, Belize and Mexico during 2015.

### Event background information

On 25 November 2015, the French authorities notified the EU of an outbreak of highly pathogenic avian influenza, subtype H5N1, in a backyard holding in the Dordogne département. Following abnormal mortality in the holding, the virus presence was confirmed on 24 November 2015 by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES). ANSES confirmed the presence of highly pathogenic avian influenza strain of the H5N1 subtype. On 30 November 2015 and 1 December, the French authorities reported that two poultry farms in the Dordogne region were also affected by A(H5) viruses, an HPAI A(H5) with pending N typing results in a commercial duck farm and an HPAI A(H5N2) in a goose farm [25].

* This designation shall not be construed as recognition of a State of Palestine and is without prejudice to the individual positions of the Member States on this issue.
Phylogenetic analysis of the H5 and N1 partial sequences showed that they are not directly related to sequences belonging to the HPAI H5N1 viruses of the A/goose/Guandong/1/96 lineage (‘Asian origin’). The virus sequences for H5 are directly linked to the low pathogenic avian influenza strains of H5 subtype circulating in Europe and that are available in databases. Equally, the sequences for N1 are directly related to those circulating in Europe. Virus cultivation is ongoing, which will allow a more complete characterisation. The local authorities assume that this highly pathogenic virus mutated from a low pathogenic virus that has previously been detected in Europe. Earlier, France had reported LPAI A(H5N1) infections in duck-fattening facilities in western France. LPAI A(H5N1) viruses have also been sporadically detected in wild birds in Europe over the last ten years.

The national crisis plan was immediately activated, in accordance with EU legislation and international requirements. A protection zone with a 3 km radius (and a surveillance zone with a 10 km radius) was established around the affected backyard holdings. Enhanced active surveillance is being carried out in other poultry holdings and the surrounding wild fauna.

The French authorities are actively following up the event. People exposed to infected birds are being monitored to immediately identify persons who develop influenza-like illness (ILI) or conjunctivitis, so that they can undergo further tests.

**Threat assessment for the EU**

**Assessment of the European situation**

The outbreak of HPAI A(H5N1) and A(H5N2) in France is restricted to one region so far. Measures to control the outbreak (culling and establishment of control and surveillance zones) have been implemented to avoid the spread of the virus to other holdings. When successfully implemented, these measures will also limit the likely exposure of humans to infected poultry.

The virus identified in the French backyard farm does not appear to be related to any of the highly pathogenic viruses currently circulating in Asia, but rather appears to have evolved from previously circulating low pathogenic A(H5N1) viruses in Europe. No avian-to-human transmission has yet been described from low pathogenic A(H5N1) viruses, and human exposure to low pathogenic A(H5N1) viruses during outbreaks in Europe has not resulted in any transmission from birds to humans. Furthermore, no human cases due to HPAI A(H5N1) have ever been reported in Europe.

The phylogenetic analysis for the HPAI A(H5N2) is pending to assess if this virus is related to the viruses circulating worldwide. No human cases related to this HPAI A(H5N2) have been observed worldwide.

The peak autumn bird migration has passed for this year. EU legislation includes provisions to prevent the introduction into other EU Member States through contaminated goods. As such, the risk of this virus spreading to countries outside France is considered to be low.

**Assessment of the global situation**

The global increase of human cases in 2014, and particularly in 2015, was mainly driven by cases in Egypt. The reintroduction of HPAI A(H5N1) in many African and Asian countries with low biosafety and biosecurity standards increased the circulation among poultry. This led to a higher risk of human exposure, especially in backyard facilities or small industrial holdings.

Small clusters of human cases were identified but all cases had been exposed to birds prior to disease onset. No sustained human-to-human transmission has been documented so far. Almost all human cases reported direct exposure to live or sick poultry – mostly backyard poultry – before onset of disease.

A correlation has been shown between the disposal of dead poultry or poultry faeces in garbage piles outside and A(H5N1) detection in backyard flocks [11]. Outdoor disposal also increased the risk of A(H5N1) spreading among households within a village. The role of domestic geese and ducks as likely asymptomatic sources of infection, particularly for free-ranging backyard poultry, is not fully understood. In addition, silent virus spread by vaccinated but infected gallinaceous poultry must be considered as a factor of spread and exposure.

Since July 2015 no human cases have been reported, although HPAI viruses are still circulating in wild bird populations, causing outbreaks in poultry holdings in Asia and Africa.

**General considerations**

Increase in reported outbreaks in domestic poultry and wild bird populations, and changes in the distribution of the outbreaks require careful monitoring. An [FAO publication](#) covers issues relating to A(H5N1) viruses including disease sampling procedures [26].
The most commonly identified risk factors associated with A(H5N1) virus infection include direct contact with infected blood or bodily fluids of infected poultry via food preparation practices; touching and caring for infected poultry [12]. Exposure to avian influenza at live bird markets also represents a risk factor for transmission to humans [13].

However, from a human health perspective, there are currently no indications of a significant change in the human epidemiology associated with clades or strains of A(H5N1). This is based on the absence of human-to-human transmission and the observation that there are no apparent changes in the size of clusters, nor are there reports of chains of infection. In addition, the newly emerged viruses of A(H5N2) and A(H5N8) clade 2.3.4.4. have been shown to lack the ability to transmit between ferrets, to exhibit low to moderate virulence in mammals and not to be transmissible via airborne infection [14, 15].

The current public health event in France does not change this view, and no humans have ever been infected with the A(H5N2) or an A(H5N1) strain circulating in Europe as low pathogenic virus. For this reason, the conclusions from previous risk assessments published by ECDC remain valid.

The main points are:

- Transmissibility of A(H5N1) ‘European type’ and A(H5N2) viruses to humans is still considered very low, requiring high infectious doses or some other – as yet unknown – factors.
- There is no evidence that these viruses have been transmitted to humans.
- The direct risk to the health of the European population from A(H5N1) ‘European type’ or A(H5N2) is extremely low.
- Persons at increased risk are mainly those who are in contact with diseased birds or poultry or their carcasses (e.g. farmers, veterinarians and labourers involved in the culling and rendering of poultry).

In EU Member States, surveillance for highly pathogenic avian influenza viruses in poultry and wild birds is strong and is carried out on a continuous basis. ECDC is closely monitoring the situation, both in the EU and worldwide, and will regularly reassess the risk that viruses of H5-type pose to humans.

Further information on preparedness and response plans and experience of dealing with HPAIV outbreaks, based on a recent workshop report, can be obtained from ECDC on request.

**Conclusions and options for response**

To date, no human infections with highly pathogenic or related low pathogenic viruses of the H5 type have ever been reported in the EU. The risk of zoonotic transmission to the general public in the EU/EEA countries is considered to be extremely low.

The risk of a foodborne transmission (e.g. eggs and meat) is considered extremely low according to EFSA.

Occupationally and otherwise exposed persons should be identified and monitored for development of influenza-like symptoms. Persons at risk are mainly those in direct contact/handling diseased birds or poultry, or their carcasses (e.g. farmers, veterinarians and labourers involved in the culling and rendering).

Workers should wear personal protective equipment (face mask, goggles/face shield/protective glasses, gloves and gown/overall) and avoid unprotected direct contact with sick or dead birds, carcasses, faeces as well as potentially contaminated environments (see ECDC guidelines and tool kit). A tutorial on the safe use of personal protective equipment that could be used to train persons directly exposed to infected poultry has previously been published by ECDC*

For further information, FAO guidance is available for consultation on the sampling of infected birds and the protection of workers [27]. Poultry workers exposed at the affected holding should be monitored for minimum of ten days in order to document possible related symptoms, including ILI with fever and cough or conjunctivitis. Local health authorities may consider actively monitoring these groups and offering them vaccination against seasonal influenza, if they are not already vaccinated. Antiviral prophylaxis, as recommended for persons exposed to avian influenza viruses, could also be considered depending on the local risk assessment (i.e. intensity of exposure).

National and regional contingency plans for the control of avian influenza in poultry and birds should be reviewed or further developed in collaboration with public health authorities.

Information about viral sequences and phylogenetic relationships will provide more details needed for risk assessment. The tool developed by EFSA as part of the FluRisk project might help to assess the risk for transmission of such viruses [16].

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**Useful links**


Link to ECDC peer reviewed surveillance articles if available: [http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20996](http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20996)

ECDC Technical Report - ECDC Guidelines: minimise the risk of humans acquiring highly pathogenic avian influenza from exposure to infected birds or animals. 21 December 2005


ECDC Tutorial on the safe use of personal protective equipment


**Rapid Risk Assessments on avian influenza**

**Avian Influenza A viruses China Feb 2014**


**H5N1 Egypt Dec 2014**


**H5N1 Egypt March 2015**


**H5N8 20 Nov 2014**


**H5N8 13 Nov 2014**

References


