

Zoonotic risks of mammal infections with Avian Influenza A(H5N1) virus

Introduction

Europe is currently hit by the worst epidemic of highly pathogenic avian influenza virus (HPAIV) in birds ever recorded. HPAIV became widely dispersed in wildlife with substantial losses in the wild bird population as well as regular spill over to commercially kept poultry.

There are growing numbers of reports of infections with the currently circulating clade 2.3.4.4b A(H5) virus in mammals, most of them due to predation on infected birds or close contacts with them. Fortunately, to date there have been no clinical human case in the EU and only a limited number of human cases worldwide, mainly in people occupationally exposed with infected poultry. However, infection of mammals gives the opportunity to the virus to acquire mutations that enhance efficient infection, replication, and spread in mammals.

Epidemiological situation of HPAI infection in mammals

Since the beginning of the pandemic of HPAIV in wild birds, individuals from several mammal species have been found positive for HPAIV in Europe (see <https://www.woah.org/en/disease/avian-influenza/#ui-id-2> and <https://www.efsa.europa.eu/en/efsajournal/pub/8191>). Most cases appeared in wildlife species such as red fox, Eurasian otter, lynx, Mustelidae, dolphin and seal, while fewer events were observed in domestic species such as ferret, cat, American mink and dog.

While most of the reports of HPAI A(H5N1) virus in mammals consist of single or at most a few animals, there were two confirmed mass mortality events of wild mammals associated with HPAIV A(H5N1) virus detections in 2022 (USA) and 2023 (Peru) and possible mammal-to-mammal transmission. Both mass mortality events concerned sea mammals (seals and sea lions) living in close contact with infected birds.

In October 2022, an outbreak of HPAI A(H5N1) in intensively farmed minks occurred in northwest Spain. A single mink farm hosting more than 50,000 minks was involved. More recently (since mid-July 2023), an outbreak caused by HPAI A(H5N1) is ongoing among farmed fur animals in Finland. Infections in foxes, American minks and raccoon dogs have been confirmed on 24 farms (dd. 21/08/23). The identified viruses belong to clade 2.3.4.4b, which is responsible for the ongoing epidemic in birds in Europe.

Genetic analysis suggests introductions from wild birds scavenging for food in farm areas. Although not scientifically proven, investigations point to direct transmission between animals. Genetic mutations which are indicative for adaptation to mammals have been found. While no human infections have been detected, control measures are being implemented to limit spread and human exposure.

In June 2023 Poland has detected numerous cases of HPAI infection in cats. A report from the Polish authorities indicated that 30 domestic cats and one caracal (dd. 21/08/23) with clinical signs and mortality were found to be infected with Influenza A(H5N1) virus. As these cases have appeared throughout many different regions of Poland, in cats with or without outdoor access, and as no further

transmission events to cats living in proximity of the infected ones have been reported, one single origin can be suspected. Cat viral sequences were highly similar, again suggesting a potential common infection source. Investigations are currently underway by Polish authorities to understand the outbreak, determine the links between cases and identify routes of exposure. Initial reports suggest that direct transmission from infected wild birds may not be the primary source. HPAI H5N1 virus was detected in one raw poultry meat sample used as feed. Further analyses are currently carried out to clarify the role of the feed. No human infections have been detected.

Also in Belgium a few cases of avian influenza infections in mammals have been found, namely in wild foxes, wild European polecats and domestic ferrets. In all cases, this was probably due to close contact with large amounts of virus, either by eating infected bird carcasses (foxes and polecats) or following intense contact with infected hobby poultry (ferrets). Detailed figures about the avian influenza cases in Belgium can be found on the following website: <https://www.sciensano.be/en/health-topics/avian-influenza/numbers>. In Belgium, and by extension in Europe, no human infections have been detected.

Risk assessment for mammals

HPAIV continue to spread and diversify globally. Viruses currently circulating in bird populations in Europe are avian-adapted viruses, i.e. they bind to avian-like receptors, transmit and replicate best in bird species. The closer and more frequent the contacts are between two susceptible species, the more likely the transmission between those species will effectively occur. This occurrence, named spill-over infection, can be facilitated by the rapid genetic evolution of influenza viruses providing the virus with increased binding properties to receptors of the non-specific host (i.e. to which the virus is less adapted). Despite the occurrence of mutations associated with increased replication in mammalian hosts, the viruses analysed retain preferential binding to avian receptors. Spill-over infections are not that common. However, the probability of this occurrence is higher at present due to the intense circulation of avian influenza viruses in wild birds and poultry farms worldwide.

It is known that felids, mustelids and Phocids are particularly susceptible to HPAI infection with most cases suspected to be the result of predation on infected carcasses of infected wild birds.

Voor **bepaalde risicoprofielen**, zoals vatbare soorten katachtigen, marterachtigen en zeehonden en dieren die een verhoogde kans hebben op nauw contact met geïnfecteerde (dode) vogels, zoals vossen en andere roofdieren, kan het risico als **laag tot matig** worden beoordeeld.

Risk for humans

Avian influenza transmission from animals to humans remains a rare event. Despite the high number of exposure events due to the large outbreaks in poultry and wild birds since 2020, no symptomatic human infection due to avian influenza A(H5Nx) has been reported in EU countries. Only sporadic human infections have been reported globally over the last few years (<https://www.ecdc.europa.eu/en/infectious-disease-topics/z-disease-list/avian-influenza/threats-and-outbreaks/situation-ah5#:~:text=Despite%20the%20high%20number%20of,reported%20from%20EU/EEA%20countries>).

For a risk assessment regarding the risks for public health, one can consult the following websites:

- ECDC (<https://www.ecdc.europa.eu/en/news-events/efsa-ecdc-eurl-ongoing-avian-influenza-outbreaks-birds-low-risk-public>)
- RAG (Belgian Risk Assessment Group: <https://www.sciensano.be/nl/projecten/coordinatie-van-de-risk-assessment-group>)

Recommendations

- Felines, martens and other mustelids, seals and other Phocids and canines (e.g. foxes), having a higher risk profile (i.e. contact with possibly infected birds) and displaying respiratory and/or neurological symptoms should be tested for a possible influenza infection. For other mammals, (avian) influenza virus infections should be included in the differential diagnosis.
- Raw meat (especially raw poultry meat in this specific case) should be avoided as feed, as it can be contaminated by HPAIV and several other pathogens. However thoroughly cooked meat remains safe. A communication campaign to inform pet owners about these risks should be set up. An example of such communication campaign can be found here: <https://www.favv-afscab.be/consumenten/dagelijksleven/bewaring/huisdierenrauwvoedsel/> (NL) <https://www.favv-afscab.be/consommateurs/viepratique/conservation/animauxcompagniealimentscrus/> (FR)
- People who come in contact with (potentially) infected animals (wild animals as well as domesticated animals) should take protective measures to reduce the risk of zoonotic transmission (from animal to human). More information regarding the risks of infection of other species with HPAIV and recommended protective measures can be found in the following document of the RAG-V-EZ: https://www.favv-afscab.be/professionnels/productionanimale/ragvez/documents/Zoonotic-risk-of-avian-influenza_V10.pdf
- Increasing awareness:
 - o Communication to wildlife rescue centres, wildlife taxi services, bird ringers and hunters regarding the biosecurity measures for manipulation/transport/housing/care of wild birds and mammals, regarding the risks of influenza infections and regarding the possibility/importance for monitoring of influenza when flu/cold symptoms occur.
 - o Communication to physicians and veterinarians regarding the risks of influenza infections and the possibility/importance for monitoring of influenza should be performed on a regular basis.
- Monitoring of avian influenza viruses in birds and mammals, including sharing of sequence data, is crucial for updated risk assessment and implementation of measures at the animal-human interface.

These recommendations will need to be reassessed and eventually adapted in function of the evolution of the epidemiological situation in Belgium.