

# Enhanced surveillance of severe avian influenza virus infections in hospital settings in the EU/EEA

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## Summary

Avian influenza virus outbreaks are continuing during the summer months, causing mass mortality in sea-breeding bird colonies, including gulls. A larger exposure of human population to sick or dead birds and mammals is expected to occur.

Transmission to humans cannot be excluded when avian influenza is circulating in wild birds and mammals and people are directly exposed without wearing protective equipment. During the summer months, infections with seasonal influenza viruses are considered to be very limited, and only a few patients with severe disease caused by the seasonal influenza virus are expected to be admitted to hospitals.

To identify sporadic severe human infections with avian influenza virus in hospital settings, the following approach is proposed:

- People admitted to hospitals with respiratory symptoms should be asked about exposure to birds (wild birds or poultry) or other wild animals (dead or alive) in the two weeks before admission.
- Consider testing for influenza virus hospitalised patients with unexplained viral encephalitis/meningoencephalitis lacking the aetiological agent diagnosis.
- All influenza A-positive samples from hospitalised patients should be subtyped for seasonal influenza viruses A(H1)pdm09 and A(H3).
- Samples positive for influenza type A virus but negative for A(H1)pdm09 or A(H3) should be immediately sent to national influenza reference laboratories for further analysis and H5 testing.

## Scope of this document

This document describes how to strengthen surveillance in hospital settings for the identification of severely affected patients infected with avian influenza virus in the EU/EEA. This document aims to complement the guidance on testing and detection of zoonotic influenza virus infections in humans in the EU/EEA, and occupational safety and health measures for those exposed at work [1].

## Target audience

This document is intended for public health authorities in the EU/EEA who deal with surveillance of respiratory viruses, for clinical societies giving guidance for testing of patients with respiratory symptoms particularly in hospital settings and for clinicians to raise awareness for possible human cases due to avian influenza in hospital settings.

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## Background

Avian influenza has caused large outbreaks in wild birds and poultry over the last three years in Europe, and 2.3.4.4b is the currently circulating A(H5N1) clade. Despite exposure to infected sick and dead birds, no human infections have been identified in the EU/EEA to date. The detections of H5 viral particle in two Spanish workers involved in culling activities during an outbreak of avian influenza at a poultry farm are considered contaminations and not true productive infections [2].

To support public health investigations related to avian influenza outbreaks, a document on testing and detection of zoonotic influenza virus infections in humans in the EU/EEA, and occupational safety and health measures for those exposed at work was published in 2022 [1].

Nevertheless, avian influenza virus outbreaks continue in EU/EEA countries, with some epidemiological changes observed recently that could contribute to a wider exposure of the general population to infected sick and dead wild birds (and mammalian species), particularly gull species that are living and breeding closer to urban areas and are affected by avian influenza outbreaks causing high mortality events.

ECDC suggests that people exposed to avian influenza virus are identified rapidly, particularly those occupationally exposed, e.g. in culling activities. Those people should be monitored (through active or passive surveillance) for 10–14 days since their last exposure to identify the occurrence of symptoms and initiate testing as soon as possible.

In addition to at-risk groups more likely to be exposed occupationally or recreationally described in the document [1], other people might have direct unprotected contact and be exposed to avian influenza viruses, e.g. when mortality events in wild birds such as gulls occur. Monitoring of these events is extremely challenging, if not unfeasible, for health authorities.

In such situations, sporadic transmission to humans could occur and people could become infected with avian influenza virus.

Avian influenza circulation and detection in wild birds with spill-over to carnivore wild mammal populations, as well as outbreaks in poultry farms, show different epidemiological characteristics during summer and winter months depending on the migratory bird season, e.g. movement and residence in summer breeding sites or migration and overwintering during colder winter months.

The spread of avian influenza viruses, causing high bird mortality, is expected to continue during the summer months, for example through mass mortality in sea-breeding bird colonies and more exposure in the general population to sick or dead wild birds as well as mammals.

## Strengthened hospital surveillance for severe human avian influenza virus infections

During the COVID-19 pandemic, ECDC published jointly with WHO operational considerations for respiratory virus surveillance in Europe that describe how to strengthen and design surveillance systems for respiratory viruses to fulfil different surveillance objectives [3].

Particularly, sentinel surveillance systems in primary and secondary care are considered important for the monitoring of respiratory viruses in the EU/EEA, but these systems are not designed and powered to early identify a newly emerging virus such as avian influenza in the general population and to implement control measures.

Based on limited evidence from the EU/EEA and globally for avian influenza viruses of clade 2.3.4.4b that are currently circulating, the symptoms of avian influenza virus infections in humans can range from asymptomatic infection to severe disease course. People with avian influenza virus infection can show symptoms of the upper and lower respiratory tract infection, but also atypical non-respiratory symptoms, such as neurological symptoms. In more severe cases, a rapid progression to severe pneumonia, sepsis with shock, acute respiratory distress syndrome, or encephalitis with fatal outcome have been reported.

According to the WHO guidelines for the clinical management of severe illness from influenza virus infections [4] and the ECDC expert opinion on neuraminidase inhibitors for prevention and treatment of influenza [5], clinical specimens for testing should be collected as quickly as possible and antiviral treatment could even start before clinical diagnosis and influenza confirmation.

To identify severe sporadic human infections with avian influenza virus, we propose the following measures for consideration:

Assumptions:

- Human infection with avian influenza virus following unprotected direct contact with infected birds, mammals, or contaminated environment, cannot be excluded.
- Data from human cases with avian influenza virus infection show that those identified with true productive infection mostly develop severe disease progression requiring hospital admission and care.
- Seasonal influenza viruses of subtypes A(H1N1)pdm09 and A(H3N2) are circulating on a very low level outside the influenza season (weeks 21–39) during the summer months (see also [www.flunewseurope.org](http://www.flunewseurope.org)) and very few severe human infections with seasonal influenza viruses are expected to be admitted to hospitals.
- Most commercial test systems used in hospital settings to test patients with respiratory symptoms only detect and separate influenza type A and B viruses but do not identify the subtype, e.g. A(H1N1)pdm09 or A(H3N2). Additional haemagglutinin specific RT-PCR assay is needed to determine the subtype.
- Any A(H5N1) or another avian influenza virus infection would likely be detected as influenza type A positive<sup>1</sup> and be missed if no subtyping, or specific testing requested based on suspicion of the treating clinician, is performed.
- Avian influenza A(H5N1) caused encephalitis and meningoencephalitis in a wide number of different infected mammalian species. Patients with viral infection of the brain with unknown aetiology would most likely not be considered for influenza virus testing.

To identify sporadic severe human infections with avian influenza virus in hospital settings, we propose the following approach:

- People admitted to hospitals with severe respiratory symptoms should be asked about history of exposure to birds (e.g. wild birds or poultry) or other wild animals (dead or alive) in the two weeks before admission.
- Consider testing for influenza virus hospitalised patients with unexplained viral encephalitis/ meningoencephalitis lacking the aetiological agent diagnosis.
- All influenza A-positive samples from hospitalised patients should be subtyped for seasonal influenza viruses A(H1pdm09) and A(H3). In case hospital laboratories do not have the assays in place to subtype influenza A viruses, specimens could also be shared with the national reference laboratories, national influenza centres, or other designated laboratories that can perform subtyping of influenza A viruses, after consulting with them.
- Samples positive for influenza type A virus but negative for A(H1)pdm09 or A(H3) should immediately be sent to the national influenza reference laboratories for further analysis and H5 testing.

A validation of existing assays (at least in silico checking the primers/probes) might be good to perform if validated commercial assays are not already in use.

## Proposed time frame

The time frame to have extended subtyping for hospitalised patients with influenza A virus infection in place is proposed from June to early October (i.e. influenza interseason period, weeks 21–39), when a small number of human patients with influenza virus infection are expected to be hospitalised and exposure to infected sick and dead wild birds might be more likely than in winter months when birds migrate to their overwintering sites.

## Infection prevention and control measures and communication

Implementation of early infection control precautions, proper education/training of healthcare staff, risk communication, and follow-up measures, which are outlined in the publications listed below, are paramount when an avian influenza virus infection in a person is identified.

## Reporting

Requirements for immediate reporting to national and international public health authorities (via the Early Warning and Response System and International Health Regulations) are outlined elsewhere [1].

Laboratory confirmed human infections with avian influenza and other novel influenza strains are notifiable under the International Health Regulations and through the Early Warning and Response System, in line with EU Decision 2022/2371 on serious cross-border threats to health and repealing Decision 1082/2013/EU [6]. This includes any relevant information that may be useful for coordinating a response, such as the type and origin of the agent, date, and place of incident or outbreak and the detection and confirmation methods. Reporting should occur within 24 hours from the laboratory diagnosis. The European Surveillance Portal for Infectious Diseases (EpiPulse) operated by

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<sup>1</sup> Some M or NS gene-based generic influenza type A/B protocols might miss H5 and give a false negative result.

ECDC should be used for the epidemiological monitoring and assessment of human infections with avian influenza, and for sharing epidemiological situation updates with EWRS. The European Surveillance System (TESSy) should additionally be used for the longer-term monitoring.

## Link to additional resources

Latest situation update of the avian influenza situation in the EU/EEA: [Avian influenza overview: Latest situation update of the avian influenza situation in the EU/EEA \(europa.eu\)](#)

Annual Epidemiological Reports: [Annual Epidemiological Reports on avian influenza \(europa.eu\)](#)

ECDC webpages: [Avian influenza \(europa.eu\)](#)

[Operational considerations for respiratory virus surveillance in Europe](#)

[Infection prevention and control and preparedness for COVID-19 in healthcare settings](#)

Editorial on avian influenza in Eurosurveillance – May 2023: [Avian influenza, new aspects of an old threat](#)

ECDC contact tracing: <https://www.ecdc.europa.eu/en/covid-19-contact-tracing-public-health-management>

ECDC toolkit: <https://www.ecdc.europa.eu/en/avian-influenza-humans/preparedness/toolkit-investigation-cases>

WHO Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases: <https://apps.who.int/iris/handle/10665/275657>

WHO Protocol for the investigation of acute respiratory illness outbreaks of unknown etiology: <https://www.afro.who.int/publications/protocol-investigation-acute-respiratory-illness-outbreaks-unknown-etiology>

WHO guidelines for investigation of human cases of avian influenza A(H5N1): <https://apps.who.int/iris/handle/10665/69416>

CDC Investigate an Outbreak: <https://www.cdc.gov/urdo/outbreak.html>

EpiPulse: [EpiPulse - the European surveillance portal for infectious diseases \(europa.eu\)](#)

TESSy: [The European Surveillance System](#)

## Acknowledgements

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