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# **Accelerated Subtyping of Influenza A in Hospitalized Patients**

# **Summary**

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory to clinicians and laboratories due to sporadic human infections with avian influenza A(H5N1) viruses amid high levels of seasonal influenza activity. CDC is recommending a shortened timeline for subtyping all influenza A specimens among hospitalized patients and increasing efforts at clinical laboratories to identify non-seasonal influenza. Clinicians and laboratorians are reminded to test for influenza in patients with suspected influenza and, going forward, to now expedite the subtyping of influenza A-positive specimens from hospitalized patients, particularly those in an intensive care unit (ICU). This approach can help prevent delays in identifying human infections with avian influenza A(H5N1) viruses, supporting optimal patient care and timely infection control and case investigation.

# **Background**

A panzootic of highly pathogenic avian influenza A(H5N1) viruses is currently affecting wild birds. In the United States, there have been outbreaks with these viruses among poultry and dairy cows, as well as infections among other animals. Since 2022, 67 total human cases of avian influenza A(H5) virus infection have been identified in the United States, with 66 of these cases occurring in 2024. Most infections in humans have been clinically mild, but one fatality has been reported. Many individuals infected with avian influenza A(H5) viruses have reported unprotected workplace exposures, such as handling infected or sick dairy cows or poultry without using recommended personal protective equipment. However, one case involved exposure to backyard poultry or wild birds. The source of the exposure in two confirmed cases in the United States could not be determined.

CDC has routinely recommended influenza testing for hospitalized patients with suspected influenza. In light of the ongoing avian influenza A(H5) virus animal outbreak in the United States, CDC now recommends subtyping of all influenza A virus-positive specimens from hospitalized patients on an accelerated basis. This accelerated subtyping is part of a comprehensive strategy to identify severe human infections with avian influenza A(H5) viruses, in addition to characterizing seasonal influenza viruses in a timely fashion.

Enhancing and expediting influenza A virus subtyping of specimens from hospitalized patients, especially from those in an ICU, can help avoid potential delays in identifying human infections with avian influenza A(H5) viruses. Such delays are more likely while seasonal influenza activity is high, as it is now, due to high patient volumes and general burden on healthcare facilities. Additional testing also ensures optimal patient care along with timely infection control. Furthermore, expediting transportation of such specimens to commercial or public health laboratories for additional testing may also accelerate public health investigation of severe A(H5) cases and sharing of information about these viruses.

• Most influenza tests ordered in clinical settings do not distinguish avian influenza A(H5) viruses from seasonal influenza A viruses; a positive result simply confirms influenza A virus infection. Therefore, using tests that identify the seasonal influenza A virus subtype will help identify whether infection with a seasonal influenza A virus is present. If a test result is positive for influenza A virus but negative for seasonal influenza A virus subtypes [i.e., A(H1) and A(H3)], the virus detected might be a novel influenza A virus, such as influenza A(H5), and specimens should be prioritized for shipment to a public health laboratory for additional testing. Alternatively, there are now a few commercial laboratories offering influenza A(H5) subtyping in the clinical setting.

Additionally, the Food and Drug Administration offers a list of influenza A typing and subtyping tests. Services like diagnostic and subtype testing that are reasonable and necessary to diagnose illness are covered in most cases by both public and private health insurers.

Subtyping is especially important in people who have a history of relevant exposure to wild or domestic animals infected or possibly infected with avian influenza A(H5N1) viruses.

CDC still considers the risk from avian influenza A(H5) viruses to the public to be low but is closely monitoring this dynamic situation. At this time, while seasonal influenza levels are high nationally, nearly all people who are currently hospitalized with influenza A virus infections probably have seasonal influenza.

#### **Recommendations for Testing of Hospitalized Patients**

In addition to jurisdiction-specific instructions for sending specimens for subtyping, CDC now recommends that all influenza A positive respiratory specimens from hospitalized patients, especially from those in an ICU, be subtyped for seasonal influenza A viruses [A(H1) and A(H3)] as soon as possible following admission—ideally within 24 hours—to support optimal patient care and proper infection prevention and control measures and to facilitate rapid public health investigation and action.

#### **Recommendations for Clinicians**

- When collecting a thorough exposure history from a patient with suspected or confirmed influenza
  who is hospitalized, ask about potential exposure to wild and domestic animals, including pets
  (e.g., cats), and animal products (e.g., poultry, dairy cows, raw cow milk and raw cow milk
  products, raw meat-based pet food), or recent close contact with a symptomatic person with a
  probable or confirmed case of A(H5).
- Implement appropriate infection control measures when influenza is suspected.
  - If avian influenza A(H5) virus infection is suspected, probable, or confirmed in a
    hospitalized patient, place the patient in an airborne infection isolation room with negative
    pressure with implementation by caregivers of <u>standard</u>, <u>contact</u>, <u>and airborne</u>
    <u>precautions</u> with eye protection (goggles or face shield).
- Test for seasonal influenza A in hospitalized patients with suspected seasonal influenza or novel influenza A virus infection such as avian influenza A virus infection, using whatever diagnostic test is most readily available for initial diagnosis.
  - o If the initial diagnostic test does not subtype [e.g., identify A(H1) and A(H3)], order an influenza A subtyping diagnostic test within 24 hours of hospital admission for patients who tested positive for influenza A.
  - Subtyping should be performed with assays available to the testing laboratory, as follows:
    - Subtyping tests should be performed in the hospital clinical laboratory, if available.
    - Alternatively, specimens should be sent to a commercial clinical laboratory.
    - If influenza A virus subtyping is not available through one of these routes, arrangements can made for influenza A virus-positive specimens to be subtyped at a public health laboratory.
- Any hospitalized patients, especially those in an ICU, with suspected seasonal influenza or avian
  influenza A(H5) should be started on <u>antiviral treatment</u> with oseltamivir as soon as possible
  without waiting for the results of influenza testing.
  - Consider <u>combination antiviral treatment</u> for hospitalized patients with avian influenza A(H5) virus infection.
- Notify the health department promptly if avian influenza A(H5N1) virus infection is suspected, probable, or confirmed in a hospitalized patient.
- Questions about appropriate clinical management or testing of hospitalized patients with novel influenza A virus infection [e.g., A(H5)], including about combination antiviral treatment dosing or testing for antiviral resistance, can be directed to the CDC Influenza Division for consultation with a medical officer via the CDC Emergency Operations Center at 770-488-7100.

### **Recommendations for Clinical Laboratories**

- Subtype and send respiratory specimens that are positive for influenza A but negative for seasonal influenza A virus subtypes [i.e., negative for A(H1) and A(H3)] to a public health laboratory as soon as possible and within 24 hours of obtaining the results. Do not batch specimens for consolidated or bulk shipment to the public health laboratory if that would result in shipping delays for any such specimen.
- If influenza A virus subtyping is not available at the hospital or the clinical laboratory of the
  treating facility, public health officials should be notified, and arrangements made for influenza A
  virus-positive respiratory specimens to be subtyped at a public health laboratory or a commercial
  laboratory with this testing capability. Specimens should be clearly linked to clinical information
  from the patient to ensure specimens from severely ill and ICU patients are prioritized.
- Immediately contact the <u>state, tribal, local, or territorial public health authority</u> if a positive result for influenza A(H5) virus is obtained using a laboratory developed test (LDT) or another A(H5) subtyping test to initiate important time-critical actions.

# **Recommendations for Public Health Laboratories**

• Complete influenza A virus subtyping assays within 24 hours of receipt and report results to CDC, as required.

#### Recommendations for the Public

- People should avoid direct contact with wild birds and other animals infected with or suspected to be infected with avian influenza A viruses.
- If you must have direct or close contact with infected or potentially infected birds or other animals, wear recommended personal protective equipment (PPE).
- Additional information on protecting yourself from avian influenza A(H5) infection is available from CDC.

#### For More Information

- H5 Bird Flu: Current Situation | CDC
- 2024-2025 Influenza Season: Surveillance for Novel Influenza A and Seasonal Influenza Viruses | CDC
- Interim Guidance for Infection Control Within Healthcare Settings When Caring for Confirmed Cases, Probable Cases, and Cases Under Investigation for Infection with Novel Influenza A Viruses Associated with Severe Disease | CDC
- Interim Guidance on Specimen Collection and Testing for Patients with Suspected Infection with Novel Influenza A Viruses Associated with Severe Disease or with the Potential to Cause Severe Disease in Humans | CDC
- Case Definitions for Investigations of Human Infection with Avian Influenza A Viruses in the United States | CDC
- Interim Guidance on the Use of Antiviral Medications for Treatment of Human Infections with Novel Influenza A Viruses Associated with Severe Human Disease | CDC

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