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CDC HEALTH ADVISORY

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Human Infection with Avian Influenza A (H5N1) Virus

Summary and Background

On January 8, 2014, the Public Health Agency of Canada reported the first confirmed case of human infection with avian influenza A (H5N1) virus identified in North America. The patient exhibited symptoms while returning from travel to Beijing, China, on December 27, 2013. For more information on this patient's travel itinerary, please refer to a Public Health Agency of Canada technical briefing at http://www.phac-aspc.gc.ca/media/nr-rp/2014/2014_0108a-eng.php. The patient was hospitalized on January 1, 2014, and subsequently died on January 3, 2014. Investigations by Canadian public health officials are ongoing. Since avian influenza A (H5N1) viruses have only been rarely, and never sustainably, transmitted from person to person, there is a very low risk of subsequent related cases. To date, no cases of human infection with avian influenza A (H5N1) viruses have been reported in the United States.

This case is a reminder that novel influenza A viruses, including avian influenza A (H5N1) virus, can infect and cause severe respiratory illness in humans. The clinical presentation of human infection with avian influenza A viruses varies considerably. **Most reports of H5N1 in humans, however, have described severe illness, including fulminant pneumonia leading to respiratory failure, acute respiratory distress syndrome, and death. Other reported H5N1 complications include encephalitis, septic shock, and multi-organ failure.**

Clinicians should consider the possibility of avian influenza A (H5N1) virus infection in persons exhibiting symptoms of severe respiratory illness who have appropriate travel or exposure history. This includes persons with recent travel (within 10 days of illness onset) to areas where human cases of avian influenza A (H5N1) virus infection have been detected or where avian influenza A (H5N1) viruses are known to be circulating in animals¹. Rapid detection and characterization of novel influenza A viruses remain critical components of national efforts to prevent further cases, evaluate clinical illness associated with them, and assess any ability for these viruses to spread among humans.

State health departments are encouraged to investigate potential human cases of avian influenza A (H5N1) virus infection as described below and should notify CDC within 24 hours of identifying a probable or confirmed case of novel influenza A virus infection, including avian influenza A (H5N1) virus infection (<http://www.cdc.gov/flu/avianflu/h5n1/case-definitions.htm>).

Clinicians and state health departments should also be aware that human infection with avian influenza A (H7N9) viruses have been reported among persons in China and Taiwan since April 2013, and may exhibit similar symptoms to those of influenza A (H5N1), including pneumonia, respiratory failure, and acute respiratory distress syndrome. Influenza A (H7N9) infections in humans have also been associated with high mortality. No cases of influenza A (H7N9) infections in humans have been reported in North America. **Potential cases of human infection with influenza A (H7N9) virus should also be investigated, using current case definitions and testing recommendations for avian influenza A (H7N9) virus (<http://www.cdc.gov/flu/avianflu/healthprofessionals.htm>).**

Interim Recommendations for Clinicians and State and Local Health Departments

Case Investigation and Testing Recommendations

Patients who meet both the clinical and exposure criteria described below should be tested for avian influenza A (H5N1) virus infection by reverse-transcription polymerase chain reaction (RT-PCR) assay using H5-specific primers and probes. Decisions on diagnostic testing for influenza using RT-PCR should be made using available clinical and epidemiologic information, and additional persons in whom clinicians suspect avian influenza A (H5N1) virus infection also should be tested. For more information on laboratory testing of persons under investigation for avian influenza A (H5N1) virus infection, please see <http://www.cdc.gov/flu/avianflu/healthprofessionals.htm>. Guidance on testing, treatment, and infection control will be updated by CDC as more information becomes available.

Clinical Illness Criteria

- i. Patients with new-onset severe acute respiratory illness requiring hospitalization (i.e., illness of suspected infectious etiology that is severe enough to require inpatient medical care in the judgment of the treating clinician).

Exposure Criteria

- i. Patients with recent travel (within 10 days of illness onset) to areas where human cases of avian influenza A (H5N1) virus infection have been detected or where avian influenza A (H5N1) viruses are known to be circulating in animals¹.

OR

- ii. Patients who have had recent close contact (within 10 days of illness onset) with suspected² or confirmed cases of human infection with avian influenza A (H5N1) virus. Close contact may be regarded as coming within about 6 feet (2 meters) or within the room or care area of a person with a suspected or confirmed case while the person was ill (beginning 1 day prior to illness onset and continuing until resolution of illness). Close contacts include healthcare personnel providing care for a person with a suspected or confirmed case, family members of a person with a suspected or confirmed case, persons who lived with or stayed overnight with a person with a suspected or confirmed case, and others who have had similar close physical contact, especially without the use of respiratory protection.

OR

- iii. Persons with an unprotected exposure to avian influenza A (H5N1) virus in a laboratory setting.

¹For a list of countries where avian influenza A (H5N1) viruses are known to be circulating in animals or where human cases of avian influenza A (H5N1) have become infected, please see http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/graph_avian_influenza/graphs_HPAI_02_01_2014.pdf and http://www.who.int/influenza/human_animal_interface/EN_GIP_20131210CumulativeNumberH5N1cases.pdf.

²Patients suspected of having infection with avian influenza A (H5N1) virus can include those with probable cases under investigation for infection with avian influenza A (H5N1) virus, and other patients for whom available clinical and epidemiologic information support a diagnosis of infection with avian influenza A (H5N1) virus (<http://www.cdc.gov/flu/avianflu/h5n1/case-definitions.htm>).

Specimen Collection and Laboratory Testing

- If infection with avian influenza A (H5N1) virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, respiratory specimens

should be collected with appropriate infection control precautions for novel influenza A virus infection and sent to the state or local health department for testing. Clinicians should obtain a respiratory specimen from these patients, place the swab or aspirate in viral transport medium, and contact their state or local health department to arrange transport and request a timely diagnosis at a state public health laboratory or CDC. Viral culture should not be attempted in these cases.

- Commercially available rapid influenza diagnostic tests (RIDTs) may not detect novel influenza A viruses in respiratory specimens. Therefore, a negative rapid influenza diagnostic test result does not exclude infection with avian influenza A (H5N1) virus. In addition, a positive test result for avian influenza A (H5N1) virus infection cannot confirm infection because these tests cannot distinguish between influenza A virus subtypes (e.g., they do not differentiate between human and animal influenza A viruses). Therefore, when RIDTs are positive for influenza A and there is concern for avian influenza A (H5N1) virus infection, respiratory specimens should be collected and sent for testing at a state public health laboratory using the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel. Clinical treatment decisions should not be made on the basis of a negative rapid influenza diagnostic test result since these tests have only moderate sensitivity.

For additional guidance on diagnostic testing of patients under investigation for avian influenza A (H5N1) virus infection, please see <http://www.cdc.gov/flu/avianflu/healthprofessionals.htm>. Guidance on testing, treatment, and infection control will be updated by CDC as more information becomes available.

Infection Control

- Standard, contact, and airborne precautions are recommended for management of hospitalized patients who may be infected with avian influenza A (H5N1) virus.

For additional guidance on infection control precautions for patients with suspected or confirmed infection with avian influenza A (H5N1) virus, please see

<http://www.cdc.gov/flu/avianflu/healthprofessionals.htm>.

Treatment and Chemoprophylaxis

- For persons hospitalized with suspected novel influenza A virus infection, including suspected avian influenza (H5N1) virus infection, clinicians should start empiric treatment with oseltamivir as soon as possible, without waiting for laboratory confirmation.
- Antiviral treatment is most effective when started as soon as possible after influenza illness onset. Early initiation of treatment provides a more optimal clinical response, although treatment of moderate, severe, or progressive disease begun after 48 hours of the onset of symptoms may still provide clinical benefit.
- Persons who meet exposure criteria for a suspected or confirmed case of avian influenza A (H5N1) virus infection should be monitored daily for 10 days for fever and respiratory symptoms. Antiviral chemoprophylaxis should be provided to close contacts according to risk of exposure (<http://www.cdc.gov/flu/avianflu/healthprofessionals.htm>).

For additional guidance on antiviral treatment of patients under investigation for avian influenza A (H5N1) virus infection with antiviral medications, or for guidance on antiviral chemoprophylaxis of exposed contacts, please see <http://www.cdc.gov/flu/avianflu/healthprofessionals.htm>. Guidance on testing, treatment, and infection control will be updated by CDC as more information becomes available.

For More Information

- General information about avian influenza viruses and how they spread (<http://www.cdc.gov/flu/avianflu/avian-in-humans.htm>)
- Past Outbreaks of Avian Influenza in North America (<http://www.cdc.gov/flu/avianflu/past-outbreaks.htm>)

- Transmission of Avian Influenza A Viruses Between Animals and People (<http://www.cdc.gov/flu/avianflu/virus-transmission.htm>)
- WHO: FAQs on avian influenza A(H5N1) virus (http://www.who.int/influenza/human_animal_interface/avian_influenza/h5n1_research/faqs/en/)

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