CDC Health Advisory

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Update on Influenza A (H5N1) and SARS: Interim Recommendations for Enhanced U.S. Surveillance, Testing, and Infection Control

Recent Developments

Influenza A (H5N1) Virus Infections

Infections of H5N1 among poultry have been confirmed in Cambodia, China, Hong Kong SAR, Indonesia, Japan, Korea, Laos, Thailand, and Vietnam (for a continually updated listing of affected countries, visit the Web site of the World Organization of Animal Health [OIE] at http://www.oie.int/eng/en_index.htm).

Human cases of influenza A (H5N1) infection have occurred in Vietnam and Thailand. On February 1, 2004, the World Health Organization (WHO) reported that laboratory test results had confirmed two new cases of human H5N1 infection in Vietnam; both patients died. The cases were in two sisters who are part of a cluster of four cases of severe respiratory illness in a single family. A detailed investigation of this cluster is under way; **limited human-to-human transmission may be one possible explanation, but direct poultry-to-human transmission cannot be ruled out, according to WHO.** To date, 10 laboratory-confirmed cases of H5N1 infection have been reported in patients in Vietnam, 8 of whom died. In Thailand, cases of H5N1 infection have been confirmed in 4 persons, 3 of whom died. Laboratory results on additional possible cases are pending. (For updated information, visit the WHO Web site at http://www.who.int/en/).

With the exception of the family cluster in Vietnam, it is believed that all human H5N1 cases resulted from contact with infected birds or surfaces contaminated with excretions from infected birds. At this time, there is no evidence of efficient person-to-person transmission in Vietnam or elsewhere.

Genetic sequencing of H5N1 viruses from human cases in Vietnam indicates that all genes are of avian origin. (The acquisition of human influenza viral genes increases the likelihood that a virus of avian origin can be readily transmitted from person-to-person.) Genetic sequencing of human H5N1 isolates from Vietnam additionally showed characteristics commonly known to confer antiviral resistance to amantadine and rimantadine, two antiviral drugs used for influenza. The remaining two antivirals (oseltamivir and zanamavir) should still be effective.

Severe Acute Respiratory Syndrome

On January 31, 2004, WHO announced that a new case of laboratory-confirmed infection with SARS-associated coronavirus (SARS-CoV) had been reported in China. This is the fourth SARS case (three confirmed, one probable) reported in China since December 16, 2003.

The most recent case occurred in a 40-year-old director of a hospital and practicing physician in Guangzhou, Guangdong Province, China. He became ill with SARS-like symptoms on January 7, 2004, and was admitted to a hospital with pneumonia on January 16 and placed in isolation. Previously reported confirmed cases include a 20-year-old woman who worked in a restaurant in Guangdong Province and became ill on December 25, 2003, and a 32-year-old man in Guangdong Province who had become ill on December 16, 2003. A fourth person (probable case) –- a 35-year-old business man from the Guangdong Province who had onset of illness on December 31, 2003 – tested positive for SARS-CoV infection at a national reference laboratory in China and on preliminary serologic tests performed by WHO SARS International Reference and Verification Network laboratories in Hong Kong.

All four patients have recovered from their illness and have been discharged from the hospital. To date, none of the contacts of these cases has developed a SARS-like illness. The source of infection in these individuals has not been determined. Samples collected from cages that housed civets at the restaurant where the waitress with confirmed SARS worked have tested positive for traces of SARS-CoV, suggesting a possible source of infection. However, evidence that civets transmit SARS-CoV to humans remains inconclusive.

Interim Recommendations: Enhanced U.S. Surveillance and Diagnostic Evaluation

CDC recommends enhanced surveillance efforts by state and local health departments, hospitals, and clinicians to identify patients at increased risk for influenza A (H5N1) and SARS. The clinical presentation and travel history of persons with influenza A (H5N1) or SARS-CoV infection may overlap. Interim recommendations for diagnostic evaluation for these agents in individuals who meet certain epidemiologic and clinical criteria follow below.

Influenza A (H5N1) Virus Infections

Testing for influenza A (H5N1) is indicated for **hospitalized** patients with:

a. radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternate diagnosis has not been established, **AND**

b. history of travel within 10 days of symptom onset to a country with documented H5N1 avian influenza in poultry and/or humans (for a listing of H5N1-affected countries, see the OIE Web site at http://www.oie.int/eng/en_index.htm and the WHO Web site at http://www.who.int/en/).

Testing for influenza A (H5N1) should be considered on a case-by-case basis in consultation with state and local health departments for **hospitalized or ambulatory** patients with:

a. documented temperature of >38°C (>100.4°F), **AND**

b. one or more of the following: cough, sore throat, shortness of breath, **AND**

c. history of contact with domestic poultry (e.g., visited a poultry farm, household raising poultry, or bird market) or a known or suspected human case of influenza A (H5N1) in an H5N1-affected country within 10 days of symptom onset.

Severe Acute Respiratory Syndrome

CDC continues to recommend consideration of testing for SARS-CoV in patients who require hospitalization for radiographically confirmed pneumonia or ARDS without identifiable etiology **AND** who have one of the following risk factors in the 10 days before the onset of illness:

- Travel to mainland China, Hong Kong, or Taiwan, or close contact with an ill person with a history of recent travel to one of these areas, **OR**

- Employment in an occupation associated with a risk for SARS-CoV exposure (e.g., health care worker with direct patient contact; worker in a laboratory that contains live SARS-CoV), **OR**

- Part of a cluster of cases of atypical pneumonia without an alternative diagnosis.

For patients with pneumonia or ARDS who have recently traveled to Guangdong Province, China, diagnostic testing for SARS-CoV should be performed immediately. For other patients, diagnostic testing for SARS should proceed for such patients as described in guidelines at www.cdc.gov/ncidod/sars/absenceofsars.htm.

Interim Recommendations: Infection Control Precautions for Influenza A (H5N1)

All patients who present to a health-care setting with fever and respiratory symptoms should be managed according to recommendations for Respiratory Hygiene and Cough Etiquette and questioned regarding their recent travel history. Isolation precautions identical to those recommended for SARS should be implemented for all hospitalized patients diagnosed with or under evaluation for influenza A (H5N1) as follows:

- Standard Precautions
  - Pay careful attention to hand hygiene before and after all patient

contact

- Contact Precautions
  - Use gloves and gown for all patient contact
- Eye protection
  - Wear when within 3 feet of the patient
- Airborne Precautions
  - Place the patient in an airborne isolation room (i.e., monitored negative air pressure in relation to the surrounding areas with 6 to 12 air changes per hour).

  - Use a fit-tested respirator, at least as protective as a NIOSH-approved N-95 filtering facepiece respirator, when entering the room.

For additional information regarding these and other health-care isolation precautions, see the Guidelines for Isolation Precautions in Hospitals. These precautions should be continued for 14 days after onset of symptoms until an alternative diagnosis is established or until diagnostic test results indicate that the patient is not infected with influenza A virus (see Laboratory Testing Procedures below). Patients managed as outpatients or hospitalized patients discharged before 14 days should be isolated in the home setting on the basis of principles outlined for the home isolation of SARS patients (see http://www.cdc.gov/ncidod/sars/guidance/i/pdf/i.pdf).

Laboratory Testing Procedures

Highly pathogenic avian influenza A (H5N1) is classified as a select agent and must be worked with under Biosafety Level (BSL) 3+ laboratory conditions. This includes controlled access double door entry with change room and shower, use of respirators, decontamination of all wastes, and showering out of all personnel. Laboratories working on these viruses must be certified by the U.S. Department of Agriculture. The same BSL 3+ laboratory guidelines are recommended for conducting virus isolation for SARS-CoV. CDC does **not recommend** that virus isolation studies on respiratory specimens from patients who meet the above criteria be conducted unless stringent BSL 3+ conditions can be met. Therefore, respiratory virus cultures should not be performed in most clinical laboratories and such cultures should not be ordered for patients suspected of having H5N1 infection.

Clinical specimens from suspect A (H5N1) cases and SARS-CoV cases may be tested by PCR assays using standard BSL 2 work practices in a Class II biological safety cabinet. In addition, commercial antigen detection testing can be conducted under BSL 2 levels to test for influenza.

To assist public health public health laboratories with SARS and respiratory illness diagnostic preparedness efforts, CDC has developed real-time PCR protocols for a number of respiratory pathogens, including influenza A and B viruses, adenovirus, metapneumovirus, *Legionella*, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*. **These protocols are currently available only to public health laboratories and have been posted at the APHL Members Only (password required) Web site www.aphl.org/Members_Only/index.cfm, under SARS. These protocols are not available in all public health laboratories, and physicians should consult with their local public health laboratory when ordering these tests.**

Specimens from persons meeting the above clinical and epidemiologic criteria should be sent to CDC if

- The specimen tests positive for influenza A by PCR or by antigen detection testing, **OR**
- PCR assays for influenza or SARS-CoV are not available at the state public health laboratory.

Because the sensitivity of commercially available rapid diagnostic tests for influenza may not always be optimal, CDC also will accept specimens from persons meeting the above clinical criteria even if they test negative by influenza rapid diagnostic testing if PCR assays are not available at the state laboratory.

Requests for testing should come through the state and local health departments, which should contact the CDC Director's Emergency Operations Center at 770-488-7100 before sending specimens for influenza A (H5N1) or SARS testing.

More Information

For further details about the reported cases of influenza A (H5N1) in Asia, see the WHO Web site http://www.who.int/en/. Additional information about influenza is available on the CDC Web site at www.cdc.gov/flu.

For more information about current U.S. SARS control guidelines, see the CDC document, "In the Absence of SARS-CoV Transmission Worldwide: Guidance for Surveillance, Clinical and Laboratory Evaluation, and Reporting" at www.cdc.gov/ncidod/sars/absenceofsars.htm. The document is part of CDC's draft *Public Health Guidance for Community-Level Preparedness and Response to Severe Acute Respiratory Syndrome (SARS)* www.cdc.gov/ncidod/sars/sarsprepplan.htm.

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