

## Cover Sheet

**DATE:** June 10, 2013

**SUBJECT:** Updated Guidelines for evaluation of severe respiratory illness associated with MERS-CoV and Human Infections with Avian Influenza A (H7N9) Viruses

**For LOCAL HEALTH  
DEPARTMENT reference only**

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**CDCP Epidemiology  
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# Information Sheet

**Date:** June 10, 2013

**Subject:** Updated Guidelines for evaluation of severe respiratory illness associated with Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Human Infections with Avian Influenza A (H7N9) Viruses

## **Background:**

H7N9 – As of June 3, 2013, Chinese public health officials have reported >130 cases of H7N9. Although several clusters of human infection with H7N9 have been identified in China, **continuous person-to-person transmission of the virus has not been proven.** At this time, **no cases of human infection with H7N9 have been detected in the United States,** despite testing of >60 persons with respiratory illness who reported recent travel to China.

MERS-CoV – As of June 7, 2013, 55 cases have been reported to World Health Organization (WHO). **No cases have been reported in the United States.** Illness onsets were from April 2012 through May 2013. Of the 55 cases, 31 were fatal, for a case-fatality rate of 56%.

**Information: Please find attached two CDC HEALTH UPDATES. One is an update on Avian Influenza A (H7N9), and includes new recommendations on who should be tested for H7N9 in the United States. The second is updated guidance for health departments and healthcare providers in the evaluation of patients for MERS-CoV infection including the expansion of availability of laboratory testing.**

**Recommendations:** Please review the attached Health Alert Network Updates (<http://www.dphhs.mt.gov/publichealth/han/>) and consider these diseases in individuals meeting the criteria for inclusion.

H7N9 – Testing is available and can be performed at the Montana Public Health Laboratory (MTPHL). Please contact MTPHL at 1-800-821-7284 with any questions, and to arrange for testing to be performed.

MERS-CoV – Testing for specimens for MERS-CoV is currently being conducted at the Centers for Disease Control and Prevention (CDC). Please contact MTPHL at 1-800-821-7284 with any questions regarding the testing of suspected cases. Arrangements can be made to perform testing as indicated.

# This is an official **CDC HEALTH UPDATE**

Distributed via the CDC Health Alert Network  
June 7, 2013, 14:00 ET (02:00 PM ET)  
CDCHAN-00347

## **Human Infections with Avian Influenza A (H7N9) Viruses**

This health advisory provides an **update** on the avian influenza A (H7N9) virus [H7N9] situation and includes new recommendations on who should be tested for H7N9 in the United States. This document replaces guidance published on April 5, 2013, in CDC Health Advisory 344 "Human Infections with Novel Influenza A (H7N9) Viruses," found at <http://emergency.cdc.gov/HAN/han00344.asp>. The updated guidance reflects the most current epidemiology of H7N9 cases, which indicates that almost all H7N9 human infections have resulted in severe respiratory illness; H7N9 has been found rarely among those with milder disease. For that reason, CDC is changing its recommendations for H7N9 testing: **The primary changes from previous guidance are (i) a new recommendation to test only patients with an appropriate exposure history and severe respiratory illness requiring hospitalization and (ii) a request that only confirmed and probable cases of human infection with H7N9 be reported to CDC.** In the previous guidance issued on April 5, CDC recommended that all persons with relevant exposure history and illness compatible with influenza, regardless of severity be tested. CDC will continue to update these recommendations as more information becomes available. The current guidance is consistent with interim surveillance recommendations by the World Health Organization for H7N9 found at [http://www.who.int/influenza/human\\_animal\\_interface/influenza\\_h7n9/InterimSurveillanceRecH7N9\\_10May13.pdf](http://www.who.int/influenza/human_animal_interface/influenza_h7n9/InterimSurveillanceRecH7N9_10May13.pdf)

### **Summary and Background**

As of June 3, 2013, Chinese public health officials have reported >130 cases of human infection with H7N9 from 10 provinces and municipalities in mainland China and Taiwan [1, 2]. Most patients were hospitalized with severe respiratory illness and reported poultry contact prior to illness onset [2, 3]. Preliminary results from influenza-like illness surveillance suggest that H7N9 has not caused widespread mild illness in China [4].

Although several clusters of human infection with H7N9 have been identified in China, **sustained person-to-person transmission of the virus has not been demonstrated. At this time, no cases of human infection with H7N9 have been detected in the United States**, despite testing of >60 persons with respiratory illness who reported recent travel to China.

Clinicians should consider the possibility of H7N9 infection in persons presenting with respiratory illness requiring hospitalization and an appropriate travel or exposure history. Influenza diagnostic testing in patients with severe respiratory illness for whom an etiology has not been confirmed may identify human cases of H7N9.

**Confirmed** and **probable** cases of human infection with H7N9 in the United States should be reported to CDC within 24 hours of initial detection. See <http://www.cdc.gov/flu/avianflu/h7n9/case-definitions.htm>. However, state health departments are encouraged to investigate all potential cases of H7N9 infection as described below in order to determine case status.

### **Interim Recommendations for Clinicians and State and Local Health Departments**

CDC recommends the following testing practices based on the current epidemiology of H7N9 cases.

### **Case Investigation and Testing**

- Patients who meet both the clinical and exposure criteria described below should be considered for H7N9 testing by reverse-transcription polymerase chain reaction (RT-PCR) methods. 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 H7N9 infection should also be tested.

### Clinical Illness Criteria

- i. Patients with new-onset severe acute respiratory infection **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).

*AND*

- ii. Patients for whom no alternative infectious etiology is identified.

### Exposure Criteria

- i. Patients with recent travel (within 10 days of illness onset) to areas where human cases of H7N9 have become infected or to areas where avian influenza A (H7N9) viruses are known to be circulating in animals<sup>1</sup>.

*OR*

- ii. Patients who have had recent close contact (within 10 days of illness onset) with confirmed cases of human infection with H7N9<sup>2</sup>. Close contact may be regarded as coming within about 6 feet (2 meters) of a confirmed case while the case was ill (beginning 1 day prior to illness onset and continuing until resolution of illness). Close contact includes healthcare personnel providing care for a confirmed case, family members of a confirmed case, persons who lived with or stayed overnight with a confirmed case, and others who have had similar close physical contact.
- If infection with H7N9 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 virulent influenza viruses 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.** For additional guidance on diagnostic testing of patients under investigation for H7N9 infection, please see <http://www.cdc.gov/flu/avianflu/h7n9/specimen-collection.htm>.
  - Commercially available rapid influenza diagnostic tests (RIDTs) may not detect H7N9 viruses in respiratory specimens. Therefore, a negative rapid influenza diagnostic test result does not exclude infection with H7N9. In addition, a positive test result for influenza A cannot confirm avian influenza virus infection because these tests cannot distinguish between influenza A virus subtypes (they do not differentiate between human influenza A viruses and novel<sup>3</sup> influenza viruses). Therefore, when RIDTs are positive for influenza A and there is concern for novel influenza A virus infection, respiratory specimens should be collected and sent for RT-PCR testing at a state public health laboratory. Clinical treatment decisions should not be made on the basis of a negative rapid influenza diagnostic test result since the test has only moderate sensitivity ([http://www.cdc.gov/flu/professionals/diagnosis/clinician\\_guidance\\_ridt.htm](http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm)).

### **Infection Control**

Clinicians should be aware of appropriate infection control guidelines for patients under investigation for infection with novel influenza A viruses. For guidance on infection control precautions for H7N9 see <http://www.cdc.gov/flu/avianflu/h7n9-infection-control.htm>.

### **Treatment**

For guidance on treatment of patients under investigation for H7N9 with antiviral medications, or for guidance on antiviral chemoprophylaxis of exposed contacts, see <http://www.cdc.gov/flu/avianflu/h7n9-antiviral-treatment.htm>.

### **For More Information**

- CDC avian influenza A (H7N9) virus information is available at <http://www.cdc.gov/flu/avianflu/h7n9-virus.htm>.
- WHO Situation Updates on avian influenza are available at [http://www.who.int/influenza/human\\_animal\\_interface/avian\\_influenza/archive/en/index.html](http://www.who.int/influenza/human_animal_interface/avian_influenza/archive/en/index.html).

- WHO "Frequently Asked Questions on human infection with A (H7N9) virus, China" is available at [http://www.who.int/influenza/human\\_animal\\_interface/faq\\_H7N9/en/index.html](http://www.who.int/influenza/human_animal_interface/faq_H7N9/en/index.html).
- The Chinese Center for Disease Control and Prevention (China CDC) "Questions and Answers about human infection with A (H7N9) avian influenza virus" is available at [http://www.chinacdc.cn/en/research\\_5311/FAQ/201304/t20130418\\_80053.html](http://www.chinacdc.cn/en/research_5311/FAQ/201304/t20130418_80053.html).
- CDC general information about avian influenza viruses and how they spread is available at <http://www.cdc.gov/flu/avianflu/avian-in-humans.htm>.

### **End Notes:**

<sup>1</sup>As of June 3, 2013, China was the only country where H7N9 viruses were known to be circulating in animals or where human cases have become infected. Patients with direct or close contact with wild birds or poultry, or animal settings, such as live poultry markets while traveling in these areas should be strongly considered for H7N9 testing. For more information on countries affected, please see the CDC avian influenza A (H7N9) information page at <http://www.cdc.gov/flu/avianflu/h7n9-virus.htm>.

<sup>2</sup>Contact investigation protocols for confirmed cases may supersede the recommendations described here; testing of close contacts with *any level* of respiratory illness may be pursued, if in the judgment of the investigators, this is warranted.

<sup>3</sup>Influenza viruses that do not typically infect humans are called "novel" influenza viruses; this includes influenza viruses that typically infect birds and swine.

### **References:**

1. Centers for Disease Control and Prevention. Emergence of Avian Influenza A(H7N9) Virus Causing Severe Human Illness - China, February-April 2013. *MMWR* **2013**; 62(18): 366-71. [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6218a6.htm?s\\_cid=mm6218a6\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6218a6.htm?s_cid=mm6218a6_w)
2. Li Q, Zhou L, Zhou M, et al. Preliminary Report: Epidemiology of the Avian Influenza A (H7N9) Outbreak in China. *N Engl J Med*. **2013** Apr 24. [Epub ahead of print]. [http://www.ncbi.nlm.nih.gov/pubmed/?term=Epidemiology+of+the+Avian+Influenza+A+\(H7N9\)+Outbreak+in+China](http://www.ncbi.nlm.nih.gov/pubmed/?term=Epidemiology+of+the+Avian+Influenza+A+(H7N9)+Outbreak+in+China)
3. Lee SS, Wong NS, Leung CC. Exposure to avian influenza H7N9 in farms and wet markets. *Lancet* May 25;381(9880):1815. doi: 10.1016/S0140-6736(13)60949-6. Epub **2013** May 10. [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(13\)60949-6/fulltext?rss=yes](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)60949-6/fulltext?rss=yes)
4. Xu C, Havers F, Wang L, Chen T, Shi J, Wang D. Monitoring avian influenza A(H7N9) virus through national influenza-like illness surveillance, China. *Emerging Infectious Diseases* [Internet], **2013** Jul [June 3, 2013]. <http://dx.doi.org/10.3201/eid1908.130662>.

*The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.*

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##This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations##

# This is an official **CDC HEALTH UPDATE**

Distributed via the CDC Health Alert Network  
June 7, 2013, 8:00 p.m. ET  
CDCHAN-00348

## **Notice to Health Care Providers: Updated Guidelines for Evaluation of Severe Respiratory Illness Associated with Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**

**Summary:** *The Centers for Disease Control and Prevention (CDC) is working closely with the World Health Organization (WHO) and other partners to better understand the public health risk posed by Middle East Respiratory Syndrome Coronavirus (MERS-CoV), a novel coronavirus that was first reported to cause human infection in September 2012. No cases have been reported in the United States. The purpose of this HAN Advisory is to provide updated guidance to state health departments and health care providers in the evaluation of patients for MERS-CoV infection including expansion of availability of laboratory testing and, in consultation with WHO, expansion of the travel history criteria for patients under investigation from within 10 to 14 days for investigation and modification of the case definition. Please disseminate this information to infectious diseases specialists, intensive care physicians, internists, infection preventionists, as well as to emergency departments and microbiology laboratories.*

### **Background**

MERS-CoV, formerly called “novel coronavirus,” is a beta coronavirus that was first described in September 2012, when it was reported to have caused fatal acute lower respiratory illness in a man in Saudi Arabia. Genetic sequence analyses have shown that this new virus is different from other known human coronaviruses, including the one that caused severe acute respiratory syndrome (SARS). Diagnosis relies on testing with real time reverse transcription polymerase chain reaction (RT-PCR) assays. There is no specific treatment for MERS-CoV infection; care is supportive.

As of June 7, 2013, 55 laboratory-confirmed cases of MERS-CoV infection have been reported to WHO—two from France, three from Italy, two from Jordan, two from Qatar, 40 from Saudi Arabia, two from Tunisia, one from the United Arab Emirates, and three from the United Kingdom (UK). Additional details can be found in the June 7, 2013 *MMWR* Early Release ([http://www.cdc.gov/mmwr/preview/mmwrhtml/mm62e0607a1.htm?s\\_cid=mm62e0607a1\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm62e0607a1.htm?s_cid=mm62e0607a1_w)). To date, all cases have a direct or indirect link to one of four countries: Saudi Arabia, Qatar, Jordan, and the United Arab Emirates. **No cases have been reported in the United States.** Illness onsets were from April 2012 through May 2013. Of the 55 cases, 31 were fatal, for a case-fatality rate of 56%. The median age of cases is 56 years. All of the patients were aged  $\geq 24$  years, except for two children, one aged 2 years and one aged 14 years.

Eight clusters of illnesses have been reported by six countries (France, Italy, Jordan, Saudi Arabia, Tunisia, and UK). These clusters provide clear evidence of human-to-human transmission of MERS-CoV. The largest cluster reported to date consists of 25 cases, 14 of which were fatal, associated with a health-care facility in Al-Ahsa governorate in Saudi Arabia. Two of the case-patients in that cluster were health-care personnel who acquired the infection after exposure to patients with confirmed MERS-CoV infection.

The first case reported by France was in a person with an underlying immunosuppressive condition who initially had abdominal pain and diarrhea and subsequently developed respiratory complications. This case raises the possibility that presentations may not initially include respiratory symptoms. Among cases reported to WHO in which more detailed information is available, most are reported to have chronic underlying medical conditions or immunosuppression; such persons may be at increased risk of MERS-CoV infection or severe disease, or both. In some instances, sampling with nasopharyngeal swabs did not detect MERS-CoV by PCR; however, MERS-CoV was detected by PCR in lower respiratory tract specimens from those same patients. Therefore, lower tract respiratory specimens should be a priority for collection and PCR testing, in addition to nasopharyngeal swabs.

## Recommendations

Recommendations and guidance on MERS-CoV case definitions, case investigation, specimen collection and shipment for testing, and infection control (including use of personal protective equipment) are available at the CDC MERS website (<http://www.cdc.gov/coronavirus/MERS/index.html>). Information and guidance posted on this website may change as we learn more about the virus. Please check CDC's MERS website regularly for the most current information. State and local health departments with questions should contact the CDC Emergency Operations Center (770-488-7100 or [eocreport@cdc.gov](mailto:eocreport@cdc.gov)).

## Surveillance

As a result of investigations suggesting incubation periods for MERS CoV may be longer than 10 days, the time period for considering MERS in persons who develop severe acute lower respiratory illness days after traveling from the Arabian Peninsula or neighboring countries\* has been extended from within 10 days to within 14 days of travel.

In particular, persons who meet the following criteria for "patient under investigation" (PUI) should be reported to state and local health departments and evaluated for MERS-CoV infection:

- A person with an acute respiratory infection, which may include fever ( $\geq 38^{\circ}\text{C}$  ,  $100.4^{\circ}\text{F}$ ) and cough; AND
- Suspicion of pulmonary parenchymal disease (e.g., pneumonia or acute respiratory distress syndrome based on clinical or radiological evidence of consolidation); AND
- History of travel from the Arabian Peninsula or neighboring countries\* within 14 days; AND
- Symptoms not already explained by any other infection or etiology, including clinically indicated tests for community-acquired pneumonia<sup>†</sup> according to local management guidelines.

In addition, the following persons may be considered for evaluation for MERS-CoV infection:

- Persons who develop severe acute lower respiratory illness of known etiology within 14 days after traveling from the Arabian Peninsula or neighboring countries\* but who do not respond to appropriate therapy; OR
- Persons who develop severe acute lower respiratory illness who are close contacts<sup>‡</sup> of a symptomatic traveler who developed fever and acute respiratory illness within 14 days of traveling from the Arabian Peninsula or neighboring countries.\*

In addition, CDC recommends that clusters of severe acute respiratory illness (SARI) should be investigated and, if no obvious etiology is identified, local public health officials should be notified and testing for MERS-CoV conducted if indicated.

CDC requests that state and local health departments report PUIs for MERS-CoV and clusters of SARI with no identified etiology to CDC. To collect data on PUIs, please use CDC's Interim Health Departments MERS-CoV Investigation Form available at <http://www.cdc.gov/coronavirus/mers/guidance.html>. State health departments should FAX completed investigation forms to CDC at 770-488-7107 or attach in an email to [eocreport@cdc.gov](mailto:eocreport@cdc.gov) (subject line: MERS-CoV Patient Form).

## Laboratory Testing

Testing of specimens for MERS-CoV is currently being conducted at CDC. The Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) on June 5, 2013, to authorize the use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay (NCV-2-12 rRT-PCR Assay) to test for MERS-CoV in clinical respiratory, blood and stool samples. This EUA is needed because, at this time, no FDA-approved tests that identify MERS-CoV in clinical specimens are available. This assay will be deployed to Laboratory Response Network (LRN) laboratories in all 50 states over the coming weeks. Updated information about laboratories with the capacity to conduct MERS testing with the NCV-2-12 rRT-PCR Assay will be provided on CDC's MERS website (<http://www.cdc.gov/coronavirus/mers/case-def.html>).

To increase the likelihood of detecting MERS-CoV, CDC recommends collection of specimens from different sites-- for example, a nasopharyngeal swab and a lower respiratory tract specimen such as sputum, bronchoalveolar lavage, bronchial wash, or tracheal aspirate. Specimens should be collected at different times after symptom onset, if possible. Lower respiratory tract specimens should be a priority for collection and PCR

testing; stool specimens are of lower priority. Specimens should be collected with appropriate infection control precautions <http://www.cdc.gov/coronavirus/mers/case-def.html>.

#### Case Definitions

The MERS-CoV case definition continues to evolve and is available at <http://www.cdc.gov/coronavirus/mers/case-def.html>. In consultation with WHO, the definition of a probable case of MERS has been updated to also include persons with severe acute respiratory infection with no known etiology with an epidemiologic link to a confirmed MERS-CoV case.

#### Infection Control

There is clear evidence of limited human-to-human transmission, possibly involving different modes, such as droplet and contact transmission, but further studies are required to better understand the risks. Until the transmission characteristics of MERS-CoV are better understood, patients under investigation and probable and confirmed cases should be managed in healthcare facilities using standard, contact, and airborne precautions. As information becomes available, these recommendations will be re-evaluated and updated as needed.

\* Countries considered to be on or neighboring the Arabian Peninsula include Bahrain, Iraq, Iran, Israel, Jordan, Kuwait, Lebanon, Oman, Palestinian territories, Qatar, Saudi Arabia, Syria, the United Arab Emirates (UAE), and Yemen.

† Examples of respiratory pathogens causing community-acquired pneumonia include influenza A and B, respiratory syncytial virus, adenovirus, *Streptococcus pneumoniae*, and *Legionella pneumophila*.

‡ Close contact is defined as 1) any person who provided care for the patient, including a health-care worker or family member, or who had other similarly close physical contact, or 2) any person who stayed at the same place (e.g., lived with or visited) as the patient while the patient was ill.

#### **For more information:**

For additional information, please consult the CDC MERS website at:

<http://www.cdc.gov/coronavirus/mers/index.html>

State and local health departments with questions should contact the CDC Emergency Operations Center (770-488-7100 or [eocreport@cdc.gov](mailto:eocreport@cdc.gov)).

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