

Chief Health Officer circular to Clinicians and Laboratories

9 April 2013

Status: Active

H7N9 Influenza

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Issued by: Dr Rosemary Lester, Chief Health Officer, Victoria
Issued to: Clinicians and Laboratories

Summary

As of 7 April, 2013, 21 cases of H7N9 influenza have been reported in China, including six deaths. Although the environmental source has not yet been definitively determined, some of the confirmed cases have been associated with contact with chickens or poultry or an animal “wet market” environment.

In patients with acute pneumonia or pneumonitis with a history of travel to China within seven days of illness onset, or contact with known confirmed or probable cases, the following is recommended:

1. Place the patient in a single room with negative pressure air-handling, or a single room from which the air does not circulate to other areas, and implement standard and transmission-based precautions (contact and airborne), including the use of personal protective equipment (PPE).
2. Investigate and manage the patient as for community acquired pneumonia. Appropriate specimens should also be collected for influenza PCR testing.
3. Arrange testing of any suspected or probable cases (see case definition) in accordance with the instructions below. Notify any suspected, probable or confirmed cases promptly to your local public health authorities. Call the Victorian Department of Health, Communicable Disease Prevention and Control Section on 1300 651 160 to arrange testing.

What is the H7N9 influenza?

Influenza (A)H7 viruses are a group of influenza viruses that normally circulate among birds. H7N9 is a reassortant derived from three different avian influenza viruses. This strain is distinct from the H1N1/09 (that caused the 2009 pandemic in humans) and H5N1 influenza. H7N9 that is genetically similar to that detected in infected humans has been detected in pigeon and poultry samples collected at a live animal market in Shanghai. Unlike other influenza strains, including highly pathogenic avian influenza H5N1, this new virus is hard to detect in poultry because this novel virus causes little to no signs of disease in animals.

Although there is no evidence of human-to-human transmission of H7N9 to date, sequence analysis indicates the virus has properties to infect mammalian cells; therefore, the potential for avian-human and human-human transmission exists but requires further investigation. Sequences previously associated with high virulence of A(H7) in humans (PB2 gene) have been detected in isolates in the current outbreak.

What is the current situation?

See WHO website on the current situation, including epidemiological updates, Q&A and guidance documents:

Disease Outbreak News <http://www.who.int/csr/don/en/index.html>

Influenza at the Human-Animal Interface http://www.who.int/influenza/human_animal_interface/en/

- A total of 21 cases have been reported from China, including six deaths. To date cases have been reported from four eastern provinces of China (Shanghai, Anhui, Jiangsu and Zhejiang).
- There continues to be no evidence of human-to-human transmission with medical observation of over 530 contacts ongoing. In Jiangsu, investigation is ongoing into a contact of an earlier confirmed case who developed symptoms of illness.
- The incubation period is not precisely known.
- There is currently no vaccine available for H7N9 influenza. Laboratory testing conducted in China has shown that the influenza A(H7N9) viruses are sensitive to neuraminidase inhibitors (oseltamivir and zanamivir). When these drugs are given early in the course of illness, they have been found to be effective against seasonal influenza virus and influenza A(H5N1) virus infection. However, at this time, there is no experience with the use of these drugs for the treatment of H7N9 infection.
- From 1996 to 2012, human infections with H7 influenza viruses (H7N2, H7N3, and H7N7) were reported in Netherlands, Italy, Canada, USA, Mexico and the United Kingdom. Most of these infections occurred in association with poultry outbreaks.

What are the symptoms?

H7N9 was initially identified in patients with severe pneumonia and/or Acute Respiratory Distress Syndrome (ARDS) but 3 recent cases have been mild. Symptoms include fever $\geq 38^{\circ}\text{C}$, cough and shortness of breath. However, information is still limited about the full spectrum of disease that infection with influenza A(H7N9) virus might cause.

Symptoms and signs of A(H7) infections during previous outbreaks mainly resulted in conjunctivitis and mild upper respiratory symptoms, with the exception of one death, which occurred in the Netherlands.

Are health workers at risk from H7N9 influenza?

The routes of transmission to humans of the H7N9 influenza have not yet been fully determined, but there is currently no evidence that this strain can spread from human to human. Infection control recommendations in this document for suspected, probable and confirmed cases aim to provide the highest level of protection for health care workers, given the current limited state of knowledge.

Has WHO recommended any travel or trade restrictions related to this new virus?

The number of cases identified in China is very low. WHO does not advise the application of any travel measures with respect to visitors to China nor to persons leaving China. There is no evidence to link the current cases with any Chinese products. WHO advises against any restrictions to trade at this time.

Who do I test for H7N9 influenza?

Testing should be considered for:

1. Individuals with acute pneumonia or pneumonitis and history of travel to, or residence in China within the previous 7 days.
2. Individuals with acute pneumonia or pneumonitis and history of contact with those in point 1 above.

3. Health care workers with acute pneumonia, who have been caring for patients with severe acute respiratory infections, particularly patients requiring intensive care, without regard to place of residence or history of travel.

How do I test for H7N9?

- Where H7N9 infection is suspected, samples should be referred to the Victorian Infectious Diseases Reference Laboratory for testing. Specimens can be handled and transported routinely. They should be clearly identified as requiring urgent testing for influenza A/H7N9, and separated from non-urgent specimens. The reference laboratory should be notified.
- Collect combined nose and throat swabs (usually from adults) or nasopharyngeal aspirates (usually from children) and place in viral transport medium. Sputum is strongly recommended wherever possible. Bronchoalveolar samples and lung biopsy should also be sent if available.
- Gloves, gown, P2 respirator and eye protection should be worn as a minimum when collecting samples from patients. If a negative pressure room is unavailable, the patient should be placed in a single room with the door closed.
- Testing for other infectious causes can be undertaken at the referring laboratory using PC2 precautions, processing of samples in a biosafety cabinet and use of PPE including a surgical mask and eye protection. Routine tests for acute pneumonia should be performed where indicated, including bacterial culture, serology, urinary antigen testing and tests for influenza viruses.
- The laboratory carrying out the influenza testing should immediately refer all unsubtypeable or presumptive H7 influenza A virus to VIDRL or the WHOCC in Melbourne.
- Laboratory staff should handle specimens under enhanced PC2 conditions, with handling of open samples in a biosafety cabinet and the use of gloves, gowns, masks and eye protection. PC3 conditions are required for virus culture.

Further details about specimen collection and testing can be found in **Laboratory investigation for patients with suspected infection with influenza A/H7N9: PHLN recommendations for laboratories (attached)**.

What are the recommended isolation and PPE recommendations for patients in hospital?

While further information is accumulating, current recommendations are for airborne transmission precautions for suspected, probable or confirmed cases.

These recommendations on isolation and PPE for suspected, probable and confirmed cases take a deliberately cautious approach by recommending measures that aim to control the transmission of pathogens that can be spread by the airborne route. These measures are detailed in [NHMRC: Australian Guidelines for the Prevention and Control of Infection in Healthcare – 2010](#) (particularly section B2.4).

In summary, transmission-based precautions for suspected, probable and confirmed cases should include:

- Placement of cases in a negative pressure room if available, or in a single room from which the air does not circulate to other areas
- Airborne transmission precautions, including routine use of a P2 respirator, disposable gown, gloves, and eye protection when entering a patient care area
- Standard and contact precautions, including close attention to hand hygiene
- If a single or negative pressure room is not available (eg in primary care settings), or if transfer of the confirmed or probable case outside the negative pressure room is necessary, asking the patient to wear a surgical face mask, if tolerated, while they are being transferred and to follow respiratory hygiene and cough etiquette.

- Triage areas should have signs asking that patients with severe respiratory tract infections with a recent history of travel to China should make themselves known so that appropriate arrangements can be made.

Case Definitions

1. Suspected case (under investigation)*

- A person with an acute febrile respiratory infection with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia, pneumonitis or Acute Respiratory Distress Syndrome (ARDS))

AND

- With one or more of the following exposures during the 7 days prior to the onset of symptoms:
 - Travel to a country† where human cases of H7N9 influenza have recently been reported, especially if there was recent direct or close contact with animals (e.g. wild birds, poultry or pigs).
 - Close contact‡ with a laboratory-confirmed case.

2. Probable Case

- A person fitting the definition of a Suspected Case but with no possibility of laboratory confirmation for H7N9 influenza, either because the patient or samples are not available for testing AND
- Not already explained by any other infection or aetiology, including all clinically indicated tests for community acquired pneumonia according to local management guidelines.

3. Confirmed Case

- A person with laboratory confirmation of infection with H7N9 influenza at a WHO National Influenza Centre.

* Although most of the cases to date have presented with a severe acute respiratory illness, mild cases have been reported. If doctors are concerned about patients presenting with milder illness, they should discuss this with the local public health authorities.

† Currently, China (excluding Hong Kong) is the only country that has recently reported human cases of H7N9 influenza.

‡ Close contacts include:

- Any person who provided care for the patient or who had other similarly close physical contact while not wearing appropriate PPE in the 7 days before symptom onset; this includes health care workers or family members.
- Any person who stayed in the same household as a probable or confirmed case while the case was symptomatic.

Advice for contacts of cases

Contacts of cases should be directed to the Communicable Disease Prevention & Control Section of the Department of Health (Ph. 1300 651 160) for advice.

Advice for travellers to China

At this time, it is advisable that travellers to China keep away from sick and dead poultry and livestock and avoid visiting live animal markets.

Advice for returned travellers

At this time, if returned travellers meet the exposure criteria for the case definition but have a less severe respiratory illness, advice regarding further management should be sought from the Communicable Disease Prevention & Control Section of the Department of Health (Ph. 1300 651 160).

Other useful links

UN Food and Agriculture Organization of the United Nations (FAO)
<http://www.fao.org/news/story/en/item/173655/icode/>

Who do I contact if I have a suspected case?

Call the Victorian Department of Health, Communicable Disease Prevention and Control Section on 1300 651 160.

For advice on any updates to this document please also contact the number above.

Yours sincerely

Dr Rosemary Lester
Chief Health Officer

Authorised by the Victorian Government, Melbourne.

Laboratory investigation for patients with suspected infection with influenza A/H7N9
PHLN recommendations for laboratories
(8th April, 2013)

A small number of human infections with a new strain of influenza A/H7N9 have recently been described in patients with pneumonia in China, specifically, Shanghai and surrounding areas. As of 7 April, 2013, 21 cases of H7N9 influenza have been reported in China, including 6 deaths. Some of the confirmed cases have been associated with contact with chickens or poultry or an animal environment but the source is yet to be determined.

At the moment, the documented human infections have caused moderate-severe pneumonia, and human-to-human spread as not been proven. However the extent of milder illness is not known. The virus is susceptible to both oseltamivir and zanamivir.

Tests are currently available in several laboratories within Australia, which can be accessed through your local Public Health Laboratory Network member. There are no serological tests available.

As there have been only a small number of cases, and none within Australia, the information about incubation period, range of clinical illness, period of virus shedding and the risk of transmission is quite limited.

Also, as only limited test evaluation has been possible, testing should only be undertaken in major human reference laboratories. It appears likely that the current influenza A matrix PCRs will perform adequately, but there are currently no reliable assays for this H7 gene. **The performance of the antigen detection tests (either rapid tests or laboratory-based) is unknown but is expected to be poor.** Culture should only be attempted in reference laboratories, and requires PC3 containment.

The purpose of testing patients fitting the current case definition is not only to detect influenza A/H7N9 but also to detect other pathogens that may more likely explain the illness.

Laboratory specimen collection and investigations for A/H7N9 should only be undertaken where there is a reasonable suspicion that they may have infection, in order to improve the reliability of the tests and to avoid overwhelming the existing capacity.

Therefore, it is important that testing for influenza A/H7N9 be limited to those patients meeting the current case definition. That requires a suitable travel history within the week preceding onset of illness and clinical evidence of infection.

Testing is not required if the patient has already had an adequate alternative diagnosis for their illness.

The request form should include the patient's travel history, dates of potential exposure, date of onset of illness, brief details of the clinical illness and results of any investigations already undertaken.

Samples should be collected and sent to the nearest PHLN laboratory for investigations. The type of specimen and day after onset of fever/symptoms that the sample should be collected can be found later in this document.

Clinicians dealing with suspected or probable influenza A should undertake the routine investigations for atypical pneumonia available in their laboratory. These tests can be undertaken in standard microbiology laboratory conditions (PC-2)

Please refer the samples for influenza A/H7N9 testing immediately: do not wait for results of other tests before referring the samples. A list of tests to investigate possible other coexisting medical conditions can be found later in this document.

For any queries about testing (or for viral transport media etc), contact your jurisdictional PHLN laboratory.

Medical or clinical queries regarding H7N9 influenza should be directed to your local public health officer, infectious diseases physician or clinical microbiologist

Recommendations for laboratory investigation of suspected influenza A/H7N9 infection

Specimens can be handled and transported routinely. They should be clearly identified as requiring urgent testing for influenza A/H7N9, and separated from non-urgent specimens. The reference laboratory should be notified.

Gloves, gown, mask and eye protection should be worn as a minimum when collecting samples from patients. For invasive samples (nasopharyngeal aspirates, BAL and other samples where aerosols may be produced) a P2 respirator mask is recommended.

Respiratory tract samples

- Currently we do not know the patterns of excretion or the duration of shedding of A/H7N9. It is recommended that samples are collected as early as possible in the clinical illness and, while there is a continuing high suspicion of active influenza A/H7N9 infection, these should be repeated every 3-4 days.
- Collect combined nose and throat swabs (usually from adults) or nasopharyngeal aspirates (usually from children) and place in viral transport medium. Sputum is strongly recommended wherever possible. Bronchoalveolar samples and lung biopsy should also be sent if available.
- Appropriate personal infection control precautions should be taken whilst specimens are being collected.
- Testing for other infectious causes can be undertaken at the referring laboratory using PC2 precautions, processing of samples in a biosafety cabinet and use of PPE including a surgical mask and eye protection.

Blood

- Collect 10ml serum tubes for acute and convalescent testing, at presentation and at days 7-10 and 21-28 after onset). This will be used to test for influenza and other potential causes of the illness.
- Serological testing for other pathogens can be undertaken in the host laboratory, or sent on to PHLN or other referral laboratories using usual referral pathways.

Tissues

- Send in sterile saline in a sealed container

Other samples

- Currently no other samples are recommended for H7N9 testing.

Routine biochemistry, haematology, bacteriology and other testing should be carried out at the facility managing the suspect patient using BSL2 precautions and in accordance with the PHLN guidelines for specimen handling.

Table 1 – Influenza A/H7N9 investigations showing specimen type and day of collection, based on days equals days after onset of illness)

Type Of Specimen	Day Specimen To Be Collected
NPA (or combined nose and throat swabs), sputum	As early as possible during the clinical illness. Repeat every 3-4 days while there is a continuing high suspicion of influenza A/H7N9 infection AND the patient remains clinically unwell AND the cause has not been determined.
Bronchoalveolar samples or lung tissue	When available
Blood	On presentation, and days 7-10 and 21-28, depending on the availability of the patient.
Lung tissue	When possible.

Typical testing protocol for suspected Influenza A/H7N9 infection

▪ Respiratory tract samples

A) Nasopharyngeal aspirate or combined nose and throat swab.
Request test for:

Influenza A/H7N9 by nucleic acid detection test
PLUS

Influenza A and B, parainfluenza types 1-3, RSV, adenovirus, human metapneumovirus, rhinovirus, enterovirus, human coronaviruses, *Chlamydophila pneumoniae*,

PLUS

Virus isolation including Influenza A/H7N9 (where available)

PLUS

Routine bacterial and fungal culture and other relevant tests for pneumonia (eg urinary antigens for *Legionella*, *S. pneumoniae*) etc.

B) Bronchoalveolar fluid, sputum, tracheal aspirates

Request test for:

Influenza A/H7N9 by nucleic acid testing.

PLUS

Mycoplasma pneumoniae, *Legionella pneumophila*, *Legionella longbeachae*, *Chlamydophila pneumoniae*, influenza A and B, parainfluenza types 1-3, RSV, adenovirus, human metapneumovirus, rhinovirus, enterovirus, human coronaviruses

PLUS

Virus isolation including Influenza A/H7N9 (where available)

PLUS

Routine bacterial and fungal culture and other relevant tests for pneumonia (eg urinary antigens for *Legionella*, *S. pneumoniae*) etc.

▪ **Blood**

Acute and convalescent (7-10 and 21-28 days after disease onset) serum.

Request test for:

Antibody to Influenza A

PLUS

Antibody to Influenza B, parainfluenza 1-3, RSV, *Legionella* sp, Q fever, adenovirus, *Chlamydophila pneumoniae*, *Chlamydia psittaci*, *Mycoplasma pneumoniae*..