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**Department of Health**

## **Laboratory investigation for patients with suspected infection**

### ***Public Health Laboratories Network recommendations for laboratories***

**28 March 2014**

In April 2013, a small number of human infections with a new strain of avian influenza A(H7N9) were described in patients with pneumonia in China, specifically, Shanghai and surrounding areas. As of 24 February 2014, 365 cases of H7N9 avian influenza have been reported in China (including Hong Kong) and Taiwan, including 116 deaths. To date, evidence suggests that all human infections were acquired in mainland China. 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 majority of documented human infections have caused moderate-severe pneumonia, and human-to-human spread as not been proven. However the full extent of milder illness is not known. Laboratory studies suggest that the virus is susceptible to both neuraminidase inhibitors including oseltamivir and zanamivir although this has not been rigorously examined in humans.

Diagnostic 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 which distinguish H7N9 avian influenza from other influenza A virus infections.

Since there has been a relatively small number of cases and none thus far within Australia, information about incubation period, range of clinical illness, period of virus shedding and the risk of transmission is limited.

**Further, as only limited test evaluation has been possible, testing should only be undertaken within, or in collaboration with, 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.



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

Laboratory specimen collection and investigations for H7N9 avian influenza 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 H7N9 avian influenza 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. Screening of samples by influenza A matrix gene PCR may be done outside the reference laboratory following discussion with the jurisdictional PCR laboratory. In that case all positive samples must be urgently referred for confirmation and subtyping. 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 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 avian influenza should be directed to your local public health officer, infectious diseases physician or clinical microbiologist**



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## **Recommendations for laboratory investigation of suspected H7N9 avian influenza infection**

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

Gloves, gown, P2 mask and eye protection should be worn when collecting samples from patients with suspected H7N9 avian influenza infection. Sample processing within the laboratory can be undertaken using PC2 precautions, processing of opened samples in a biosafety cabinet and use of PPE including a surgical mask and eye protection. Virus cultures can only be opened and a PC3 facility, and all live virus must be retained within a PC3 facility.

### **Respiratory tract samples**

- Currently we do not know the patterns of excretion or the duration of shedding of H7N9 avian influenza. 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 H7N9 avian influenza 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.
- 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 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 avian influenza testing.

**Routine pneumonia biochemistry, haematology, bacteriology and other testing should be carried out at the facility managing the suspect patient using PC-2 precautions and in accordance with the PHLN guidelines for specimen handling.**



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**Table 1 –H7N9 avian influenza investigations showing specimen type and day of collection, based on days equals days after onset of illness)**

<b>Type Of Specimen</b>	<b>Day Specimen To Be Collected</b>
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 H7N9 avian influenza infection AND the patient remains clinically unwell AND the cause has not been determined.
Bronchoalveolar samples or lung tissue	When available
Blood	Serum on presentation and on days 7-10 and 21-28 after disease onset.
Lung tissue	When possible.

**Typical testing protocol for suspected H7N9 avian influenza 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, *Chlamydomphila pneumoniae*,

PLUS

Virus isolation (where available)

PLUS

Routine tests as per local protocols for pneumonia including bacterial and fungal culture and other relevant (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*, *Chlamydomphila pneumoniae*, influenza A and B, parainfluenza types 1-3, RSV, adenovirus, human metapneumovirus, rhinovirus, enterovirus, human coronaviruses



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PLUS

Virus isolation (where available)

PLUS

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

#### ▪ **Blood**

Serum at presentation and on days 7-10 and 21-28 after disease onset.

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*.