1 Title

HA Guidance for Laboratory Diagnosis of Human Swine Influenza* (HSI) / Influenza A (H1N1).

2 Background

It aims at achieving early diagnosis of severe cases and virus isolation for monitoring of virological profile of the isolates. The laboratory network\(^1\) between Department of Health (DH) and Hospital Authority (HA) on molecular diagnosis of emerging infections has been fully activated to provide rapid molecular test (RT-PCR) for HSI.

3 Preferred Specimens for RT-PCR Test for HSI / H1N1

3.1 Collect the following types of specimens, in accordance with the recommended infection control measures;

3.2 Send specimens to hospital laboratory as soon as possible.

<table>
<thead>
<tr>
<th>Specimen(^2)</th>
<th>Collection</th>
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<tbody>
<tr>
<td>Nasopharyngeal swab (NPS) or A combined oro-pharyngeal (throat) and nasal swab in the same T/M bottle or</td>
<td>Use swabs with a synthetic tip (e.g. flocked swab, polyester or Dacron), vigorously swab mucous membrane and place into viral transport media (“T/M”).</td>
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<tr>
<td>Nasopharyngeal aspirate (NPA) or Endotracheal aspirate (for intubated patient) or Bronchoalveolar lavage (BAL) if available</td>
<td>Place the aspirate into viral transport media (“T/M”)</td>
</tr>
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\(^1\) Laboratory network includes laboratories of Public Health Laboratory Centre, Queen Elizabeth Hospital (QEH), Queen Mary Hospital (QMH), Princess Margaret Hospital (PMH), Prince of Wales Hospital (PWH), Tuen Mun Hospital (TMH) and United Christian Hospital (UCH).

\(^2\) Testing for novel influenza A (H1N1) virus: [http://www.cdc.gov/h1n1flu/specimencollection.htm](http://www.cdc.gov/h1n1flu/specimencollection.htm)

* The **Human Swine Influenza (HSI)** refers to the new influenza virus causing the outbreak first reported in Mexico and subsequently spread to other countries. The virus was renamed by WHO as **Influenza A (H1N1)** on 30 April 2009.
4 Handling of Specimen

4.1 Labeling and Laboratory Request Form

Specimen must be labeled with 2 unique patient identifiers matching the information on the request form. Generate a GCRS request form to enable result capture into ePR and eFlu.

4.2 Packaging

Specimen should be labeled and transported in a triple packaging system in accordance with the guidance outlined in Guidelines on Biosafety in the Clinical Laboratory. Reference: http://www.chp.gov.hk/files/pdf/Guidelines_on_Biosafety_in_the_Clinical_Laboratory_2nd_Edn.pdf

4.3 Transportation

Send specimens to the laboratory as soon as possible. For outside hospital transport, they should be kept at 4°C and upright during transport to minimize the possibility of spillage.

5 Diagnostic Tests of HSI

5.1 PCR Tests

PCR assay to detect current HSI virus H1 genes (HSI-H1); PCR for M gene is optional. It could detect influenza strains of all sub-types including H5N1 and H9N2. PCR for human influenza A-H1 and H3 should be performed on a selective basis.

5.2 Viral Culture

Virus isolation requires a BSL-3 facility. The turnaround time may be up to 1 week. Influenza strains of other sub-types, e.g. H5N1, H9N2, could also be detected.

5.3 Paired Sample for Serology Study

To demonstrate a four-fold or more rise in HSI influenza A (H1N1) virus specific antibodies.

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5.4 Limited Role of Rapid Influenza Antigen Test

The Rapid Influenza Antigen Test detects a range of animal influenza A subtypes, including H5N1 and H9N2. While it may detect the HSI Influenza A (H1N1) virus, it may also give false negative results due to its lower sensitivity.

In reporting of result, limitations of the rapid antigen test should be added, e.g. A positive result cannot distinguish influenza A subtypes; a negative result does not exclude influenza virus infection.

6 HSI / Influenza A (H1N1) Test in HA Hospitals (see flowchart in Annex I)

6.1 HA hospitals namely QMH, PWH, TMH, PMH, QEH and UCH are currently providing rapid PCR tests on HSI.

6.2 Service arrangement for PCR assays: each PCR assay takes about 3 hours to complete and in order to shorten the interval from patient admission to laboratory diagnosis, the PCR tests are performed on a 7-day-a-week basis, with one to three test runs per day depending on situation. Please consult hospital microbiologists for the specific testing schedule.

6.3 For patient diagnosis:
   i. Patients tested negative by the hospital laboratory could be taken off isolation or discharged if clinically fit;
   ii. For serious/critical cases, send a sample to PHLC for parallel PCR testing.
   iii. Specimens should also be sent to PHLC for virus culture.
   iv. Refer to the “HA guideline for Triage and Management of Patients with ILI in Mitigation Phase” effective 28 Sept 2009

6.4 For patient discharge:
   i. Refer to the “HA guideline for the Management of the Confirmed Cases of Human Swine Influenza (HSI) at Designated Hospitals”;
   ii. Do not send samples to PHLC for PCR testing.

6.5 Outside office hours, PHLC will have a staff to receive specimens for urgent human swine influenza testing. Please call medical staff at 6909-1776 for testing arrangement.

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6.6 The total maximum capacity of tests per day in these 6 HA laboratories would be around 1,000 tests per day. Under extreme situation, round-the-clock service could be implemented to nearly double the testing capacity.

6.7 The HA hospital laboratories are working closely with the DH PHLC in protocol setting, technology transfer, quality assurance program and confirmation of diagnosis in a timely basis.

6.8 Repeat HSI PCR test is indicated despite of an earlier negative HSI PCR result for any patient showing deterioration in clinical or CXR conditions.

7 Laboratory Biosafety

Processing of clinical specimens (e.g. routine handling of serum and blood samples, preparing smears from patient specimens, and packaging of specimens for transport) should be conducted in a biosafety level 2 facilities. When a procedure or process cannot be conducted within a BSC, an appropriate combination of personal protective equipment (PPE) (including respiratory and eye protection) and physical containment devices (e.g. centrifuge safety cups or sealed rotors) MUST be used. All laboratory workers should wear a laboratory gown, a pair of gloves, and other appropriate PPE when handling specimen. PPE must be removed before leaving the laboratory. Personnel must wash their hands often – especially after handling infectious materials and animals, before leaving the laboratory working areas, and before eating.

References

2. Ruest A, Michaud S, Deslandes S, Frost EH. Comparison of the Directigen flu A+B test, the QuickVue influenza test, and clinical case definition to viral culture and reverse transcription-PCR for rapid diagnosis of influenza virus infection. J Clin Microbiol 2003;41:3487-93
3. Guidance to Influenza Laboratories. WHO Diagnosing Swine Influenza A/H1N1 Infections of current concern 25 April 2009
5. Biosafety Guidelines for Human Swine Influenza A (H1N1) CHP May 2009
6. Laboratory biorisk management for laboratories handling human specimens suspected or confirmed to contain influenza A (H1N1) causing the current international epidemics WHO 6 May 2009.
7. CDC Interim Guidance on Specimen Collection, Processing, and Testing for Patients with Suspected Novel Influenza A (H1N1) Virus Infection. 11 May 2009 http://www.cdc.gov/h1n1flu/specimencollection.htm

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**Note:**

<table>
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<tr>
<td>PMH</td>
<td>Princess Margaret Hospital</td>
</tr>
<tr>
<td>QEH</td>
<td>Queen Elizabeth Hospital</td>
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<tr>
<td>PWH</td>
<td>Prince of Wales Hospital</td>
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<tr>
<td>TMH</td>
<td>Tuen Mun Hospital</td>
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