

## Exercise 5

### Case Management of Suspect Avian Influenza A (H5N1) Infection in Humans - Case Management and Public-Health Action

#### Objectives:

- Identify clinical features of avian influenza A (H5N1) infections in humans
- Demonstrate epidemiologic skills necessary to assess exposure to sources of avian influenza A (H5N1)
- Provide recommendations to health-care providers in the management of influenza A (H5N1) patients
- Minimize the risk of spread or further human illness associated avian influenza A (H5N1)

#### Instructions:

In this exercise, you will work with your group to decide on recommendations for health-care providers on case management and also the public-health actions you will need to take when alerted to a potential avian influenza H5N1 case.

Each segment will be followed by a series of questions. Your facilitator or one person in your group should read the information aloud to group members. Then, work as a group to generate one answer for each question asked.

Time allotted: 2 hours

#### Background

It's Friday afternoon, September 1, 2006. You are at work at the local health department when you get a phone call from Dr. Patel at the university student health clinic. Dr. Patel has been treating a 21-year-old college student named Ben. On August 30, Ben had a high fever and shortly thereafter, he began to have a sore throat. Ben came into the clinic on August 31. He had a fever of 30° C/102.2° F. No other respiratory symptoms were observed.

In speaking with Ben about his recent activities, Dr. Patel learned Ben spent the past two months in Indonesia working on a research project. He arrived back in the United States on August 28.

Dr. Patel prescribed Ben azithromycin and sent him home. Ben has returned to the clinic today with a cough and shortness of breath. Dr. Patel has been hearing about avian influenza A (H5N1) in humans through educational outreach from the State and Local health departments.

**Question 1** – What are common signs and symptoms of seasonal influenza and avian influenza A (H5N1) in humans?

### Additional Background Information

Based on his physical examination, Dr. Patel has decided to admit Ben overnight to the university hospital to receive intravenous (IV) fluids and antibiotics.

Dr. Patel is aware of animal and human cases of avian influenza A (H5N1) in Indonesia. However, since Ben didn't have any cough when he first presented, Dr. Patel didn't think it was influenza. Now that Ben has a cough and shortness of breath, Dr. Patel decided to do a rapid test for influenza A and the result was negative.

**Question 2** – Does a negative result for a rapid influenza A test rule out the possibility that a person is infected with avian influenza A (H5N1)?

**Question 3** – Based on the information at hand, how would you classify Ben according to your case definitions (see Appendix A)? Why?

**Question 4** – Dr. Patel will be hospitalizing Ben. Would you recommend Ben be placed in isolation? Why or why not?

### Recommendations

Dr. Patel asks you “Could this be avian influenza A (H5N1)? What should I do?” You have recommendations for testing and treatment, but first you would like some more information

**Question 5** – What information would you collect from Dr. Patel? Based on what you have already heard you plan to interview Ben, but what additional information would you like for Dr. Patel to get from Ben now?

### Information from Dr. Patel

Dr. Patel has the following information on Ben.

Name: Benjamin Diaz      DOB: 04/15/1985      Race: Hispanic, non-white  
Address: 453 Berkshire Lane #3D, Collegetown, NC 29896  
Home phone: none  
Cell phone: 919.555.8695  
Occupation: student

Contact Name: Dr. Sunil Patel  
Contact Address: University Student Health Center, 300 Patterson Road,  
Collegetown, NC 29894  
Work phone: 919.555.6589  
Pager: 919.555.2874

Additionally, Dr. Patel has learned that:

Ben's project required him to go to rural areas of East Java Province. Ben had contact with more than 50 residents of East Java and notes that many households had chickens that roamed freely in and out of the house. He recalls seeing some dead poultry in a yard where he was conducting an interview, and notes that one of his older subjects was difficult for him to interview due to a cough and respiratory infection, so he had to put his ear close to his mouth to understand him. You find out that H5N1 influenza has been reported in this part of the country. Most cases of H5N1 influenza in humans have been due to transmission from infected poultry or poultry products to people, but you know a real worry with this virus is that it could change rapidly to a virus capable of person-to-person transmission, sparking a deadly epidemic.

So far, you cannot reliably determine whether infected poultry or infected people were Ben's principle exposure.

Ben hasn't spoken to any of his project members except for his advisor, Cassie. She just returned from Indonesia two days ago and was fine when Ben spoke with her.

*\*Please use this information to start filling out a case history – see Appendix B for the WHO standard case report form\**

**Question 6** – Has this new information changed Ben’s case classification? Why or why not?

**Question 7** – What recommendations would you offer about testing for avian influenza A (H5N1)?

**Question 8** – What recommendations would you offer about treatment for Ben as a suspect avian influenza A (H5N1) case?

**Question 9** – Once you hang up with Dr. Patel, what should you do?

#### Update from Dr. Patel’s Office

Dr. Patel’s office calls you an hour later with the information that Ben has now been placed in isolation under the care of Dr. Dorian. Dr. Dorian’s pager number is 210.555.8926.

**Question 10** – What follow up actions would you take?

#### Dr. Dorian

Dr. Dorian returns your page around 3:00 p.m. He has spoken with Dr. Patel who has brought him up to speed on Ben’s situation. Ben has been admitted into the hospital, where he has been placed in a negative pressure isolation room. Ben was placed on IV fluids. Nurse Todd is with Ben collecting specimens from Ben’s oropharyngeal airway. After specimens have been collected, Ben will be given a dose of oseltamivir.

Ben’s fever is 39.2 C/102.6 F, and he is now complaining of a headache in addition to the sore throat, cough and shortness of breath. Blood work and a chest X-ray were ordered, but Dr. Dorian does not have the results.

You ask Dr. Dorian if it would be possible for you to interview Ben. Dr. Dorian agrees to let you interview Ben, but asks you come soon.

**Question 11** – What personal protection steps should you take when speaking with Ben?

**Question 12** – With your group, develop five to 10 key questions that should appear on a questionnaire that you would administer to Ben.

### Laboratory Findings

When you arrive at the university hospital, you head directly to the nurse's desk on the floor where Ben is staying. The nurse pages Dr. Dorian, who appears shortly thereafter. He has a few minutes to talk to you about Ben.

Oropharyngeal and nasopharyngeal swabs have been collected and will be forwarded to the state public-health laboratory for testing. Ben was given oseltamivir.

The following are results from Ben's blood work up and chest x-ray:

<u>Initial laboratory studies</u>	<u>Normal Values</u>
- Leukocyte count of 2800/mm <sup>3</sup>	4,300 - 10,800/mm <sup>3</sup>
- Lymphocyte count of 640/mm <sup>3</sup>	1500 - 4000/mm <sup>3</sup>
- Hemoglobin of 12.5 g/dl	12 - 18 g/dl
- Platelet count of 125,000/mm <sup>3</sup>	150,000 - 400,000/mm <sup>3</sup>
Blood glucose 93.6 mg/dL	39.6 - 126.0 mg/dL
Liver function tests are normal	
Chest x-ray is clear	

**Question 13** – Based on these results, how would you classify Ben's leukocyte, lymphocyte, platelet counts as well as his hemoglobin level? Are these signs compatible with avian influenza A (H5N1)?

### Ben's Interview

You learn Ben arrived in Indonesia on June 16 and went directly to East Java Province, where he stayed in a rural village going door-to-door to interview residents. Project members were assigned to different villages throughout Indonesia, but his advisor, Cassie, was based in East Java Province. She occasionally visited the village to collect Ben's interviews and came to the village on August 26 to collect his last interviews. Otherwise, Ben did not see any of the other project members.

Ben had his own room in a small hotel in the village and made a few friends during his stay. As he told Dr. Patel, he recalled seeing dead chickens and had contact with at least one person who was ill. He returned to the United States on Stargaze Airlines FL#543. It was a 26-hour direct flight, arriving on August 28. His parents picked him up at the airport. He stayed the night with his parents and traveled back to the University the next day.

Ben has one roommate, a medical student on rotation in another state. Ben has not seen the roommate since he left for Indonesia.

Below are the details of Ben's close contacts and their contact information:

Name: Joe Diaz	Relationship: Father	Contact: 210.555.9686
Name: Jaclyn Diaz	Relationship: Mother	Contact: 210.555.9686
Name: Cassie Livingston	Relationship: Advisor	Contact: cannot recall

*\*Please update your case report forms with this information.\**

**Question 14** – With this information, what steps would you take next?

## The Weekend

You spend your Saturday trying to contact Ben's parents and his advisor, Cassie. You manage to track Ben's parents down on Saturday afternoon, September 2, at the hospital. They have just arrived to visit Ben.

They tell you they do not have any symptoms. You complete a contact form for each one.

You receive a phone call from your contact at the CDC. World Health Organization investigators have been working with Indonesian authorities in East Java Province and have determined that influenza A (H5N1) is present in the village where Ben was working. Human-to-human transmission among two families there cannot be ruled out at this point.

**Question 15** – Do you think Ben became infected through human-to-human transmission? What other information would you want to know?

**Question 16** – Would you recommend Ben's parents receive the influenza A (H5N1) vaccine?

## The Weekend (continued)

You are in contact with Dr. Dorian on Saturday and learn Ben's condition is worsening. He is showing signs of respiratory distress and decompensation. He requires supplemental oxygen to maintain normal oxygen levels. Furthermore, his chest x-ray reveals bilateral infiltrates, his blood glucose has risen, and his liver enzymes (AST and ALT) are elevated.

Later that day, you learn from your supervisor that Ben's oropharyngeal swab tested positive by RT-PCR for avian influenza A (H5). Sunday afternoon, the CDC laboratory in Atlanta confirmed that the virus was H5N1. Ben is now a confirmed case. You contact Ben's parents to recommend they receive chemoprophylaxis for influenza A (H5N1) if they are not already.

Finally, on Sunday evening, you manage to get a hold of Cassie. She tells you she has not been feeling well since Friday evening. She just returned from Indonesia on August 30 and thought it was just jet lag. But then she began to run a fever, and subsequently, developed a headache and a cough.

**Question 17** – What recommendations do you offer Ben’s parents? As a group, create a short script for how you would explain your recommendations to his parents.

**Question 18** – What implications does this diagnosis have for potential human-to-human transmission of avian influenza?

**Question 19** – What would you recommend Cassie do? What kind of follow up (case or contact) would you conduct for Cassie?

**Question 20** – Now that Ben is a confirmed case of avian influenza H5N1 and you are following up with Cassie’s contacts, what other actions do you need to take?

**Discussion Question** – What non-pharmaceutical interventions do you recommend, if any, to protect the community? What single over-riding communications objective (“SOCO”) do you want to communicate to the public?

### Conclusion

During the following week, Ben’s respiratory symptoms improved and the fever resolved. Less than a week later he recovered, but was kept in isolation.

Unfortunately, Cassie’s condition deteriorated rapidly. Four days after being hospitalized, Cassie died of multi-organ failure. Tests for influenza A (H5N1) were positive.

No other cases of H5N1 influenza were found among contacts of Ben or Cassie. Whether the Indonesian cases of avian influenza A (H5N1) were transmitted from person to person, or directly from infected birds, was never able to be determined. Any exposure to poultry or poultry products was never documented for Cassie. It is possible that Ben and Cassie were infected through person-to-person transmission, exposure to infected poultry or exposure to contaminated environments. Additional genetic analyses of the H5N1 virus isolated from these cases were undertaken in order to look for genetic changes that could indicate an increased ability of the virus to transmit among humans, but no such changes were found.

## **Appendix A: Interim Case Classification Guidelines**

The case classifications outlined below have been developed as preliminary guidance for use in the event of an avian influenza A (H5N1) outbreak in U.S. domestic poultry and should be adapted, as necessary, for the specific outbreak conditions. This guidance is based on the current state of knowledge regarding human infection with influenza A (H5N1) viruses; however, it may be modified for use during poultry outbreaks caused by other notifiable avian influenza viruses. As of this writing, influenza H5N1 has not been identified among animals or humans in the United States. In addition, no sustained human-to-human transmission of influenza H5N1 has been documented anywhere in the world, consistent with WHO Pandemic Phase 3 (Pandemic Alert Period)\*. This guidance will be updated as our knowledge of the epidemiology of influenza H5N1 changes.

Proposed Interim Influenza Division/CDC Case Definitions of Influenza A (H5N1) in Humans

### **Report under investigation**

Additional information needed on clinical and exposure information

### **Suspect case**

Documented temperature  $\geq 38$  C ( $\geq 100.4$  F) and one of the following: cough, sore throat, and/or respiratory distress AND

One of the following exposures within 10 days of onset

- a. Direct exposure to sick or dead domestic poultry
- b. Direct exposure to surfaces contaminated with poultry feces
- c. Consumption of raw or partially cooked poultry or poultry products
- d. Close contact (within 1 meter or 3 feet) of an ill patient with confirmed or suspected avian influenza A (H5N1) virus infection
- e. Works with live HPAI (H5N1) virus in a laboratory
- f. Laboratory test for avian influenza A (H5N1) is pending, inadequate or unavailable

### **Confirmed H5N1 case**

Positive for avian influenza A (H5N1) virus by one of the following methods

- a. Isolation of H5N1 from viral culture
- b. Positive RT-PCR for H5N1
- c. Four-fold rise in H5N1 specific antibody titer by microneutralization assay in paired sera
- d. Positive IFA for H5 antigen using H5N1 monoclonal antibodies

### **Not a case**

Negative avian influenza A (H5N1) virus testing result from a sensitive laboratory testing method using adequate and appropriately timed clinical specimens



## Appendix B: WHO template for case report form

[http://www.who.int/csr/disease/avian\\_influenza/guidelines/global-surveillance.pdf](http://www.who.int/csr/disease/avian_influenza/guidelines/global-surveillance.pdf)

### Case report form - Influenza A/H5

Case unique identifier \_\_\_\_\_

#### 1. Reporting details

Name of reporting Country or Territory \_\_\_\_\_

Date of report to National Health Authorities (dd/mm/yyyy) \_\_\_\_/\_\_\_\_/\_\_\_\_

Contact details of person submitting the report

Name \_\_\_\_\_

Institution/Organization \_\_\_\_\_

Address \_\_\_\_\_

Telephone \_\_\_\_\_

Fax

E-mail \_\_\_\_\_

First administrative level from where person was reported \_\_\_\_\_

(Defined as first public-health jurisdictional level below the national level)

Second administrative level from where person was reported \_\_\_\_\_

(Defined as second public-health jurisdictional level below the national level)

City/town/village from where person was reported \_\_\_\_\_

Date that person first came to the attention of local public-health authorities

(dd/mm/yyyy) \_\_\_\_/\_\_\_\_/\_\_\_\_

#### 2. Demographic details

Sex Male  Female  Unknown

Date of birth (dd/mm/yyyy) \_\_\_\_/\_\_\_\_/\_\_\_\_

Age \_\_\_\_\_ expressed in  
Years  Months

Current contact details Full address \_\_\_\_\_

Country \_\_\_\_\_

Telephone \_\_\_\_\_

Fax \_\_\_\_\_

Nationality \_\_\_\_\_

Ethnicity \_\_\_\_\_

### 3. Signs and symptoms

Date of onset of illness (dd/mm/yyyy) \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_  
 Body temperature higher than or equal to 38°C\* Yes  No  Unknown   
 Cough Yes  No  Unknown   
 Sore throat Yes  No  Unknown   
 Shortness of breath Yes  No  Unknown

### 4. History of admission to hospital

Has the person been admitted to hospital Yes  No  Unknown

If Yes, complete table<sup>1</sup> below

**Note:** If the person became ill while in hospital, include these details of this hospital stay under Hospital 01 in the table. Under these circumstances the date of admission should precede the date of onset of symptoms.

	Name of the hospital or hospital identifier	Second administrative level where hospital is located	Date of admission to hospital (dd/mm/yyyy)	Has the person been isolated or cohorted	Date isolated or cohorted (dd/mm/yyyy)	Date person discharged from hospital <sup>2</sup> (dd/mm/yyyy)
Hospital 01				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		
Hospital 02				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		
Hospital 03				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		
Hospital 04				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		
Hospital 05				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		

<sup>1</sup> Add as many lines as needed to accommodate all hospitals in which the case was admitted

<sup>2</sup> Date case discharged from hospital: this corresponds to the date of discharge OR date of transfer OR date of death

**To be completed ONLY once**

Termination date of hospital stay (correspond to date of discharge from **final** hospital, or date of death) (dd/mm/yyyy)

\_\_\_\_/\_\_\_\_/\_\_\_\_

During any of the hospital admissions was the person:

Isolated or cohorted    Yes     No     Unknown     If Yes, date of isolation in **final** hospital (dd/mm/yyyy)

\_\_\_\_/\_\_\_\_/\_\_\_\_

Mechanically ventilated    Yes     No     Unknown

Admitted to an intensive care unit    Yes     No     Unknown

## 5. Travel history

During the 10 days (U.S. modification) prior to the onset of symptoms, did the person travel to or reside **outside** the reporting country or territory? Yes  No

Unknown

If Yes, complete itinerary in table<sup>3</sup> below

Place of departure	Country / territory of departure	HPAI outbreak reported in the animal populations of country/territory of departure	Date of departure (dd/mm/yyyy)	Primary means of transport 1. Plane 2. Boat 3. Train 4. Bus 5. Other	Place of arrival	Country / territory of arrival	HPAI outbreak reported in the animal populations of country/territory of arrival	Date of arrival (dd/mm/yyyy)
		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>					Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>					Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>					Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>					Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>					Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>					Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	

**Note:** Although detailed information contained in this table is not included in the line listing, WHO may request for it to be made readily available should it be needed for international outbreak control purposes.

<sup>3</sup> Add as many lines as needed to accommodate all places visited

During the 10\* days prior to the onset of symptoms, did the person travel to or reside in areas **within** the reporting country or territory? Yes  No  Unknown

If Yes, complete itinerary in table<sup>4</sup> below

Area of departure (Second administrative level)	HPAI outbreak reported in the animal populations of area of departure	Date of departure (dd/mm/yyyy)	Primary mean of transport 1. Plane, 2. Boat, 3. Train, 4. Bus, 5. Other	Area of arrival (Second administrative level)	HPAI outbreak reported in the animal populations of area of arrival	Date of arrival (dd/mm/yyyy)
	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>				Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	

<sup>4</sup> Add as many lines as needed to accommodate all places visited

## 6. Occupational exposure

During the 10\* days prior to the onset of symptoms, has the person been working:

**6a** In an at-risk animal-related occupation<sup>5</sup>      Yes    No    Unknown

**6b** As a worker in laboratory where samples are tested  
for influenza A/H5 viruses      Yes    No    Unknown

**6c** As a health-care worker      Yes    No    Unknown

## 7. History of exposure to animal populations

During the 10\* days prior to the onset of symptoms, has the person:

	<i>7a</i>	<i>7b</i>	<i>7c</i>
	Contact (within 1 meter or 3 feet) with any live or dead animal of species listed	Entered settings where animal species were confined or had been confined in the previous six weeks	If Yes to <i>7a</i> or <i>7b</i> , and exposure occurred outside the reporting country/territory, list all countries/territories where these exposures occurred
Domestic fowl <sup>6</sup>	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	_____ _____ _____
Wild birds	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	_____ _____ _____
Swine	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	_____ _____ _____

<sup>5</sup> At-risk animal-related occupations include occupations such as: domestic fowl or swine farm worker, domestic fowl processing plant worker, domestic fowl culler (catching birds, bagging birds, transporting birds, disposing of dead birds), worker in live animal market, chef working with live or recently killed domestic fowls, dealer or trader of pet birds.

<sup>6</sup> Domestic fowl are birds that are commonly reared for their flesh, eggs or feathers and kept in a yard or similar enclosure, including chickens, ducks, geese, turkeys, guinea-fowls.

## 8. History of exposure to human cases

During the 10\* days prior to the onset of symptoms, has the person been in contact (within touching or speaking distance) with:

**8a** A confirmed human case of influenza A/H5 infection Yes  No  Unknown

If Yes, indicate unique identifier of confirmed case identified in 8.a. \_\_\_\_\_

**8b** A person with an unexplained acute respiratory illness that later resulted in death Yes  No  Unknown

**8c** Any other person for whom diagnosis of influenza A/H5 is being considered<sup>7</sup> Yes  No  Unknown

**8d** If Yes to 8a or 8b or 8c, the person is part of a cluster<sup>8</sup>, tick "Applicable" Applicable  Not applicable

**8e** If Applicable, is the cluster: Already known , indicate cluster identifier<sup>9</sup> in 8f  
Newly identified , assign and indicate cluster<sup>9</sup> identifier in 8f

**8f** Indicate cluster identifier<sup>9</sup> \_\_\_\_\_

What is the setting of this cluster

- Household
- Extended family
- Hospital
- Other residential institution
- Military barracks
- Recreational camps
- Other , specify \_\_\_\_\_

### Summary of exposure history

No reported at-risk animal exposure and no laboratory occupational exposure:

tick "Applicable" if "No" to **6.a.**, and **6.b.**, and **all 7.a.**, and **all 7.b.**

Applicable  Not applicable

Exposure history is unknown or undetermined:

Tick "Applicable" if "Unknown" or **blank** to all the following items: **6.a.**, and **6.b.**, and **6.c.**, and **all 7.a.**, and **all 7.b.**, and **8.a.**, and **8.b.**, and **8.c.**

Applicable  Not applicable

<sup>7</sup> a person for whom diagnosis of influenza A/H5 viral infection is being considered: include all case categories that are not confirmed.

<sup>8</sup> A "cluster" is defined as two or more persons for whom the diagnosis of influenza A/H5 is being considered (including those persons who have died of an unexplained acute respiratory illness) with onset of symptoms within the same two-week period and who are associated with a specific setting such as a household, extended family, hospital, other residential institution, military barracks or recreational camp.

<sup>9</sup> Cluster identifier: Suggested to use unique identifier of the first identified case in the cluster as cluster identifier.

**9. Laboratory investigation results**

Positive influenza A by rapid test Yes  No   
Unknown

High influenza A/H5 specific antibodies detected in a single serum specimen Yes  No   
Unknown

If Yes, indicate titer \_\_\_\_\_

Positive viral culture for influenza A/H5 Yes  No   
Unknown

Positive polymerase chain reaction (PCR) for influenza A/H5 Yes  No   
Unknown

Positive immunofluorescence antibody (IFA) test for H5 antigen using H5 monoclonal antibodies Yes  No   
Unknown

4-fold rise in H5-specific antibody titer in paired serum samples Yes  No   
Unknown

Has influenza A/H5 virus subtype been identified Yes  No   
Unknown

If Yes, specify \_\_\_\_\_

Were samples or isolates sent for further confirmation to a WHO reference laboratories for diagnosis of influenza A/H5 infection <sup>10</sup> Yes  No   
Unknown

If Yes, indicate laboratory:

National Institute of Infectious Diseases, Japan Yes  No   
Unknown

Centers for Disease Control and Prevention, US Yes  No   
Unknown

National Institute for Medical Research, UK Yes  No   
Unknown

St. Jude Children's Research Hospital, US Yes  No   
Unknown

National Influenza Center - Government Virus Unit

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<sup>10</sup> See Annex 6: WHO reference laboratories for diagnosis of influenza A/H5 infection

Hong Kong - SAR China

Yes  No

Unknown

The University of Hong Kong, Queen Mary Hospital

Hong Kong - SAR China

Yes  No

Unknown

Institut Pasteur, France

Yes  No

Unknown

Other

Yes  No

Unknown

If Yes, specify \_\_\_\_\_

### 10. Prophylaxis against influenza

Was the person vaccinated against influenza in the six months prior to the onset of symptoms

Yes  No

Unknown

If Yes, in which country \_\_\_\_\_

During the 10\* days prior to the onset of symptoms has the person been taking any of the following medications

	Medication		Was the medication taken every day during this 10* day period
Oseltamivir phosphate (Tamiflu®)	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	If Yes,	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>
Zanimivir (Relenza®)	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>
Amantadine (Symadine®, Symmetrel®)	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>
Rimantadine (Flumadine®)	Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>		Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>



## Appendix C

# This is an official CDC HEALTH UPDATE

Distributed via Health Alert Network  
Wednesday, June 07, 2006, 19:50 EDT (7:50 PM EDT)  
CDCHAN-00246-2006-06-07-UPD-N

## Updated Interim Guidance for Laboratory Testing of Persons with Suspected Infection with Avian Influenza A (H5N1) Virus in the United States

This update provides revised interim guidance for testing of suspected human cases of avian influenza A (H5N1) in the United States and is based on the current state of knowledge regarding human infection with H5N1 viruses. The epidemiology of H5N1 human infections has not changed significantly since February 2004. Therefore, CDC recommends that H5N1 surveillance in the United States remain at the enhanced level first established at that time. However, this revised interim guidance provides an updated case definition of a suspected H5N1 human case for the purpose of determining when testing should be undertaken and also provides more detailed information on laboratory testing. Effective surveillance will continue to rely on health-care providers obtaining information regarding international travel and other exposure risks from persons with specified respiratory symptoms as detailed in the recommendations below. This guidance will be updated as the epidemiology of H5N1 changes. Note: CDC is revising its interim guidance for infection control precautions for avian influenza A (H5N1). These will be issued as soon as they are available.

### Current Situation:

The avian influenza A (H5N1) epizootic (animal outbreak) in Asia has expanded to wild birds and/or poultry in parts of Europe, the Near East and Africa. Sporadic human infections with H5N1 continue to be reported and have most recently occurred in China, Egypt, Indonesia, Azerbaijan, Cambodia, and Djibouti. In addition, rare instances of probable human-to-human transmission associated with H5N1 viruses have occurred, most recently in a family cluster in Indonesia. So far, however, the spread of H5N1 virus from person to person has been rare, inefficient and unsustainable. The total number of confirmed human cases of H5N1 reported as of June 7, 2006, has reached 225. The case fatality rate for these reported cases continues to be approximately 50 percent. As of this date, H5N1 has not been identified among animals or humans in the United States.

The epizootic in Asia and parts of Europe, the Near East and Africa is not expected to diminish significantly in the short term, and it is likely that H5N1 infection among birds has become enzootic in certain areas. It is expected that human infections resulting from direct contact with infected poultry will continue to occur in affected countries. Since no sustained human-to-human transmission of influenza H5N1 has been documented anywhere in the world, the current phase of alert, based on the World Health Organization (WHO) global influenza preparedness plan, remains at Phase 3 (Pandemic Alert).<sup>\*</sup> In addition, no evidence for genetic reassortment between human and avian influenza A virus genes has been found. Nevertheless, this expanding epizootic continues to pose an important and growing public health threat. CDC is in communication with WHO and other national and international agencies and continues to monitor the situation closely.

### Reporting and Testing Guidelines:

CDC recommends maintaining the enhanced surveillance efforts practiced currently by state and local health departments, hospitals, and clinicians to identify patients at increased risk for avian influenza A (H5N1). Guidance for enhanced surveillance was first described in a HAN update issued on February 3, 2004, and most recently updated on February 4, 2005.

Testing for avian influenza A (H5N1) virus infection is recommended for:

A patient who has an illness that:

- requires hospitalization or is fatal; AND
- has or had a documented temperature of  $\geq 38^{\circ}\text{C}$  ( $\geq 100.4^{\circ}\text{F}$ ); AND
- has radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternate diagnosis has not been established; AND
- has at least one of the following potential exposures within 10 days of symptom onset:

A) History of travel to a country with influenza H5N1 documented in poultry, wild birds, and/or humans,<sup>†</sup> AND had at least one of the following potential exposures during travel:

- direct contact with (e.g., touching) sick or dead domestic poultry;
- direct contact with surfaces contaminated with poultry feces;
- consumption of raw or incompletely cooked poultry or poultry products;
- direct contact with sick or dead wild birds suspected or confirmed to have influenza H5N1;
- close contact (approach within 1 meter [approx. 3 feet]) of a person who was hospitalized or died due to a severe unexplained respiratory illness;

B) Close contact (approach within 1 meter [approx. 3 feet]) of an ill patient who was confirmed or suspected to have H5N1;

C) Worked with live influenza H5N1 virus in a laboratory.

Testing for avian influenza A (H5N1) virus infection can be considered on a case-by-case basis, in consultation with local and state health departments, for:

- A patient with mild or atypical disease<sup>‡</sup> (hospitalized or ambulatory) who has one of the exposures listed above (criteria A, B, or C); OR
- A patient with severe or fatal respiratory disease whose epidemiological information is uncertain, unavailable, or otherwise suspicious, but does not meet the criteria above (examples include: a returned traveler from an influenza H5N1-affected country whose exposures are unclear or suspicious, a person who had contact with sick or well-appearing poultry, etc.)

Clinicians should contact their local or state health department as soon as possible to report any suspected human case of influenza H5N1 in the United States.

Specimen Collection and Testing Guidelines:

- Oropharyngeal swab specimens and lower respiratory tract specimens (e.g., bronchoalveolar lavage or tracheal aspirates) are preferred because they appear to contain the highest quantity of virus for influenza H5N1 detection, as determined on the basis of available data. Nasal or nasopharyngeal swab specimens are acceptable, but may contain less virus, and therefore, not be optimal specimens for virus detection.

- Detection of influenza H5N1 is more likely from specimens collected within the first three days of illness onset. If possible, serial specimens should be obtained over several days from the same patient.

- Bronchoalveolar lavage is considered to be a high-risk aerosol-generating procedure. Therefore, infection control precautions should include the use of gloves, gown, goggles or face shield, and a fit-tested respirator with an N-95 or higher rated filter. A loose-fitting powered air-purifying respirator (PAPR) may be used if fit-testing is not possible (for example, if the person has a beard). Detailed guidance on infection control precautions for health care workers caring for suspected influenza H5N1 patients is available.||

- Swabs used for specimen collection should have a Dacron tip and an aluminum or plastic shaft. Swabs with calcium alginate or cotton tips and wooden shafts are not recommended.§ Specimens should be placed at 4°C immediately after collection.

- For reverse-transcriptase polymerase chain reaction (RT-PCR) analysis, nucleic acid extraction lysis buffer can be added to specimens (for virus inactivation and RNA stabilization), after which specimens can be stored and shipped at 4°C. Otherwise, specimens should be frozen at or below -70°C and shipped on dry ice. For viral isolation, specimens can be stored and shipped at 4°C. If specimens are not expected to be inoculated into culture within two days, they should be frozen at or below -70°C and shipped on dry ice. Avoid repeated freeze/thaw cycles.
- Influenza H5N1-specific RT-PCR testing conducted under Biosafety Level 2 conditions is the preferred method for diagnosis. All state public-health laboratories, several local public-health laboratories, and CDC are able to perform influenza H5N1 RT-PCR testing, and are the recommended sites for initial diagnosis.
- Viral culture should NOT be attempted on specimens from patients suspected to have influenza H5N1, unless conducted under Biosafety Level 3 conditions with enhancements.
- Commercial rapid influenza antigen testing in the evaluation of suspected influenza H5N1 cases should be interpreted with caution. Clinicians should be aware that these tests have relatively low sensitivities, and a negative result would not exclude a diagnosis of influenza H5N1. In addition, a positive result does not distinguish between seasonal and avian influenza A viruses.
- Serologic testing for influenza H5N1-specific antibody, using appropriately timed specimens, can be considered if other influenza H5N1 diagnostic testing methods are unsuccessful (for example, due to delays in respiratory specimen collection). Paired serum specimens from the same patient are required for influenza H5N1 diagnosis: one sample should be tested within the first week of illness, and a second sample should be tested 2-4 weeks later. A demonstrated rise in the H5N1-specific antibody level is required for a diagnosis of H5N1 infection. Currently, the microneutralization assay, which requires live virus, is the recommended test for measuring H5N1-specific antibody. Any work with live wild-type highly-pathogenic influenza H5N1 viruses must be conducted in a USDA-approved Biosafety Level 3 enhanced containment facility. Visit <http://www.cdc.gov/flu/h2n2bsl3.htm> for more information about procedures and facilities recommended for manipulating highly pathogenic avian influenza viruses.

Laboratory testing results positive for influenza A (H5N1) in the United States should be confirmed at CDC, which has been designated as a WHO H5 Reference Laboratory. Before sending specimens, state and local health departments should contact CDC's on-call epidemiologist at (404) 639-3747 or (404) 639-3591 (Monday – Friday, 8:30 AM - 5:00 PM) or (770) 488-7100 (all other times).

#### Travel Health Notice:

CDC has not recommended that the general public avoid travel to any of the countries affected by H5N1. However, CDC does recommend that travelers to these countries avoid poultry farms and bird markets or other places where live poultry are raised or kept. For details about other ways to reduce the risk of infection, see [http://www.cdc.gov/travel/other/avian\\_influenza\\_se\\_asia\\_2005.htm](http://www.cdc.gov/travel/other/avian_influenza_se_asia_2005.htm).

#### More Information:

Department of Health and Human Services at [www.pandemicflu.gov](http://www.pandemicflu.gov)

World Health Organization at

World Organization for Animal Health (OIE) at [http://www.oie.int/eng/en\\_index.htm](http://www.oie.int/eng/en_index.htm)

\*For the current WHO Pandemic Phase, see [http://www.who.int/csr/disease/avian\\_influenza/phase/en/index.html](http://www.who.int/csr/disease/avian_influenza/phase/en/index.html).

† For a listing of influenza H5N1-affected countries, visit the CDC website at <http://www.cdc.gov/flu/avian/outbreaks/current.htm>; the OIE website at [http://www.oie.int/eng/en\\_index.htm](http://www.oie.int/eng/en_index.htm); and the WHO website at [http://www.who.int/csr/disease/avian\\_influenza/en/](http://www.who.int/csr/disease/avian_influenza/en/).

‡ For example, a patient with respiratory illness and fever who does not require hospitalization or a patient with significant neurologic or gastrointestinal symptoms in the absence of respiratory disease.

|| Interim recommendations for infection control in health-care facilities caring for patients with known or suspected avian influenza are available at <http://www.cdc.gov/flu/avian/professional/infect-control.htm>.

§ Specimens can be transported in viral transport media, Hanks balanced salt solution, cell culture medium, tryptose-phosphate broth, veal infusion broth, or sucrose-phosphate buffer. Transport media should be supplemented with protein, such as bovine serum albumin or gelatin, to a concentration of 0.5% to 1%.

Information regarding Laboratory Biosafety Level Criteria can be found at <http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4s3.htm>.

##This Message was distributed to State and Local Health Officers, Public Information Officers, Epidemiologists, State Laboratory Directors, Weapons of Mass Destruction Coordinators and HAN Coordinators, as well as Public Health Associations and Clinician organizations##