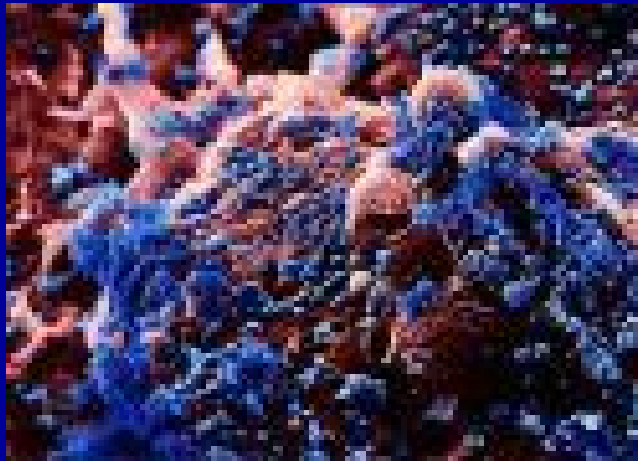


Module 6: Case Management of Suspect Human Avian Influenza Infection



Part 1: Background information on clinical features and management of avian influenza

Learning Objectives

- **Recognize clinical features of H5N1 in humans**
- **Understand how information about the patient *before* onset of illness can help you suspect infection**
- **Know the types of treatment options available**

Part 1 Session Overview

- **Clinical features**
- **Epidemiologic information**
 - Risk for infection
 - Transmission
- **Laboratory diagnosis**
- **Current antiviral medications**
- **Group exercise**

Illness Scenario

- **5-year-old Ahmad sick for five days**
 - Fever
 - Watery diarrhea
 - Headache
 - Cough
 - Short of breath
- **No one else sick**
- **Ahmad and a friend play with chickens**

Question: *Is this avian influenza?
What should Dr. Sara do?*

Clinical Features

General Information

	Human influenza	Avian influenza
Vulnerable Age Groups	<ul style="list-style-type: none">• All ages affected• Highest rates in children < 5 years• Most serious complications in elderly >60 years	<ul style="list-style-type: none">• Children• Adolescents• Healthy young adults• High fatality rate in all groups
Time from exposure to illness	<ul style="list-style-type: none">• Mean 2 days• Range: 1 – 5 days	<ul style="list-style-type: none">• Mean 2 – 3 days• Range: 2 – 8 days

Signs and Symptoms

Human Influenza

Avian Influenza (H5N1)

Type of infection

Upper and lower respiratory

Lower respiratory with pneumonia

Fever

Yes

Yes

Headache

Yes

Yes

Cough

Yes

Yes

Respiratory symptoms

Varies; sore throat to difficulty breathing

Difficulty breathing, tachypnea, sputum

Gastrointestinal symptoms

Uncommon, except children, elderly

Variable, watery diarrhea, vomiting, abdominal pain

Recovery

2-7 days

High mortality

Unusual Presentations

- **Knowledge of avian influenza infection in humans changes as we learn more**
- **Unusual presentations**
 - **Initial absence of respiratory symptoms**
 - **Severe watery diarrhea**
 - **Altered mental status, loss of consciousness**

Clinical Features among Patients with H5N1 (2)

Presentation (%)	HK (N=18)	Thai (N=17)	VT (N=10)	HCM (N=10)	Cam (N=4)
● Fever	94	100	100	100	100
● Cough	67	100	100	100	100
● Dyspnea	6	100	100	100	NA
● Diarrhea	17	41	70	NA	50
● Myalgia	11	53	0	20	NA
● Pulm. Infiltrate	61	100	100	100	100

Clinical Course of H5N1 Illness, December 2003 – April 2006

- **Median time from illness onset to hospitalization: 4 days (range, 0 - 18 days)**
- **Case-fatality rate: 56%**
- **Median time from illness onset to death: 9 days (2 - 31 days)**

Clinical Features among Patients with H5N1 (3)

Outcomes (%)	HK (N=18)	Thai (N=17)	VT (N=10)	HCM (N=10)	Cam (N=4)
Respiratory failure	44	76	90	70	100
Renal dysfunction	22	29	10	20	NA
Time from onset of illness to death (d)	23 (8-29)	12 (9-16)	9 (4-17)	12.8 (4-21)	8 (6-10)
Death (%)	33	71	80	80	100

(N Engl J Med 2005;353:1374-85.)

Complications

Seasonal Influenza

- Ear infection, sinusitis
- Bronchitis, bronchiolitis
- Pneumonia
 - viral or secondary bacterial
- Exacerbation of chronic conditions
- Muscle inflammation
- Neurologic Disease
 - Seizures
 - Brain inflammation
 - Reye's syndrome

Avian Influenza

- Almost all develop pneumonia
- Acute Respiratory Distress Syndrome (ARDS)
- Multi-organ failure
- Encephalopathy
- Mucosal bleeding

Clinical Complications- Avian Influenza

- **Acute Respiratory Distress Syndrome**
- **Respiratory failure**
 - May occur within a few days to 2 weeks after illness onset
- **Multiple organ failure**
 - Renal dysfunction
 - Cardiac problems
 - ↓ lymphocytes and platelets
 - Hypotension
 - Arrhythmia

Normal lymphocytes

1500 - 4000 / mm³

Normal platelet count

150,000 - 400,000 / mm³

Imaging

X-ray changes are common in the lungs of avian influenza patients

- **Non-specific changes**
- **Diffuse or patchy infiltrates**
- **Fluid in the space surrounding the lungs**
- **Cavities uncommon**



BBC News. <http://bbb.co.uk>
Saturday, 3 December 2005

Avian Influenza Chest X-Ray



Day 5 —————> Day 7 —————> Day 10

**Chest x-ray of an avian influenza patient,
shown by day of illness**

Tran Tinh Hien, Nguyen Thanh Liem, Nguyen Thi Dung, et al. *New England Journal of Medicine*. 18 March, 2004. vol. 350 no. 12. pp 1179-1188. ¹⁵

Radiologic Findings of 17-H5N1 Patients, Thailand, 2004

Radiologic findings	Survived (N=5)	Died (N=12)	P
CXR (early)			
- interstitial	1	1	0.51
- lobar, patchy	4	11	
CXR (late)			
- ARDS (diffuse bilateral)	1	12	0.02
- No ARDS	4	0	

Clinical Laboratory Findings

Commonly associated with avian influenza:

- **Drop in white blood cell count (lymphocytes)**
- **Mild to moderate drop in blood platelet count**
- **Increased aminotransferases (liver enzymes)**

Hani and Ahmad

Question:

Do you think Ahmad has signs and symptoms of avian influenza? Why or why not?

Epidemiologic Information

History: Risk Factors for Infection

Within 7-10 days before symptoms begin:

- Close contact with live, sick, or dead birds
- In setting with confined birds
- Contact with contaminated surfaces or environments
- Travel or residence in area affected by avian influenza outbreaks in animals

Note: There is no risk of getting H5N1 by eating well cooked food



History: Risk Factors for Infection

- Uncertain risk of person-to-person spread
- **Within 7-10 days before symptoms begin:**
 - Face-to-face contact
 - Touching or within 1 meter of suspected or diagnosed H5N1 patient without proper precautions
 - Touching or being within 1 meter of a person who has severe pneumonia or dies from an acute respiratory illness without proper precautions

Hani and Ahmad

Question:

Do you think Ahmad is at risk for avian influenza H5N1 infection?

Why or why not?

Hani and Ahmad

Question:

Has Ahmad had an exposure that could lead to transmission?

Using All of The Information



A Clinician Should Suspect H5N1 Infection if a Patient Has:

- **Unexplained acute respiratory illness with fever**
- **Exposure within 7-10 days before symptoms to:**
 - **Suspect / diagnosed H5N1 patient**
 - **Poultry or wild birds**
- **Residence in or recent travel to an area with known H5N1 activity in poultry**

Use All Information

- **Clinical signs compatible with avian influenza**
- **History compatible with exposure to avian influenza**
- **If yes → this is a suspected case →**
 - **Send samples for laboratory confirmation**
 - **Initiate treatment**
 - **Implement appropriate infection control practices**
 - **Alert public health authorities**

Ahmad's Situation

- **5-year-old Ahmad sick for five days**
 - Fever
 - Watery diarrhea
 - Headache
 - Cough
- **No one else sick**
- **Ahmad and a friend play with and hold chickens**

Hani and Ahmad

Question:

Would you suspect avian influenza H5N1 infection? Why or why not?

Hani and Ahmad

Question:

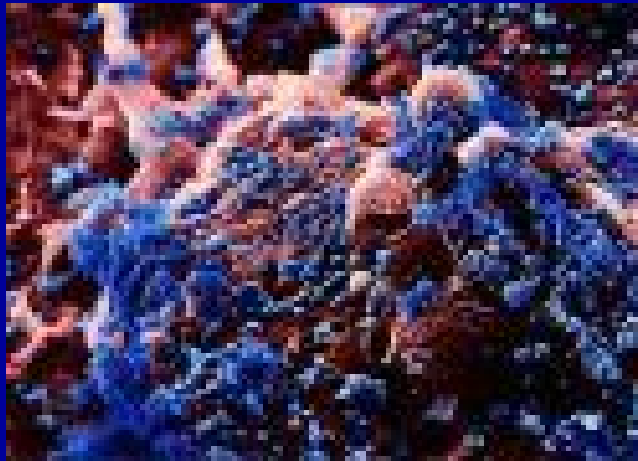
What would you tell Dr. Sara to do?

Part 1 Summary

- **Ask about recent exposure and contact with humans or animals that may have had avian influenza H5N1 infection.**
- **Virology laboratory can confirm H5N1, but you should not wait for the results before initiating treatment or implementing appropriate infection control measures.**
- **Individuals with avian influenza H5N1 infection may progress rapidly to respiratory failure.**

Questions?

Case Management of Suspect Human Avian Influenza Infection



Part 2: Case Management of Suspected Avian Influenza Cases

Learning Objectives

- **Collect appropriate clinical and exposure information**
- **Recognize laboratory tests used for a suspected case patient**
- **Know how to advise on treatments and interventions for suspected case-patients and their contacts**

Session Outline

- **Data to use in managing a suspect case**
 - Clinical data
 - Information from medical charts
 - Epidemiologic context (exposures)
- **Clinical specimens for influenza diagnosis**
- **Administration of medical care**

Assess Suspected Avian Influenza Patients

Assess Suspected Avian Influenza Patients

Does the patient have avian influenza?

- 1. Confirm and / or collect clinical history and physical exam data**
- 2. Evaluate the epidemiologic context**
- 3. Consider clinical, laboratory, and epidemiologic information together**

Clinical Data to Collect

- **Date of illness onset**
- **Symptoms**
- **Clinical measurements**
- **Complications**
 - Type
 - Date of onset
- **Any clinical specimens collected for laboratory testing**

Sample Patient Chart:

Exposure History

Contact with ill people? (If yes, date and name, relationship to patient)

Contact with diseased poultry (Live or dead)? (If yes, date and location)

Recent travel? (If yes, date and location)

Other close patient contacts (Household members, close coworkers)

Epidemiologic Data

- **Potential exposure to H5N1**
 - Occupational exposure
 - Travel or residence in area affected by avian influenza outbreaks in animals
 - Direct contact with dead or diseased birds or other animals in affected area
 - Close contact with a person with unexplained moderate or severe acute respiratory illness



Warning! Even if NO reports of ill poultry in a province, there could be disease in that area, especially if poultry influenza vaccines are used 39

What laboratory tests should be performed for a Suspected Case of Avian Influenza?

Suspected Case: Diagnosis

- **Diagnosing avian influenza**
 - Specimen collection
 - Testing

Clinical Specimens

- **Respiratory**

- Throat swabs and nasal swabs
- Collect as soon as possible
- Collect tracheal specimens from intubated patients

- **Blood**

- Useful for detection of virus RNA
- Antibodies (convalescent sample)

Lab Tests for Influenza A

- **Rapid tests**
 - Commercial kits
 - Results in 15 – 30 minutes
 - NOT sensitive for H5
- **Virus culture**
 - Results in 2 – 10 days
 - Must be done in a special lab
- **PCR**
 - Detects viral genes
 - Results in a few hours
 - Uses respiratory sample, serum or culture
 - Can be specific for H5N1

Diagnosing Avian influenza

- Many countries are developing capacity to test for H5N1 by PCR.
- Regional reference labs can perform PCR, viral culture for H5N1.
 - Do you know where you would send samples for testing if there were a suspected human case of avian influenza?

Diagnosing Avian influenza

- **Rapid antigen tests are insensitive and do not distinguish H5N1 from other influenza viruses**
- **We shouldn't rely on the Rapid Detection Kits?**

Case Management

- **Antivirals**
 - Consider age group
- **Supportive care**
- **Antibiotics**

Current Antiviral Treatment

Neuraminidase Inhibitor

- **Two drugs available**
 - Oseltamivir and zanamivir
 - Should be given as soon as possible
 - Effective for treatment and prevention
 - Used for seasonal and avian influenza



Oseltamivir Treatment in Seasonal Influenza (5 days)

Adults:

75 mg twice a day for 5 days

Children:

<1 year, not studied adequately

≤ 15 kg - 30 mg twice a day

>15 kg to ≤23 kg - 45 mg twice a day

>23 kg to ≤40 kg - 60 mg twice a day

>40 kg - 75 mg twice a day



Oseltamivir Use in H5N1

- **Best dosage for H5N1 uncertain**
 - Use the dose recommended for seasonal influenza
 - Longer treatment (7 to 10 days) or higher doses of unproven benefit
- **Dosage for post-exposure prevention**
 - Once daily for 7 to 10 days after last exposure
- **Side Effects**
 - Nausea and vomiting
 - Skin rash

Zanamivir in H5N1 Illness

- Inhaled by mouth via special device
 - May be used for ≥ 5 years of age
- Unstudied in human H5N1 illness
- Treatment dosage
 - 2 inhalations (10 mg), once in morning and night for 5 days
- Side effects
 - Wheezing, and breathing problems



Supportive Care

Hospital care for proven or suspected avian influenza cases should include the capacity to:

- **Isolate the patient**
- **Provide supplemental oxygen and ventilation**
- **Provide intensive care support for organ failure**
- **Provide low dose corticosteroids for sepsis**

Supportive Care (Continued)

- **Assess respiratory status (transcutaneous oxygen saturation)**
- **Provide supplemental oxygen as indicated**
- **Ventilatory support**
- **Fluids, pressors as needed for hypotension**
- **No aspirin for children < 18 years of age**
 - **Use paracetamol or ibuprofen**

Other Treatments

- **Antibiotics**

- If H5N1 is confirmed, antibiotics can be used for treatment of suspected bacterial infection but not as prophylaxis

- **Corticosteroids**

- Consider low-dose hydrocortisone for sepsis
- Unknown if high dose useful in H5N1 illness
- Risk of side effects

Part 2 Summary

- **Laboratory testing is essential to confirm the diagnosis of avian influenza H5N1**
- **Multiple clinical samples should be collected for influenza diagnosis**
- **Antiviral therapy with oseltamivir should be initiated as soon as possible.**

Glossary

Seasonal Influenza

Expected rise in influenza occurrence among humans living in temperate climates; occurs during the winter season with strains of influenza that have minor changes from season to season.

Avian Influenza

Subtypes of influenza A virus that causes influenza among fowl and poultry and sometimes cause zoonotic infections in humans or other species.

References and Resources

- Writing Committee of WHO Consultation on Human Influenza A/H5. *NEJM* 2005; 353:1374- 1385
- Tran Tinh Hien, et al. Avian Influenza A (H5N1) in 10 Patients in Vietnam. *N Engl J Med* 2004; 350:1179-1181.
- Preliminary clinical and epidemiological description of influenza A (H5N1) in Viet Nam 12 February 2004.
http://www.who.int/csr/disease/avian_influenza/guidelines/vietnamclinical/en/index.html

