32 *Avian Flu—Is the Danger Still there?*

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Abstract: Avian flu is an infection, caused by Avian influenza viruses occurring naturally, among birds. Wild birds and aquatic birds act as reservoir for these viruses. In 1997, first human case of avian influenza was reported. Since then more than 200 human cases have been reported from different parts of the world, namely from eastern Asia, South-east Asia and Europe. Humans do not have natural immunity against avian influenza viruses and this infection in humans causes very high mortality. Among the various avian flu viruses H5N1 virus is of considerable importance as it causes serious disease in humans and has a very high case fatality rate. There is growing concern about a possible pandemic due to these avian influenza viruses.

INTRODUCTION

"Avian Flu" is an infection caused by avian (bird) influenza viruses, which occur naturally among birds. Wild birds and aquatic birds carry these viruses in their intestines but do not get sick.

However, avian influenza is very contagious and can cause devastating epidemics in domesticated birds (chickens, ducks, etc.). Infected birds shed influenza virus in their saliva, nasal secretions and feces. Susceptible birds become infected when they come in contact with contaminated secretions or excretions.

The "Avian Influenza" outbreaks among domestic poultry have been occurring for a long time in different parts of the world. In last two decades Far-East and China have emerged as epicenter of Avian Flu. Although avian influenza usually does not infect humans, rare cases of human infection with avian influenza have been reported since 1997. More recently, more than 200 confirmed cases of human infection with Avian Influenza A (H5N1) have been reported. During an outbreak of avian influenza among poultry, there is a possible risk to people who have contact with infected birds or surfaces contaminated with secretions or excretions.[1-3]

VIRUS

The avian influenza viruses belong to family Orthomyxoviridae. The family contains 5 general, i.e. Influenza A, Influenza B, Influenza C, Thyrotovirus and Isavirus. All past influenza pandemic have been caused by influenza A viruses. Influenza A virus can be of several sub-types. These sub-types differ due to the presence of glycoproteins on the surface of virus; Hemagglutinins (HA) and Neuraminadase (NA). There are 18 known HA sub-types and 9 known NA sub-types. Many different combinations of HA and NA are possible.

H5 subtype can be of either high pathogenic or low pathogenic strain (HPAI and LPAI). H7 and H9 subtype have caused infection in humans rarely. [4]

TRANSMISSION

The main mode of transmission is by consumption of uncooked or partly cooked poultry. Virus can also be transmitted by contact with surfaces contaminated by secretions or by excretions. Swimming or bathing in water contaminated by infected birds, using chicken droppings as manure in fields can also be hazardous. During an outbreak of avian influenza among poultry, there is a possible risk to people who have close contact infected birds or contaminated surfaces. *So far there has been only one documented case of human to human transmission.*

CLINICAL FEATURES

The clinical signs and symptoms of avian influenza (H5N1) may be more protean. During 1997, epidemic in Hong Kong patients exhibited fever, headache, malaise, myalgia, sore throat, cough and rhinitis. Although uncommon, conjunctivitis and gastrointestinal symptoms were also reported. In 2004, epidemic in Vietnam prominent clinical signs and symptoms were those of severe influenza syndromes with fever, cough, diarrhea and shortness of breath. 70% of patients had gastrointestinal symptoms. In 2004, epidemic in Thailand, prominent symptoms were fever, cough, sore throat, rhinorrhea, myalgia and shortness of breath. For confirmed cases of H5N1 reported to WHO by Oct. 31, 2006.[5] see Table 32.1.

LABORATORY DIAGNOSIS

Laboratory identification is commonly performed using direct antigen detection, virus isolation in cell culture, or detection of influenza specific RNA by reverse transcriptase polymerase chain reaction (RT-PCR). In recent years commercial influenza rapid detection kits have become available. These are mostly antigen detection tests which produce results within 30 minutes.[6,7]

Rapid Detection Tests

Rapid detection tests for influenza can be performed on a variety of specimens, i.e. nasal aspirates, nasal washings, sputum, nasopharyngeal swabs and throat swabs. Specimens should be collected as close to the onset of symptoms as possible and not after 4-5 days in adults as virus shedding typically diminishes. In younger children, viral shedding may occur for longer periods and the collection of specimens for testing after 5 days may still be useful. These tests detect a common antigen present on all influenza A and B viruses. However, rapid tests cannot differentiate subtypes of influenza A. Sensitivity and specificity of these tests are 70-75% and 90-95% respectively. During periods of influenza prevalence clinical diagnosis can be highly predictive of influenza (PPV 79-87%, NPV 39-75%).

Immunofluorescent Antibody Staining

The sensitivity of influenza detection in respiratory specimens by immunofluorescent staining ranges between 70-100%, specificity 80-100%, PPV 85-94%, and NPV 96-100%.

Viral culture is considered the gold standard. Polymerase chain reaction assays detect both viable and non-viable influenza virus RNA and are in general more sensitive than culture.

Role of Rapid Test in Clinical Situations[8]

Rapid antigen testing should be carried out when results will influence a clinical decision:

1. Patient management: Patients with lower respiratory tract illness, especially children and adults with medical conditions increasing their risk for developing various complications.
2. Isolation and cohorting of confirmed cases and reduction of inappropriate use of antibiotics.
3. Institutional outbreak management.
4. Semi-closed community outbreak management
5. International travelers.
6. Surveillance.

ANTIVIRAL AGENTS FOR H5N1 INFLUENZA[9]

- Only neuraminadase inhibitors, i.e. zanamivir and oseltamivir should be used for avian influenza:

Zanamivir

- Children: Approved for children ≥ 7 years for treatment.
- 2 inhalations of 5 mg blisters (10 mg), twice a day.
- For Chemoprophylaxis—10 mg OD for persons ≥ 5 years.

Oseltamivir

- Approved for use in persons ≥ 1 year.
- Dose varies according to body weight:
  - ≤ 15 kg-30 mg BD
  - ≤ 15-23 kg-45 mg BD
  - 23-40 kg-60 mg BD
  - ≥ 40 kg 75 mg BD

  Chemoprophylaxis

  - ≤ 15 kg-30 mg OD
  - 15-23 kg-45 mg OD
  - 23-40 kg-60 mg OD
  - ≥ 40 kg-75 mg OD

  Persons aged > 65 years—no reduction in dosage.

Persons with Impaired Renal Function

Zanamivir no dose adjustment for a 5 day course

Oseltamivir—creatinine clearance 15-30 ml/ minute-75 mg OD.

Chemoprophylaxis—75 mg OD.

No dosage recommendation for those undergoing dialysis.

Persons with liver disease: Neither of these agents have been studied in these patients.

Persons with seizure disease: Seizure activity has been noted in the post-marketing use but epidemiological studies have not reported any increased risk of seizures.

Side Effects

Zanamivir —Decrease in FEV_1 by 25%, diarrhea, nausea, sinusitis and bronchitis.

Patients with asthma or chronic obstructive pulmonary disease who use *Zanamivir* are advised to keep a fast acting bronchodilator readily available and consult their physicians if they experience breathing difficulty.

Oseltamivir: Nausea and vomiting. These symptoms are minimized if it is taken with food.

Use during pregnancy: These drugs should be used only when potential benefits justifios the potential risk to fetus.

Infection Control Recommendations for Avian Influenza in Health care Facilities[10,11]

- Use standard and droplet precautions when providing care for patients with acute febrile respiratory illness.
- Respiratory hygiene/cough etiquette.
- Early recognition and reporting of these cases.

- Isolation for suspected and confirmed cases.
- Family members and visitors should be restricted and should use full barrier precautions.
- Treat patient's waste as contaminated with virus
- For dishes, laundry, eating utensils use standard precautions.
- Use long sleeved gown with plastic apron, gloves, face shield, visor or goggles, N95 or EU FP2 mask or surgical mask.
  Facial protection and hand washing are the priorities among the precautions.

Duration of A1
Infection Control Precautions

- Adults (> 12 year)—7 days after resolution of fever.
- Children (< 12 year)—21 days after symptoms onset.

Current WHO Travel Recommendations[12,13]

Advice to Countries

- No travel restrictions to countries currently having outbreaks of H5N1 avian influenza.
- No routine screening of travelers coming from affected countries.

Advice to Travelers

- Travelers to area affected by avian influenza should avoid direct and unprotected exposure to infected birds including feces and undercooked meat and eggs.
- To avoid contact with live animal market, poultry farms or caged poultry.

Use of Seasonal Flu Vaccine in Humans at Risk for H5n1 Infection[14]

- All persons expected to be in contact with poultry or poultry farms.
- Healthcare workers involved with daily care of known or confirmed human cases of H5N1.
- Healthcare workers in emergency care facilities in areas where there is confirmed occurrence of influenza H5N1.

Influenza Pandemic Considerations

Past influenza pandemics occurring in the 20th century, apparently all arose from the Eurasian avian lineage of viruses. Influenza pandemic strains can emerge from the avian lineage either through the process of genetic reassortment between human and avian influenza strains, or through gradual adaptation to the pandemic strains.[15,16]

Current research indicates that 1957 and 1968 pandemics occurred through genetic reassortment. The 1918 pandemic strains, apparently did not originate through a reassortment event, rather, it is likely that an avian strain initially infected humans and gradually adapted to the human population over time to become a pandemic strain.

Of the various avian influenza subtypes H5N1 is of greatest concern due to:
This subtype mutates rapidly[17,18]

- Causes severe disease in humans with a high case fatality rate.
- The virus has spread rapidly throughout the poultry flock in Asia.
- The virus is continuing to spread to other areas of the world including Central Asia, Europe and Africa.
- Recent genetic sequencing performed on viral strains from Turkey, showed that the strains contain two mutations, which may make the virus better adapted to humans.
- The current H5N1 strain is highly pathogenic for humans who do not have natural immunity against it.

At this point there is no evidence of genetic reassortment between avian H5N1 and human viruses, although this remains a concern. The potential for gradual adaptation of H5N1 to humans over time with evolution into a pandemic strain is also a possibility.

A study published in July 2006 attempted to determine whether a synthetic influenza virus made by combining H5N1 avian flu and a human flu virus, would be more contagious than the natural avian H5N1 virus. Findings showed that it was not more easily spread to a ferret model.

According to WHO, at this time the pandemic alert level for H5N1 influenza is at phase 3; a new viral subtype is causing disease in humans but it is not yet spreading efficiently and sustainably. Concern about a possible human pandemic is further heightened by the fact that a long period has elapsed since the H3N2 pandemic of 1968, known as Hong Kong Flu.[19-22]

Pre-pandemic vaccines have been produced by the manufacturers using clade 1 virus (rgA) Vietnam 1194/2004 (NBRG-14) and rgA/Vietnam 1203/2004 (CDCRG-1) and SURG-161052). Clinical trials have been conducted or are underway in several countries and stockpiling of clade 1 vaccines has begun in some countries. However, it is not known if the next influenza pandemic will be caused by H5N1 viruses or which of the clade or sub-clades of H5N1 would be responsible should one occur.[23,24]

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