Emerging Infectious Disease (1): Avian Influenza

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Abstract

Avian influenza is one of the two terrible virus infections, and the other one is severe acute respiratory syndrome (SARS) in early 21th century. Studies showed most avian influenza infections of human were directed invaded by the virus (most H5N1 Strain) from poultry but some case reports suspected the possibility of human-to-human transmission. The most frightening possibility is the reassortment of the high pathologic avian influenza with common human influenza virus. If this occurred, a new virus pandemic, like Spanish flu, may come and cause millions of people die. The most important effort is to halt further spread of epidemics in poultry population. Culling the infected and suspected infected poultry widely is needed. It is also essential to have good hand hygiene, have adequate general precaution and educate people to decrease the opportunity for exposure to poultry or their droppings. Health worker have to wear enough precaution in the hospital. The scientists must do their best to develop vaccine against avian influenza as soon as possible.*(Ann Disaster Med. 2005;3 Suppl 2:S40-S46)*

Key words: Avian Influenza; Virology; Poultry; H5N1

Introduction

"Avian influenza" is highly concerned by the public since the outbreak of H5N1 subtype in Hong Kong in 1997. A total of 18 cases of human influenza virus infection had been identified and six of them died.[1] The Hong Kong government worked hard to control the disease and killed millions of poultry. The outbreak was under control since 1999 until two cases were reported in February 2003. At the same time, a total of 89 human infection with influenza A (H7N7), including 1 resulting in the death of a Dutch veterinarian, occurred and decimated the Dutch poultry industry.[2,3] Since mid-December 2003, 8 Asian countries—Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam—have reported outbreaks of highly pathogenic avian influenza caused by the H5N1 strain among poultry and more than 100 million poultry died.[4] Then another outbreak of avian influenza A infection in human was identified in January 2004.[5] Throughout the year of 2004, 45 patients were infected by the H5N1 virus and 32 victims died.[6] According the report of world health organization, 44 cases have been detected in 18 cities and provinces of Vietnam and 19 of them have died from mid-December 2004 to 14 April 2005.

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Avian influenza was concerned not only about its high mortality rate but also the risk of pandemic threat to human, like the influenza pandemic during 1918-1919. We therein reviewed current knowledge about avian influenza, including the virology, epidemiology, diagnosis and management of this disease.

Classification

Influenza virus was classified as A, B and C based on their nucleoprotein (NP) and matrix (M1) protein.[7] All avian influenza viruses belong to Influenza A virus. Type A virus have been isolated from a wide range of species, including humans, pigs, horses, seals, ferrets, mink, whales and birds. Influenza A virus can be divided into subtypes by the surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA). To date, 15 different hemagglutinin (H1-H15) and 9 neuraminidase (N1-N9) proteins have been identified.[8] The HA, NA subtypes circulated in human being were limited, only H1, H2, H3 and N1, N2 presented. In contrast, almost all virus subtypes exist in avian species.

Antigenic Variation

The antigenicity of influenza virus changes gradually by point mutation (antigenic drift) or drastically by genetic reassortment (antigenic shift).[9] Antigenic drift was driven by the immunological pressure among virus and enforced replacement of human influenza virus vaccine strain every several years.[10] Antigenic shift is caused by either direct transmission of nonhuman influenza viruses to humans or the reassortment of genes from two different influenza viruses that have infected a single cell.[11] Pigs may serve as an intermediate host for the reassortment of human and avian influenza viruses[4] because they could be infected by both. During antigenic shift, a new strain that most humans have no immunity might occurred and could have the potential to cause severe global outbreaks. So far, the H5N1 influenza virus infecting human was mostly from avian virus antigen and there is no direct evidence of reassortment.

Severe influenza pandemics in human history

There were several influenza pandemics in human history. The most well-known and serious one is the "Spanish flu" which occurred during the year of 1918 to 1919. The causative strain was influenza virus H1N1. It occurred during the World War I and resulted in at lest 25 to 50 millions of people died. Most of them were young soldiers and the amount was at least double the number of soldiers killed by the enemy on the war field.[4] Some people think the influenza stopped the World War I. Other pandemics included the Asian influenza (1957, H2N2), Hong Kong flu (1968, H3N2) and Russian flu (H1N1) and were less lethal than the Spanish flu.

Transmission of Avian Influenza Virus

Transmission to poultry

All birds are thought to be susceptible to infection with avian influenza viruses. Wild waterfowl and migrating bird populations provided an extensive natural reservoir for influenza A virus.[12] Their secretion, saliva or feces contain much virus. If they contact with domestic poultry, the disease will spread. Furthermore, their dropping or saliva may contaminate water, river, feed or even human shoes, and cause wide spread of poultry infection. The symptoms

of infected poultry may range from mild upper respiratory airway symptoms to rapid death. The highly pathogenic avian influenza (HPAI) could cause millions of poultry die and much economic loss, like the Pennsylvanian outbreak in 1983.[13] The "wet market", where live poultry was sold under crowded, is also a focus of disease transmission.[14] As the traveling poultry leaves their breeding ground and start to migrate, the influenza virus may travel from one country to another.[12] This traveling period was compatible with the peak period between late summer and early winter.

Transmission from poultry to human

There were several episode of human infection since 1997. The H5N1 outbreak in Hong Kong in 1997 resulted in 18 people infected and 6 of them died. In 1999, H9N2 virus was isolated from 2 children with mild influenza-like symptom in Hong Kong and both are recovered. In 2003, several influenza outbreaks were noted. In Hong Kong, H5N1 virus infected two family members after returning from China and one of them died. Also in Hong Kong, H9N2 infected one child and the child recovered. In the Netherlands, H7N7 virus outbreak occurred and 83 patients were infected. One of the 83 patients died, most of the others have the symptoms of conjunctivitis. The largest outbreak of H5N1 avian influenza rage in several Asian countries and tens of people die since Jan 2004. There was also an outbreak of H7N7 virus in British Columbia, Canada in 2004 and 5 patients were infected. Most of them only have mild symptoms of conjunctivitis.[15] One case control study was performed as the outbreak in Hong Kong in 1997. [16] The result demonstrated exposure to live poultry in the week before the onset of illness as the most risk factor of avian influenza virus infection. Neither traveling, eating nor preparing poultry products and recent exposure to persons with respiratory illness showed significant association.

Human-to-Human Transmission

So far, most reports suggested that human H5N1 virus infection resulted from direct contact with infected birds or surfaces contaminated with their secretions. However, some evidence revealed the possibility of human-to-human transmission. Dr. Brideges[17] noted that the health care workers who cared H5N1 infected people had a significantly higher seropositive rate than nonexposed ones (3.7 % v.s. 0.7%). Limited human-to-human transmission is a reasonable explanation. In the Netherlands, 3 family members of farm workers were infected during the H7N7 outbreak in 2003.[18] In 2004, a 11 year-old girl died of avian influenza H5N1. Her mother and aunt then got infected after taking care of her and her mother at last died. Neither her mother nor her aunt had the history of exposure to infected poultry. Human-to-human infection was highly suspected.[19]

Clinical presentation

Most people infected with avian influenza H5N1 in 1997 represented fever, sore throat and cough. More serious symptoms include dyspnea secondary to virus pneumonia, acute respiratory distress syndrome, multiple organ failure and death.[20,21] Some people presented with gastrointestinal symptoms, renal failure and pancytopenia but all of them are not usually predominant. Cytokine dysfunction was noted after influenza virus infection. A burst of cytokine production after H5N1 might result in multiple

organ failure.[4]

In the episode of H5N1 virus infection in Vietnam in January 2004, 10 patients (mean age, 13.7 years) were reported[22] and nine of them had a clear history of direct contact with poultry. All patients presented with fever (temperature 38.5 to 40.0 ℃), respiratory symptoms, and clinically significant lymphopenia (median lymphocyte count, 700 per cubic millimeter). The median platelet count was 75500 per cubic millimeter and seven patients have diarrhea. All patients showed marked abnormalities on chest radiography. However, atypical presentation with severe diarrhea and coma without respiratory tract symptoms was also reported.[23] The mortality rate was high (80%). Other avian influenza virus outbreak caused by non-H5N1 strain caused minor symptoms and most patients only symptoms of conjunctivitis.

Laboratory diagnosis

Laboratory testings are indicated under the conditions listed below:[24]

1. Testing are indicated for hospitalized patients with

(1) radiographically confirmed pneumonia, acute respiratory distress syndrome, or other severe respiratory illness for which an alternate diagnosis has not been established and

(2) history of travel to a country with documented H5N1 avian influenza within 10 days of symptom onset

2. Testings should be considered on a case-by-case basis in consultation with state and local health departments for hospitalized or ambulatory patients with

(1) temperature >38℃ (>100.4) ℉ **and**

(2) one or more of the followings: cough, sore throat, shortness of breath **and**

(3) history of contact with domestic poultry (eg, visited a poultry farm, household raising poultry, or bird market) or a known or suspected human case of influenza H5N1 in an H5N1-affected country within 10 days of symptom onset.

The nasopharyngeal aspirate obtained within 3 days of the onset of symptoms is the best specimen for influenza virus detection. The H5N1 influenza virus can be detected by rapid antigen tests, virus culture and reverse transcriptase-polymerase chain reaction (RT-PCR).[4,25]

Treatment

The current H5N1 strains are resistant to amantadine and rimantadine but are susceptible to neuraminidase inhibitors (oseltamivir and zanamivir).[4] These drugs are effective for prophylaxis and treatment of influenza A virus infection and may play an important role in reducing the severity and spread of infection during the first stages of a pandemic.[26] Within 48 hours after exposed to H5N1 avian influenza virus, oseltamivir should be used for prophylaxis.

Prevention

Prevention is the most important part of avian influenza control. There are several methods as follows:

Early identify HPAI disease in poultry and cull them

Early recognize avian influenza is the first step to prevent it. Speed is of the essence: the earlier the official intervention, the fewer the number of birds that will need to be killed. Any approach adopted must ensure complete elimi-

nation of the virus.[4,27] Outbreak of HPAI should be considered if there are reliable reports of any poultry establishment experiencing an unusually high mortality rate (e.g. >1% daily mortality for 2 days in commercial settings and > 5% for village poultry farms) and where the mortality is associated with one or more of the following signs: depression and respiratory disease, swollen heads, cyanosis of the combs or wattles, and possibly neurological signs and diarrhea. Culling the infected poultry and decontaminate the infected area are the most effective ways to prevent spread of the disease.

General precaution

It is very important to keep away from the poultry or anything which may be contaminated by the infected poultry. Using protective gloves and washing hands with soap frequently can prevent avian influenza effectively. The virus has some characters including inactivation by 56 ℃ in 3 hours, 60℃ in 30 minutes, inactivation by acid PH, oxidizing agents, sodium dodecyl sulphate, lipid solvents, detergents, and bleach. It can be easily inactived by 5 % bleach or cooked the poultry.

Patient isolation

It is important to isolate suspected persons for 14 days after onset of the symptoms, no matter at home or in the hospital.[28] Isolation precautions for patients hospitalized with suspected or confirmed avian influenza H5N1 must be the same as severe acute respiratory syndrome, which include:[29]

(i) Standard precaution: strict hand hygiene before and after all patient contacts

(ii) Contact precautions: use gloves and gown for all patient contact

(iii) Eye protection: wear when within 3 feet (1m) of the patient

(iv) Airborne precautions: place the patient in an airborne isolation room, use a fit-tested respirator, at least as protective as an NIOSH-approved N-95 filtering facepiece respirator, when entering the room

Vaccine

Current inactivated trivalent human influenza vaccine provides no protection against the H5 and H7 avian influenza strains.[4] However, an important role for the vaccine is to prevent co-infection of seasonal human influenza and avian influenza in one human body. The co-infection may increase the risk of virus reassortment and create a new highly contagious virus. Until now, no H5 or H7 vaccine was available.

Conclusion

Avian influenza is one of the two terrible virus infection besides severe acute respiratory syndrome (SARS) in the early 21th century. SARS pandemic seems subsided now but the avian influenza is still violating human. Until now, studies showed most avian influenza infections of human were directed invaded by the virus (most H5N1 stain) from poultry. Although some case reports suspected the possibility of human-to-human transmission but there was no direct evidence to prove it. The high mortality rate of HPAI infection needs to be concerned. However, the most frightening possibility is the reassortment of the HPAI with common human influenza virus. If this happened, a new virus pandemic, like Spanish flu, which caused millions of victims might occur. The most important thing is to halt further spread of epidemics in poultry population. It is also essential to have

good hand hygiene, have adequate general precaution and educate people to decrease the opportunity for exposuring to poultry or their droppings. Health worker have to wear enough precaution in the hospital. The scientists must do their best to develop vaccine against avian influenza as soon as possible.

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