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Avian influenza: What PAs need to know

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Avian influenza A(H5N1) virus infects people infrequently, but when it does the mortality rate is high. As of January 14, 2006, 148 human cases of avian influenza, with 79 deaths, had been reported to the World Health Organization (WHO).[1] Cases have been reported in Cambodia, China, Indonesia, Thailand, Vietnam, and Turkey.[1]

Most cases have occurred after people had direct or close contact with infected poultry or contaminated surfaces; in a few instances, however, the disease appears to have been spread by person-to-person transmission. Scientists are concerned that the H5N1 virus could mutate into a form that could spread easily from one person to another. The human population has little or no immune protection against H5N1 infection, so if the virus were to gain this capacity, an influenza pandemic could begin. This article reviews available information and prepares PAs to respond to the anticipated flood of calls and questions from patients alamed by the media coverage of a possible avian flu pandemic.

Background and incidence

Avian influenza, or "bird flu," is a contagious disease of animals caused by influenza A viruses that normally infect birds and, less commonly, swine. Most infected birds are completely asymptomatic; however, some develop chronic respiratory tract infections or CNS disease.[2,3] In birds, the majority of strains of influenza A virus replicate in the lungs and the cells lining the intestines, and the virus is shed in high concentration in feces.

Influenza viruses belong to the family Orthomyxoviridae, and there are three main types: influenza A, B, and C. All three cause disease in humans. Type A influenza is the most common cause of seasonal influenza outbreaks, type B influenza generally causes severe disease only among children, and type C influenza is uncommon in humans. To date three flu pandemics, all due to influenza A viruses, have occurred. In 1918, H1N1 killed a reported 500,000 persons in the United States and 20 million worldwide. Type H2N2 killed 70,000 in this country in 1957, and type H3N2 killed 34,000 in the United States in 1968.[4]

An emergency hospital in Camp Funston, Kan, during the 1918 flu pandemic.

Photo: National Museum of Health and Medicine, Armed Forces Institute of Pathology, Washington

The current outbreaks of highly pathogenic avian influenza (H5N1) began in Southeast Asia in 2003.[5] In the past two years in this area, the number of cases of human and avian infections has increased dramatically. Malaysia reported its first outbreak of H5N1 infection in poultry in 2004. More reports followed—from Russia, adjacent parts of Kazakhstan, and Mongolia.[2,6] In October 2005, an outbreak of H5N1 infection was confirmed in poultry in Turkey and Romania.[2] Although seroprevalence studies are lacking, this expanding geographic distribution of avian influenza indicates that more human populations are at risk.[7,8]

Transmission

Human influenza is transmitted by inhalation of infectious droplets or droplet nuclei, by direct contact, and perhaps indirectly by fomites.[6,8] To date, the evidence suggests that transmission of influenza A(H5N1) occurs from bird to human and perhaps from environment to human; limited, nonsustained human-to-human transmission is also possible.[8] Most infected patients have a history of direct contact with birds.[3,8]

Human exposure to the H5N1 virus is considered most likely to occur during slaughter, defeathering, butchering, and preparation of infected poultry for cooking.[8,9] However, other exposures have been implicated—

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playing with or handling poultry and consuming duck blood or undercooked poultry, for example.[8] Human-to-human transmission is most likely to result from intimate contact, and the outbreaks of several household clusters of infection point to this possibility.[8] The risk of nosocomial transmission to health care workers has been low.[8,10] No case of human-to-human transmission by small-particle aerosols has been identified.[9]

Clinical manifestations

The clinical spectrum of human influenza A(H5N1) ranges from mild or subclinical infection to fulminant disease with high mortality.[5,8,11] The incubation period for avian influenza H5N1 may be longer than those for other known human influenza viruses, with most signs and symptoms appearing 2 to 8 days after exposure.[8,12,13] These most frequently include high fever (102.5°F [39°C]) and the typical influenzalike illness with lower respiratory tract symptoms.[2,3,11] Nausea, vomiting, diarrhea, abdominal pain, pleuritic chest pain, and bleeding from the nose and gums have been reported in the early stages of disease in some patients.[8,13]

On examination of patients, lower respiratory tract manifestations including respiratory distress, tachypnea, and inspiratory crackles are common. Radiographic changes are variable and may include diffuse, multifocal, or patchy infiltrates; interstitial infiltrates; and segmental or lobular consolidation with air bronchograms.[8] Progression to respiratory failure has been associated with acute respiratory distress syndrome and ground-glass infiltrates on chest radiography.[8] Other important complications of infection include multiorgan failure, pulmonary hemorrhage, pneumothorax, pancytopenia, and sepsis syndrome.[8,12]

Diagnostic evaluation

A detailed travel and exposure history is critical in the diagnostic evaluation of patients with suspected avian influenza. The history should document specific exposures to humans with known or suspected H5N1 infection as well as any contacts with poultry in H5N1-affected countries.

Laboratory findings commonly seen with avian influenza A(H5N1) are leukopenia (particularly lymphopenia), thrombocytopenia, and elevated aminotransferase levels.[8] The diagnostic yields of different tests to detect influenza A(H5N1) are not well defined; however, virus and viral RNA levels may be more easily detected in pharyngeal than in nasal samples. Commercially available rapid serologic tests are of low sensitivity and specificity for detecting influenza A(H5N1). Reverse transcription polymerase chain reaction assays, while not widely available, appear to be better for detecting influenza A(H5N1) from clinical samples;

TABLE 1

Infection control and prevention measures for avian influenza

Traveler precautions
Avoid direct contact with poultry; avoid touching surfaces possibly contaminated with poultry feces or secretions
Do not ingest undercooked eggs or foods from poultry
Practice good hand hygiene, especially if cooking or handling poultry
Contact a health care provider if fever or respiratory symptoms develop within 1-2 weeks after returning from an area with documented cases of avian influenza
Hospital isolation precautions
Manage patients with standard, contact, droplet, and airborne precautions (hand hygiene, gloves, gowns, and eye protection)
Place patients in a negative-pressure room if available or in a private single room; discourage visitation
Limit the number of interactions between health care workers and patients and the exposure of the patient to the hospital environment as much as possible
Monitor the health status and temperatures of infected patients twice daily; report any new febrile illness to hospital personnel
Sick health care workers should not be involved in direct patient care
Consider postexposure prophylaxis with oseltamivir for health care workers exposed to secretions, infectious aerosols, or other body fluids that occur as a lapse in aseptic technique, and for persons performing high-risk procedures
Close contact precautions
Practice good hand hygiene, do not share cooking utensils, and avoid face-to-face contact with suspected infected persons
Consider using masks and eye protection
Obtain postexposure prophylaxis with oseltamivir
Monitor health status and check temperature twice daily for 7 days after the last exposure; contact health personnel for appropriate evaluation and testing should a febrile illness arise

The above recommendations are a general summary of published guidelines.[2,3,8,18]

these tests must be performed by laboratories that meet criteria for standard biosafety level (BSL) 2 conditions.[8,10] Acute-phase (within 1 week of symptom onset) and convalescent-phase (more than 3 weeks after onset) serum samples should be collected and stored locally in case further testing for antibody to the avian influenza virus is needed. Specimens from persons meeting the clinical and epidemiologic criteria for suspected avian influenza should be sent to the CDC for further analysis utilizing a laboratory with BSL 3 conditions.[14]

Treatment

The traditional treatments for influenza have been the neuraminidase inhibitors oseltamivir (Tamiflu) and zanamivir (Relenza) and the M2 inhibitors amantadine (Symmetrel) and rimantadine (Flumadine). If given early (within 48 hours of symptom onset), these drugs can reduce the severity and duration of seasonal influenza.

In vitro, avian influenza A(H5N1) is susceptible to oseltamivir and zanamavir but is often resistant to amantadine and rimantidine.[8,15] Neuraminidase inhibitors should be given as early as possible in the course of human disease due to influenza A(H5N1). The optimal dosage and duration of treatment are uncertain. The usual dosage of oseltamivir is 75 mg twice daily, but higher dosages, such as 150 mg twice daily, may be considered.[8]

Because of avian influenza, the availability of the neuraminidase inhibitors has become a concern.[2,3] At present manufacturing capacity, it would take a decade to produce enough oseltamivir to treat 20% of the world's population.[2] Individual stockpiling of antiviral drugs is not recommended, but WHO recently encouraged health authorities to consider stockpiling antiviral drugs in anticipation of a pandemic.[2,3] Each state or local government should draw up a plan to deal with an influenza pandemic. To help aid the planning process, materials such as a planning guide are available from agencies including the CDC.

Infection control and prevention

Because of the spread of the pathogenic influenza A(H5N1) virus from birds to humans and the associated high mortality rate, control and prevention measures have become increasingly important. These include control and vaccination of poultry, vaccination of humans, and the infection control and prevention measures listed in Table 1 (page 20).

Before 2004, Thailand was one of the world's major exporters of poultry and produced approximately 1 billion chickens per year. Several measures were taken there after the H5N1 virus was first isolated in January 2004. Initially, all poultry; their products, feed, bedding, and waste; and manure from infected flocks were destroyed.[10] Veterinary surveillance and long-term control measures continue with collaboration among farmers, industries, public health authorities, academic institutions, and the government.[5]

The United States Department of Agriculture (USDA) is working to protect bird populations, a measure which can help to protect people. The USDA works closely with international organizations to assist affected countries with disease prevention, management, and elimination. Since 1998, USDA scientists have tested more than 12,000 wild migratory birds for influenza in the Alaska flyway. None have tested positive for the more dangerous strains of bird flu.[16] As a primary safeguard, the USDA maintains trade restrictions on the importation of poultry and poultry products from countries where the H5N1 strain has been detected. Additionally, the USDA maintains a bank of avian influenza vaccine for birds, which contains 40 million doses that would be available in the event of an outbreak in the United States. The USDA currently is expanding this existing avian influenza vaccine bank to add another 30 million doses.[16]

Although vaccines for human influenza viruses have become an important part of worldwide prevention efforts, human vaccines effective against the H5N1 virus are not yet available. Influenza vaccine is traditionally grown in fertilized chicken eggs. Not surprisingly, this approach to developing a vaccine against H5N1 has met with high rates of failure.[17] While research on a viable cell culture system using recombinant technology is progressing, an approved and available vaccine is not on the immediate horizon. Several clinical trials are under way to test whether experimental vaccines will be fully protective and to determine whether different formulations can economize on the amount of antigen required.[2]

The CDC recommends that persons who are hospitalized with severe, febrile respiratory illnesses and who have a history of recent travel to an area with avian influenza activity be managed using the isolation procedures recommended for severe acute respiratory syndrome (SARS).[18] It is essential that local public health authorities and infection control personnel be notified if a case of avian influenza is suspected.

Conclusion

The widespread persistence and spread of the H5N1 influenza virus in poultry poses two main risks for human health. The first is the risk of direct infection as the virus passes from poultry to humans, resulting in potentially severe disease. Of the few avian influenza viruses that have infected humans, the H5N1 strain has caused the largest number of human deaths.[2] Unlike typical seasonal influenza, where infection causes only mild respiratory symptoms in most people, the disease caused by the H5N1 virus follows an unusually aggressive clinical course, with rapid deterioration and high mortality.[2,8]

The second and more worrisome risk is that the avian influenza A(H5N1) virus, through genetic recombination, will change into a form that is highly infectious to humans and has the ability to spread easily from person to person. Such a mutation has not yet happened, but it could mark the start of a global pandemic.[2] The recent spread of the virus to poultry and wild birds in new areas also increases the likelihood of more human infections.

While the timing and severity of the next pandemic cannot be predicted, the probability that a pandemic will occur has increased.[11] In August 2005, all countries received a document outlining recommended strategic actions for responding to the threat of an avian influenza pandemic.[2] Recommended actions aim to strengthen national preparedness, reduce opportunities for a pandemic virus to emerge, improve the early warning system, delay initial international spread, and accelerate vaccine development.[2] A continued global effort is required to ensure an effective response to this important and potentially life-threatening problem. □

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