Bird flu: A Throbbing Stone In An Infectious Era

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Abstract

Avian influenza is an infection caused by avian (bird) influenza (flu) viruses. These influenza viruses occur naturally among birds. Wild birds worldwide carry the viruses in their intestines, but usually do not get sick from them. However, avian influenza is very contagious among birds and can affect some of the domesticated birds, including chickens, ducks, and turkeys, and kill them.1

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 or with surfaces that are contaminated with secretions or excretions from infected birds. Domesticated birds may become infected with avian influenza virus through direct contact with infected waterfowl or other infected poultry, or through contact with surfaces (such as dirt or cages) or materials (such as water or feed) that have been contaminated with the virus.1

EPIDEMIOLOGY

Avian influenza disease which was first identified in Italy more then 100 year ago occurs worldwide. In 1997, the first cases of human infection with the avian influenza A (H5N1) virus were reported in China, Hong Kong Special Administrative Region (Hong Kong SAR). These 18 cases included 6 deaths and coincided with outbreaks of highly pathogenic H5N1 in poultry on farms and in markets selling live poultry. [1] Now this disease is spreading to Thailand, Vietnam, Korea, and Pakistan. Therefore, it poses a sufficient threat to India too! In mid-2003, the highly pathogenic H5N1 virus began to circulate widely in poultry in parts of south-east Asia, spreading within months to affect 8 countries in an outbreak unprecedented in its geographical extent and is therefore of particular public health concern. The disease remained confined to animals and humans in South-East Asia until mid-2005, when the virus expanded its geographical range through parts of central Asia to Europe, Africa and the Middle East. Between 1 December 2003 and 30 April 2006, 205 laboratory-confirmed cases and 113 deaths were reported to WHO from 9 countries. During that same period, the World Organisation for Animal Health reported outbreaks of H5N1 infection in domestic or wild birds in approximately 50 countries. H5N1 variants have demonstrated a capacity to directly infect humans in 1997, and have done so again in Vietnam in January, 2004. Infection causes a wide spectrum of symptoms in birds, ranging from mild illness to highly contagious and rapidly fatal disease resulting in severe epidemics. [2,3]

TRANSMISSION FROM AVIAN TO HUMAN

Transmission to humans occurs only when they come in contact with the surfaces contaminated with the secretions from infected birds. Severity of Clinical symptoms depends on the virulence of the pathogenic forms of the virus which may vary from low to high pathogenic form.

VIRULENCE CAUSED BY INFLUENZA VIRUS

Infection with avian influenza viruses in domestic poultry causes two main forms of disease that are distinguished by low and high extremes of virulence. The “low pathogenic” form may go undetected and usually causes only mild symptoms (such as ruffled feathers and a drop in egg production). However, the highly pathogenic form spreads more rapidly through flocks of poultry. This form may cause disease that affects multiple internal organs and has a mortality rate that can reach 90-100% often within 48 hours.

HUMAN INFECTION WITH AVIAN INFLUENZA VIRUSES

There are many different subtypes of type A influenza viruses. These subtypes differ because of changes in certain proteins on the surface of the influenza A virus (hemagglutinin [HA] and neuraminidase [NA] proteins). There are 16 known HA subtypes and 9 known NA subtypes of influenza A viruses. Many different combinations of HA

and NA proteins are possible. Each combination represents a different subtype. All known subtypes of influenza A viruses can be found in birds.

Usually, "avian influenza virus" refers to influenza A viruses found chiefly in birds, but infections with these viruses can occur in humans. The risk from avian influenza is generally low to most people, because the viruses do not usually infect humans. However, confirmed cases of human infection from several subtypes of avian influenza infection have been reported since 1997. Most cases of avian influenza infection in humans have resulted from contact with infected poultry (e.g., domesticated chicken, ducks, and turkeys) or surfaces contaminated with secretion/excretions from infected birds. The spread of avian influenza viruses from one ill person to another has been reported very rarely, and has been limited, inefficient and unsustained.

"Human influenza virus" usually refers to those subtypes that spread widely among humans. There are only three known A subtypes of influenza viruses (H1N1, H1N2, and H3N2) currently circulating among humans. It is likely that some genetic parts of current human influenza A viruses came from birds originally. Influenza A viruses are constantly changing, and they might adapt over time to infect and spread among humans.

During an outbreak of avian influenza among poultry, there is a possible risk to people who have contact with infected birds or surfaces that have been contaminated with secretions or excretions from infected birds.

CLINICAL MANIFESTATIONS

It may range from typical human influenza-like symptoms (e.g., fever, cough, sore throat, and muscle aches) to eye infections, pneumonia, severe respiratory diseases (such as acute respiratory distress). Other severe and life-threatening complications may also occur. The symptoms of avian influenza may depend on the subtype of viruses which caused the infection. [3]

CLINICAL TRIALS

Studies done in laboratories suggest that some of the prescription medicines approved in the United States for human influenza viruses should work in treating avian influenza infection in humans. However, influenza viruses can become resistant to these drugs, so these medications may not always work. Additional studies are needed to demonstrate the effectiveness of these medicines. [3]

HEALTH RISKS POSED TO HUMAN DUE TO H5N1 OUTBREAK

Of the few avian influenza viruses that have crossed the species barrier to infect humans, H5N1 has caused the largest number of detected cases of severe disease and death in humans. However, it is possible that those cases in the most severely ill people are more likely to be diagnosed and reported, while milder cases go unreported. [2]

Of the human cases associated with the ongoing H5N1 outbreaks in poultry and wild birds in Asia and parts of Europe, the Near East and Africa, more than half of those people reported infected with the virus have died. Most cases have occurred in previously healthy children and young adults and have resulted from direct or close contact with H5N1-infected poultry or H5N1-contaminated surfaces. In general, H5N1 remains a very rare disease in people. The H5N1 virus does not infect humans easily, and if a person is infected, it is very difficult for the virus to spread to another person.

While there has been some human-to-human spread of H5N1, it has been limited, inefficient and unsustained. For example, in 2004 in Thailand, probable human-to-human spread in a family resulting from prolonged and very close contact between an ill child and her mother was reported. In June 2006, WHO reported evidence of human-to-human spread in Indonesia. In this situation, 8 people in one family were infected. The first family member is thought to have become ill through contact with infected poultry. This person then infected six family members. One of those six people (a child) then infected another family member (his father). No further spread outside of the exposed family was documented or suspected.

Nonetheless, because all influenza viruses have the ability to change, scientists are concerned that H5N1 virus one day could be able to infect humans and spread easily from one person to another. Because these viruses do not commonly infect humans, there is little or no immune protection against them in the human population. If H5N1 virus were to gain the capacity to spread easily from person to person, an influenza pandemic (worldwide outbreak of disease) could begin. [4]

No one can predict when a pandemic might occur. However, experts from around the world are watching the H5N1 situation in Asia and Europe very closely and are preparing for the possibility that the virus may begin to spread more easily and widely from person to person. [4]

DIAGNOSIS

The diagnosis of influenza A (H5N1) virus infection should be included in the differential diagnosis of all persons presenting with acute febrile respiratory illness in those countries or territories where influenza A (H5N1) viruses have been identified as a cause of infection in animal populations. It should also be included in the diagnosis of anyone with possible exposure to suspected or confirmed A (H5N1) virus-infected patients or to samples containing the virus. Commonly the presenting signs and symptoms of A (H5N1) illness are non-specific, and a detailed exposure history needs to be elicited, including any close/direct contact with sick or dead poultry, wild birds, other severely ill persons, travel to an area with A (H5N1) activity, or work in laboratory handling samples possibly containing A (H5N1) virus. The use of commercially available, rapid site-of-care influenza detection tests for individual patient diagnosis is generally not recommended. Current tests have low sensitivity in A (H5N1) virus-infected patients, and a negative rapid test result does not exclude human infection with avian influenza viruses and a positive test does not distinguish from infection by other influenza viruses. [5]

Specimens for H5N1 diagnosis should be collected according to WHO guidance and tested at one of the laboratories recognized as capable of diagnosing H5N1, such as WHO Collaborating Centres or a H5 Reference Laboratory. Collection of multiple respiratory specimens (nasal, throat, endotracheal aspirates from intubated patients) from suspected A (H5N1)-infected patients should be done preferably before antiviral treatment has commenced but it should not delay the initiation of such treatment. Additional respiratory specimens can also be collected after treatment has started. Public health and hospital authorities should be alerted immediately. [5]

TREATMENT AND VACCINATION FOR H5N1 VIRUS IN HUMANS

The H5N1 virus that was found to be major cause of human illness and death in Asia is resistant to amantadine and rimantadine, two antiviral medications commonly used for influenza. Two other antiviral medications, oseltamavir and zanamavir, would probably work to treat influenza caused by H5N1 virus, but additional studies still need to be done to demonstrate their safety and effectiveness. [1]

Treatment modalities recommended for the clinical management of human H5N1 virus infection is shown in table 1.

(Ref: Department of Health and Human Services Centers for Disease Control and Prevention)

RECOMMENDATIONS FROM WHO ON MANAGEMENT ASPECTS ,

When there is evidence for sustained human-to-human transmission of H5N1 or another novel avian influenza virus emerges, strict recommendations need to be developed. Whenever feasible, sequential clinical data collection and virological sampling (for analysis at WHO-designated laboratories) should be performed during treatment or should apparent failures of chemoprophylaxis occur. Self-medication in the absence of appropriate clinical or public health advice is discouraged. When considering chemoprophylaxis for H5N1 infection, priority should be given to standard infection control practices. This includes protection of health care workers and individuals involved in eradication of animals infected with H5N1 virus as well as household contacts of H5N1 patients.

For treatment of patients with confirmed or strongly suspected human infection with the H5N1 virus, where neuraminidase inhibitors are available for therapy:

Clinicians should administer oseltamivir treatment (strong recommendation); zanamivir might be used as an alternative (weak recommendation).

In these patients, clinicians should not administer amantadine or rimantadine alone as a first-line treatment (strong recommendation).

Clinicians might administer a combination of a neuraminidase inhibitor and an M2 inhibitor if local surveillance data show that the H5N1 virus is known or likely to be susceptible (weak recommendation), but this should only be done in the context of prospective data collection.

For treatment of patients with confirmed or strongly suspected H5N1 infection, where neuraminidase inhibitors are not available for therapy:

Clinicians might administer amantadine or rimantadine as a first-line treatment if local surveillance data show that the H5N1 virus is known or likely to be susceptible to these drugs (weak recommendation).

In general, decisions to initiate antiviral chemoprophylaxis should be guided by the risk stratification described below. Stratification is based on observational data for reported

cases of human H5N1 infection and on high quality data from studies of seasonal influenza.

High risk exposure groups are currently defined as:

- Household or close family contacts of a strongly suspected or confirmed H5N1 patient, because of potential exposure to a common environmental or poultry source as well as exposure to the index case.

Moderate risk exposure groups are currently defined as:

- Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal) if personal protective equipment may not have been used properly.
- Individuals with unprotected and very close direct exposure to sick or dead animals infected with the H5N1 virus or to particular birds that have been directly implicated in human cases.
- Health care personnel in close contact with strongly suspected or confirmed H5N1 patients, for example during intubation or performing tracheal suctioning, or delivering nebulised drugs, or handling inadequately screened/sealed body fluids without any or with insufficient personal protective equipment. This group also includes laboratory personnel who might have an unprotected exposure to virus containing samples.

Low risk exposure groups are currently defined as:

- Health care workers not in close contact (distance greater than 1 metre) with a strongly suspected or confirmed H5N1 patient and having no direct contact with infectious material from that patient.
- Health care workers who used appropriate personal protective equipment during exposure to H5N1 patients.
- Personnel involved in culling non-infected or likely non-infected animal populations as a control measure.
- Personnel involved in handling sick animals or decontaminating affected environments (including animal disposal), who used proper personal protective equipment.

Where neuraminidase inhibitors are available:

- In high risk exposure groups, including pregnant women, oseltamivir should be administered as chemoprophylaxis, continuing for 7–10 days after the last exposure (strong recommendation); zanamivir could be used in the same way (strong recommendation) as an alternative.
- In moderate risk exposure groups, including pregnant women, oseltamivir might be administered as chemoprophylaxis, continuing for 7-10 days after the last exposure (weak recommendation); zanamivir might be used in the same way (weak recommendation).
- In low risk exposure groups oseltamivir or zanamivir should probably not be administered for chemoprophylaxis (weak recommendation). Pregnant women in the low risk group should not receive oseltamivir or zanamivir for chemoprophylaxis (strong recommendation).
- Amantadine or rimantadine should not be administered as chemoprophylaxis (strong recommendation).

Where neuraminidase inhibitors are not available:

- In high or moderate risk exposure groups, amantadine or rimantadine might be administered for chemoprophylaxis if local surveillance data show that the virus is known or likely to be susceptible to these drugs (weak recommendation).
- In low risk exposure groups, amantadine and rimantadine should not be administered for chemoprophylaxis (weak recommendation).
- In pregnant women, amantadine and rimantadine should not be administered for chemoprophylaxis (strong recommendation).
- In the elderly, people with impaired renal function and individuals receiving neuropsychiatric medication or with neuropsychiatric or seizure disorders, amantadine should not be administered for chemoprophylaxis (strong recommendation).

We recommend that countries develop their own guidelines for the assessment of human patients in whom there is a suspicion of influenza A (H5N1) infection. These should include the criteria required to initiate treatment pending confirmatory laboratory testing. Such guidelines will reflect geographical location with respect to recent outbreaks of avian influenza H5N1 in birds and the locally available resources.

Figure 1

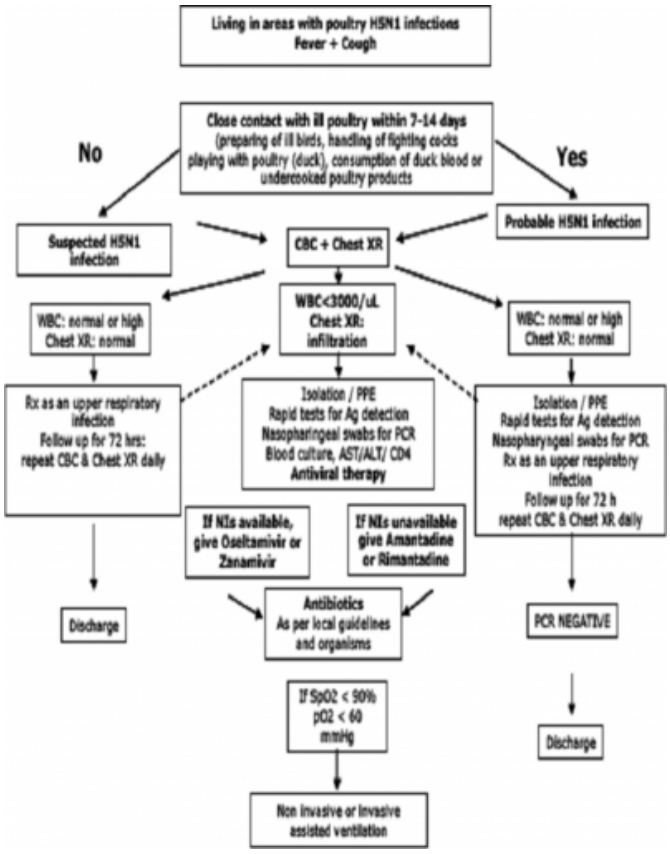

Figure 2

Table1 . Summary of treatment modalities for clinical management of human A(H5N1) virus infection.

Recommended Modalities	Strategies
Antivirals	Oseltamivir is the primary treatment of choice. Consider modified regimens (see text).
Antibiotics	Empiric treatment[1] for community-acquired pneumonia (CAP) per published guidelines pending microbiologic results (e.g. 2-3 days);
Oxygen therapy	Monitor oxygen saturation and maintain SaO_2 over 90% with nasal cannulae or face mask.
IPPV (Invasive positive pressure ventilation)	Early intervention recommended for ARDS. Use lung protective, low tidal volume, low pressure ventilation to prevent barotrauma and conservative fluid management.
Low dose systemic corticosteroids	Appropriate for refractory septic shock complicating ARDS (e.g. hydrocortisone intra venous 200mg per day in divided doses (50 mg every 6 hours) in adults).
NSAIDs, antipyretics (Non-steroidal anti-inflammatory drugs)	Paracetamol given orally or by suppository will generally be sufficient in most cases as an anti-pyretic treatment.
Infection control	Whenever risk of infectious aerosols, use particulate respirator (N95, FFP2 or equivalent), eye protection, gowns, gloves and an airborne precaution room or negative pressure room.

PREVENTIVE MEASURES

Some preventive measures can be adopted to ensure the prevention of bird flu especially for the individuals who are in direct contact with birds such as in poultry farms. Avoiding contact with live birds, especially infected ones, and good hygiene practices such as the washing of hands after handling poultry, are recommended precautions against bird flu. As an added precaution, poultry products should be thoroughly cooked at more than 100 °C. An influenza vaccine will not be able to offer any protection against bird flu. However, those at higher risk of developing complications from flu, i.e., the very old, the very young, and those with a chronic illness, are advised to take flu jabs to minimize complications and the spread of normal flu. [3]

FUTURE RECOMMENDATIONS

Some of the recommendations based on the established guidelines especially for those who are at high to moderate risk or who require emergent treatment to avoid the serious consequences are given below:

- Avoid the direct contact with the places contaminated with the infectious agents.
- Always prefer to avoid raw or uncooked meat.
- Take chemoprophylaxis in case of high risk group based on the standard recommendations.
- Contact your physician in case of suspected clinical symptoms for further management.

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