

2012

Avian Influenza: Clinical and Epidemiological Information for Paramedics and Emergency Healthcare Workers

Erin Smith
erin.smith@med.monash.edu.au

Ben Coghlan

Karin Leder

Recommended Citation

Smith, E., Coghlan, B., & Leder, K. (2006). Avian Influenza: Clinical and Epidemiological Information for Paramedics and Emergency Healthcare Workers. *Australasian Journal of Paramedicine*, 4(1).
Retrieved from <http://ro.ecu.edu.au/jephc/vol4/iss1/3>

This Journal Article is posted at Research Online.
<http://ro.ecu.edu.au/jephc/vol4/iss1/3>

CLINICAL PRACTICE

Article 990175

Avian Influenza: Clinical and Epidemiological Information for Paramedics and Emergency Healthcare Workers

Erin Smith^a, Ben Coghlan^b and Karin Leder^c

^a Research Fellow, Centre for Ambulance and Paramedic Studies, Monash University, Melbourne, Australia, and Coordinator, Cochrane Collaboration Pre-hospital and Emergency Health Field.

^b Medical Epidemiologist, Burnet Institute, Melbourne, Australia, and Master of Applied Epidemiology Program, National Centre for Epidemiology and Population Health, Australian National University.

^c Head, Infectious Diseases Unit, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia, and Physician, Victorian Infectious Diseases Service, Royal Melbourne Hospital, Victoria, Australia.

Keywords: avian influenza; bird flu; emergency health care worker; epidemiology; H5N1; infection control; infectious diseases; influenza; influenza A virus; pandemic; prehospital

What is Avian Influenza?

Avian influenza, or “bird flu”, is an infectious disease caused by avian influenza viruses that are found naturally in wild birds. The virus is transmitted between birds but usually does not result in disease. However, the virus can be transmitted from wild birds to domestic poultry. In general, domestic poultry, especially chickens, are much more likely to suffer serious disease than wild birds.

There are two main forms of the disease in birds distinguished by low and high extremes of virulence.¹ The low pathogenic form may go undetected with limited signs of illness in poultry, while the highly pathogenic form can spread rapidly, resulting in disease that affects multiple internal organs with high mortality (up to 90-100%). H5N1 is a highly pathogenic type of avian influenza A virus.

All infected birds shed massive volumes of influenza virus in their saliva, nasal secretions and faeces, contaminating environments and infecting other birds in close proximity. The Food and Agricultural Organization of the United Nations states that just one gram of contaminated faeces contains enough live virus to infect another one million birds.

In 1996, the highly pathogenic Influenza A/ H5N1 virus was first isolated from a farmed goose in Guangdong Province, China.² In 1997, outbreaks of H5N1 were reported in poultry farms and wet markets in Hong Kong. By July 2003, H5N1 had become increasingly lethal for mammals and had even begun to kill wild waterfowl, its natural hosts.² From mid 2003 the virus spread rapidly and widely: outbreaks in poultry were reported in Thailand, Korea, Viet Nam, Japan, Indonesia, China, Malaysia, Cambodia, Mongolia, Russia, Kazakhstan, Turkey, Romania, Croatia, Iraq, Iran and Nigeria.

Can it infect humans?

While the current risk of H5N1 transmission to humans is low, there have been 173 human cases and 93 deaths (case fatality rate of 54%) reported to the World Health Organization (WHO) between 2002 and February 27, 2006.³ In 1997 the first case of avian to human transmission was documented in Hong Kong, where the virus killed 6 of the 18 human cases detected (case fatality rate of 33%).⁴ Close contact with live infected poultry was implicated as the source of human infection, with the virus jumping directly from birds to people. Additional human infections have been detected in China, Cambodia, Indonesia, Iraq, Thailand, Viet Nam and Turkey.

Limited nosocomial transmission to healthcare workers has occurred: one case of serious illness in a nurse following exposure to an infected patient was reported in Viet Nam.⁷ In contrast to SARS, however, hospital acquired infections have not typically resulted in severe disease.^{5,6}

Has it spread outside of Asia?

H5N1 virus has spread beyond Asia to eastern Europe, the middle east, northern Africa, and is possibly spreading westward through Europe.^{8,9} Since the beginning of February 2006, 13 new countries have reported H5N1 infection in wild or domestic birds: India, Iraq, Nigeria, Azerbaijan, Bulgaria, Greece, Italy, Slovenia, Iran, Austria, Germany, Egypt, India and France.³ Malaysia also declared a new outbreak of H5N1 in poultry in February 2006, after being disease free for over a year.³ An unprecedented number of birds have been infected and the virus appears to have escaped its reservoir in wild birds to now also be endemic in domestic poultry.

How is avian influenza different from the seasonal type of influenza?

Every year several strains of flu circulate around the globe. The Centers for Disease Control and Prevention (CDC) in the United States reports that 5-20% of the American population are infected with seasonal influenza annually, leading to over 200,000 hospitalisations and about 36,000 deaths. The populations most at risk for seasonal influenza are infants under the age of 2 years, adults aged 65 years and older, and individuals with chronic medical conditions. On the other hand, avian influenza has predominantly caused disease in previously healthy children and young adults, mimicking the pattern of the infamous 1918 influenza pandemic.

Seasonal influenza can be transmitted readily from human-to-human. It is spread by respiratory droplets caused by coughing and sneezing. The incubation period is short, usually 1 to 3 days. Most healthy adults shed live virus as early as one day before the development of symptoms and up to five days after the onset of illness. Consequently, people infected with seasonal influenza can transmit the virus to others *before* exhibiting signs or symptoms themselves.

Although H5N1 infected people may also shed the virus before they become symptomatic, H5N1 is far less infective for humans and the incubation period appears to be far longer than other influenza viruses - estimates have ranged from 2 to 8 days after exposure.^{10,11,12} WHO recommends that infection control practices for adults should remain in place for 7 days after resolution of an adult patient's fever. For children aged 12 years and younger who may shed virus for prolonged periods, infection control practices should be continued for 21 days after the onset of the illness.

Vaccinations are available for seasonal influenza. However, because the influenza virus mutates rapidly, resulting in new circulating strains each year, vaccination against one strain of the virus will not necessarily be protective against a new strain in the following year. This

is why health care workers are required to have a new shot of the seasonal influenza vaccination annually. Similarly, although prototype vaccines against the current circulating strain of H5N1 infecting humans have been developed and are being trialled, these may not provide adequate immunity if the virus changes.

How is avian influenza transmitted?

To date, most human infections have occurred from close contact with sick birds. Exposure to live poultry or contact with surfaces contaminated with secretion/ excretions from infected birds has been associated with disease in humans.^{1,7}

More recently, transmission of the infection has been observed in a wider range of animal species: in zoos in Thailand and Cambodia large cats (tigers, leopards) and birds of prey (hawks, eagles) have become ill after being fed raw chickens infected with H5N1.^{13,14,15} On the other hand, no significant risk of human infection with H5N1 has been established from eating or preparing poultry products¹⁶, and basic food hygiene handling and cooking practices appear to be adequate to inactivate the virus and prevent infection.

While direct transmission of the virus between animal species and from bird-to-human are concerning, the more worrying prospect is the potential for human-to-human transmission of the virus. So far, only one convincing case of possible human-to-human transmission has been reported in Thailand, where a mother with no history of contact with birds developed avian influenza following prolonged, unprotected exposure to her child who was dying of H5N1.^{17,18} Additional human-to-human transmissions have been suggested in several household clusters in Viet Nam.¹²

The risk of environment-to-human transmission is still unclear, but given that the virus is relatively hardy and able to survive outside a host for days even weeks if ambient conditions are optimal, several other modes of transmission are theoretically possible. Contamination of hands from infected fomites or handling untreated poultry faeces - widely used as fertilizer in some countries - could lead to self-inoculation.⁷ Similarly, because the infection has evolved in an animal reservoir intimately connected to water (wild ducks, geese and shorebirds), contaminated water bodies represent a considerable source of infection for all birds and may also be a source of infection for humans - oral ingestion, direct intranasal or conjunctival inoculation with exposure to contaminated water could constitute a risk.

What are the clinical features of infection with H5N1?

Symptoms have ranged from typical human influenza-like symptoms (fever, cough, sore throat, rhinorrhea, headache, myalgia) to eye infections, pneumonia and severe respiratory diseases (Acute Respiratory Distress Syndrome).¹ All patients in South-East Asia have had a high fever (>38°C), while watery diarrhoea (without blood) has been described in 25-70% of cases.¹⁹ Indeed, gastrointestinal complaints may precede respiratory symptoms by up to one week complicating early clinical diagnosis. Severe lower respiratory symptoms tend to develop within about five days from the onset of first symptoms. Respiratory distress, tachypnoea, and inspiratory crackles are common findings on examination. Atypical clinical manifestations, such as encephalopathy and gastroenteritis, have also been reported.^{20,21,22} Although surveillance systems generally detect only severe manifestations of the disease, milder clinical disease and asymptomatic cases have been detected. Most cases so far identified have been in previously healthy, children and young adults.

Mortality

Just over half of all patients throughout the world confirmed as having H5N1 infection have died (case fatality rate: 54%). However, the overall mortality rate for all cases is probably

much lower.²¹ Mortality rates have been highest among infants and young children. A case fatality rate of 89% was reported among patients aged 15 years or younger in Thailand, with death occurring approximately 9-10 days following onset of illness (range 6-30 days). The cause of death is usually respiratory failure or multi-organ failure.^{11,12}

Treatment: Antivirals and other care

Antiviral drugs, some of which can be used for both treatment and prevention, have been found to be clinically effective against influenza A virus strains in otherwise healthy adults and children. These antiviral drugs could be used to contain an outbreak and reduce fatalities while a vaccine is prepared.²⁶

The primary treatment option is a class of drugs called the neuraminidase inhibitors, of which Oseltamivir (Tamiflu) is the best known. These drugs work by preventing the virus from escaping its host cells in the lungs. However, it is not yet clear how effective Tamiflu is against H5N1: reports from Southeast Asia suggest limited but emerging resistance, while a recent Queensland study suggested neuraminidase inhibitors may be ineffective in either preventing infection or reducing viral shedding during an influenza pandemic.²⁷ (There is high level resistance of H5N1 to the M2 inhibitor class of antivirals, such as amantadine and rimantadine, and these are not recommended for treatment.) Thus, antiviral treatment must be used in conjunction with appropriate barriers like personal protective equipment, distancing of infected and uninfected individuals, and sound personal hygiene practices.

The current production of neuraminidase inhibitors is inadequate to meet worldwide demand for stockpiling for pandemic preparedness let alone sufficient to fulfil the global need if a pandemic occurred in the near future. Moreover, there is a particular shortfall in countries most at risk in our region. Added to this, is uncertainty regarding the optimal way to use these medications during a pandemic: should they be used for pre-exposure prophylaxis, post-exposure prophylaxis, or merely for treatment after symptoms have developed? Health care workers known to have been exposed to confirmed cases of avian influenza are likely to be offered prophylaxis, but pre-exposure prophylaxis for all healthcare workers for the duration of a pandemic would not be feasible due to cost and supply issues.

Supportive care would include antipyretics, oxygen therapy with mechanical ventilation if required, and antibiotics for concurrent bacterial pneumonias. During the Severe Acute Respiratory Syndrome (SARS) outbreak in 2003, nebulisers were identified as potentiating in-hospital spread of the virus. Nebuliser use should therefore be minimised in both the ambulance (pre-hospital) and hospital environments to limit infection among healthcare workers.

Prevention:

1. Personal Protection

Personal Protective Equipment (PPE) reduces but does not completely eliminate the likelihood of infection. PPE will only be effective if used correctly during all contacts with infected patients. Each pre-hospital or emergency healthcare service will have regulations for the use of PPE that should be followed by all staff during the transport and treatment of patients with suspected or confirmed avian influenza. These regulations will include the use of standard universal precautions including masks, gloves, eyewear and protective overalls/uniform covers.

Respiratory protection (masks) can significantly reduce the danger of infection by viruses providing they are used and worn correctly. The following types of protective masks are available:

Paper Masks

Paper masks offer little protection against viruses as they have no filter. Furthermore, they tear easily due to moisture build up from respirations, sweat and saliva.

Surgical Masks

Surgical masks are designed to prevent transmission of infections to others from coughing and sneezing – not to provide protection to wearers from airborne infections. However, they do provide limited protection against viruses; the amount of protection is related to features of the virus and the host (for example the viral load necessary to cause infection and the degree of viral shedding by the infected person).²⁸

N-95 Masks

The WHO and the CDC recommended that healthcare workers should wear N-95 masks or higher level protection when in contact with SARS patients. N-95 masks generate static electricity which is effective in stopping very small particles from adhering to the surface of the mask. The N-95 masks are used to protect against highly transmissible respiratory infections such as tuberculosis. However, they are uncomfortable to wear for long durations and adequate protection relies on proper fitting.

P1, P2 or P3 Masks

These masks filter out fine particles and provide greater protection than standard surgical masks. P3 masks filter out a higher proportion of fine particles than P2 and P1 masks and are the European alternative to the American N-95 masks.

The effectiveness of surgical masks, even when multiple masks are worn or when they are frequently replaced, is much less than that of N-95 masks²⁶ or P2 and P3 masks. The expense of the P3 and N-95 masks however may restrict their availability and the difficulty in wearing these masks for extended periods may militate against their use for all but in-hospital patient care.

2. Other measures

Hand washing is an effective and important component for preventing the transmission of infection. Alcohol solutions or scrubbing with soap and water is sufficient. Healthcare workers should also avoid touching their mouth, eyes, and nose after contact with an infected patient.

The ambulance itself may act as a mobile fomite if an infected person has been transported. Each ambulance service will have regulations for infection control. These regulations should include procedures for disposing of wastes, sharps and disposable uniform covers, handling linen and uniforms, and cleaning and disinfecting both equipment and the ambulance interior.

3. Vaccination

Vaccination is likely to remain the principal means of combating pandemic avian influenza.²³ A French company has been developing a vaccine for H5N1 against strains from Hong Kong and Viet Nam, which has been shown to promote an immune response in healthy adults. Similarly, CSL in Australia has recently announced successful trials of a prototype vaccine against a southern Vietnamese strain of the virus.²⁴ Both of these vaccines rely on a production method that uses embryonated eggs - a relatively slow process - and only produce vaccines against a specific strain. In the United States, the CDC has begun developing an egg-independent strategy.²⁵ This technique could accelerate production of vaccine, induce an

immune response without the need for adjuvants and may even be effective against multiple genetic drift variants.

However, these vaccines are not yet commercially available and research continues to determine their clinical usefulness, particularly in children and adults aged over 65 years. Furthermore, if a strain evolves that is easily transmitted between humans these prototype vaccines may not provide full or adequate protection.

Because it is not possible to predict in advance the makeup of a particular strain that will cause a pandemic, vaccines cannot be developed before the emergence of a pandemic strain (unless of course the US CDC technology proves successful). Consequently, it is estimated that between 4 to 8 weeks will be required to develop an effective vaccine against a pandemic strain once it evolves and is detected. It may take longer to produce adequate quantities to protect a population. Once a vaccine becomes available, it is likely that healthcare workers would be among the first to receive the vaccination.

Will H5N1 avian influenza be the next pandemic?

Based on historical patterns, influenza pandemics have occurred, on average, three to four times each century. Each time a pandemic occurs, the virus mutates and a new virus subtype emerges. However, we are unable to predict with any precision when a new pandemic will occur, or what the virus subtype will be.

There are three prerequisites for a new human influenza pandemic:

1. the emergence of a new influenza virus to which the population has little or no immunity against (and which there is no effective vaccine);
2. the ability of the virus to replicate in human beings and cause disease; and
3. a virus that is efficiently transmitted from human-to-human.

The first two of these prerequisites have been met and, disturbingly, there are some signs that the virus is becoming more adapted to humans.

Epidemiological modelling estimates from the US and the UK have suggested that if an avian influenza pandemic does occur, the worldwide death toll could exceed the 1918 Spanish Flu epidemic that claimed between 50 and 100 million lives. Our best hope of averting this “worst case scenario” is sound and thorough preparation combined with early detection through sensitive surveillance systems. Both of these rely, in part, on the understanding and cooperation of our frontline emergency healthcare personnel.

Acknowledgements

The Master of Applied Epidemiology program is funded by the Australian Government Department of Health and Ageing.

References

1. Centers for Disease Control, Department of Health and Human Services. Key facts about Avian Influenza (Bird Flu) and Avian Influenza A (H5N1) Virus. Key Facts, November 25, 2005
2. The World Health Organization. H5N1 Avian Influenza: Timeline. Available at http://www.who.int/csr/disease/avian_influenza/Timeline_28_10a.pdf (Accessed January 18, 2006)
3. The World Health Organization. Available at http://www.who.int/csr/disease/avian_influenza/en/index.html (Accessed February 28, 2006)
4. Monto AS. The threat of an Avian Influenza Pandemic. *The New England Journal of Medicine* 2005; 352(4):323-325.
5. Liem NT, World Health Organization International Avian Influenza Investigation Team, Vietnam, Lim W. Lack of H5N1 avian influenza transmission to hospital employees, Hanoi, 2004. *Emerging Infectious Diseases* 2005;11:210-215.
6. Schultsz C, Dong VC, Chau NVV, et al. Avian influenza H5N1 and healthcare workers. *Emerging Infectious Diseases* 2005;11:1158-1159.
7. The World Health Organization. Avian Influenza Fact Sheet: 15 January 2004. Available at http://www.who.int/csr/don/2004_01_15/en/ (Accessed 1 December, 2005)
8. Chen H, Smith JD, Zhang SY, et al. Avian flu: H5N1 virus outbreak in migratory waterfowl. *Nature* 2005;436:191-192.
9. Liu J, Xiao H, Lei F, et al. Highly pathogenic H5N1 influenza virus infection in migratory birds. *Science* 2005;309:1206-1206.
10. Yuen KY, Chan PK, Peiris M, et al. Clinical features and rapid viral diagnosis of human disease associated with avian influenza A H5N1 virus. *Lancet* 1998;351:467-471.
11. Chotpitayasunondh T, Ungchusak K, Hanshaoworakul W, et al. Human disease from influenza A (H5N1), Thailand, 2004. *Emerging Infectious Diseases* 2005;11:201-209.
12. Hien TT, Liem NT, Dung NT, et al. Avian influenza A (H5N1) in 10 patients in Vietnam. *The New England Journal of Medicine* 2004;350:1179-1188.
13. Keawcharoen J, Oraveerakul K, Kuiken T et al. Avian influenza H5N1 in tigers and leopards. *Emerging Infectious Diseases* 2004;10:2189-2191.
14. Kuiken T, Rimmelzwan G, van Riel D et al. Avian H5N1 influenza in cats. *Science* 2004;306:241.
15. Thanawongnuwech R, Amonsin A, Tantilertcharoen R et al. Probable tiger-to-tiger transmission of avian influenza H5N1. *Emerging Infectious Diseases* 2005;11:699-701.
16. Mounts AW, Kwong H, Izurieta HS et al. Case-control study of risk factors for avian influenza A (H5N1) disease, Hong Kong, 1997. *Journal of Infectious Disease* 1999;180:505-508.
17. Ungchusak K, Auewarakul P, Dowell SF, et al. Probable person-to-person transmission of Avian Influenza A (H5N1). *The New England Journal of Medicine* 2005; 352(4):333-340.
18. Hien TT, de Jong M, Farrar J. Avian Influenza – A challenge to global health care structures. *The New England Journal of Medicine* 2004;351(23):2363-2365.
19. Tran TH, Nguyen T, Nguyen TD et al. Avian influenza A (H5N1) in 10 patients in Vietnam. *N Engl J Med.* 2004;350:1179-88.
20. Apisarnthanarak A, Kitphati R, Thongphubeth K, et al. Atypical avian influenza (H5N1). *Emerging Infectious Diseases* 2004;10:1321-1324.
21. The World Health Organization. WHO inter-country-consultation: influenza A/H5N1 in humans in Asia: Manila, Philippines, 6-7 May 2005. Available at http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_7/en/. (Accessed December 8, 2005).

22. de Jong MD, Cam BV, Qui PT, et al. Fatal Avian influenza A (H5N1) in a child presenting with diarrhea followed by coma. *New England Journal of Medicine* 2005;352:686-691.
23. Stephenson I. Are we ready for pandemic influenza H5N1? *Expert Review of Vaccines* 2005;4(2):151-155.
24. Hoelscher MA, Garg S, Bangari DS et al. Development of adenoviral-vector-based pandemic influenza vaccine against antigenically distinct human H5N1 strains in mice. *The Lancet* 2006; 367:475-481
25. The Age. Bird flu vaccine hope. February 17 2006. Available at: <http://www.theage.com.au/news/national/bird-flu-vaccine-breakthrough/2006/02/17/1140064237494.html> (Accessed Feb 17, 2006).
26. Anonymous. Avian Influenza should be ruffling our feathers. *Lancet Infectious Diseases* 2004 Oct;4(10):595.
27. Jefferson T, Demicheli V, Rivetti D, Jones M, Di Pietrantonj C Rivetti A. Antivirals for Influenza in Healthy Adults: Systematic Review. *The Lancet* 2006;367(9507):303-313.
28. Derrick JL, Gomersall CD. Protecting healthcare staff from severe acute respiratory syndrome: filtration capacity of multiple surgical masks. *Journal of Hospital Infection* 2005;59:365-368.

Author Disclosure

The authors have no financial, personal or honorary affiliations with any commercial organization directly involved or discussed in this study.

This Article was peer reviewed for the *Journal of Emergency Primary Health Care* Vol.4, Issue 1, 2006