AVIAN INFLUENZA IN HUMANS

NSW CONTROL GUIDELINES FOR PUBLIC HEALTH UNITS

1. Summary

This guideline is concerned with the public health response to people with avian influenza (AI) infection, and people who have been exposed to another person or birds with AI infection.

It is not concerned with human pandemic influenza. In the unusual event that an AI strain transforms into one that is easily transmitted between humans, it is no longer avian influenza, but becomes human (and possibly pandemic) influenza. The response to human pandemic influenza is described in the national and state influenza pandemic management plans. The pandemic phases are outlined in the Australian Heath Management Plan for Pandemic Influenza.[1] The case definitions have been developed to apply to all AI strains regardless of their pathogenicity classification in birds (see section 7). This recognises that any strain of avian influenza could emerge as a public health threat.

Public health priority
Urgent. Respond to a suspected case immediately on notification. Report details of the case to [Communicable Disease Branch (CDB)] within 1 hour of notification. [CDB] should report confirmed cases to the National Incident Room on day of notification. Data entry should be completed within the same working day.

Case management
Suspected cases must be cared for in a single room, and if available, a negative pressure room. Cases should be treated with neuraminidase inhibitors, ideally within 48 hours of onset.

Contact management
Contacts of confirmed cases and infected birds must be rapidly identified, counselled about their risk, provided with neuraminidase inhibitors (if indicated), and placed under surveillance for 10 days after the last exposure.

2. The disease

Infectious agents
Avian influenza A virus. All AI viruses are influenza A viruses which are further divided into subtypes determined by haemagglutinin (H) and neuraminidase (N) antigens. At present, 16 H subtypes and 9 N subtypes have been identified in birds. Each AI virus has one of each H and N subtype occurring in many different combinations. The virulence is associated with the genetic properties of the virus.[2] AI viruses are classified as highly pathogenic avian influenza (HPAI) and low pathogenicity avian influenza (LPAI) in conformity with criteria established in relation to poultry by the World Organisation for

Animal Health (OIE).[3] Hence the use of the terms HPAI or LPAI only refers to the virulence of the AI virus in birds.

To date, only H5 and H7 subtypes have been known to cause outbreaks of HPAI in birds. Both LPAI and HPAI viruses can however rarely cause illness in humans following very close contact. It is believed that human pandemic influenza strains may arise from AI viruses.[2] No assumption can be made about the clinical significance of a novel AI virus in humans based on the pathogenicity designation in birds.[4] One HPAI strain, the H5N1 avian influenza virus, has caused serious infections in humans and deaths during poultry outbreaks overseas.[5] One LPAI, H7N9, has caused serious infections in humans and deaths in China however has not been linked with clinical disease in birds.[6]

Note: As information as to risks and timelines becomes better documented public health staff should review the latest literature on transmission and timelines during investigations.

Reservoir

The species in the orders *Anseriformes* (ducks, geese, swans) and *Charadriiformes* (shorebirds, waders, gulls) are regarded as important reservoir hosts and disseminators of AI viruses, but rarely display clinical signs of infection.[2] In this document, these reservoir birds are referred to collectively as "waterbirds". However it is reasonable to assume all avian species are susceptible to AI infection.[3]

Mode of transmission

Bird-to-bird

Infected birds may shed virus in their saliva, nasal and respiratory secretions, and faeces depending on many factors such as the type of bird, the virus subtype and the presence of other diseases. Faeces of infected birds can contain large amounts of virus with faecal-oral transmission the predominant mode of spread between birds. Asymptomatic waterbirds may directly or indirectly introduce the virus into poultry flocks via contaminated excretions from infected birds or via contaminated environments.[7] Secondary dissemination is by fomites, movement of infected poultry, and possibly airborne. LPAI infection is primarily a localised infection in poultry and HPAI infection typically presents as a more systemic infection.[7]

Bird-to-person

Transmission of AI infection from birds to humans is rare. When it has occurred, it is believed to have resulted from close contact with infected poultry or breathing in dust contaminated with their excretions. The virus can survive on poultry products (including eggs and blood), [8] however no infection has been documented from eating properly cooked eggs and meat from infectious birds. Transmission has been thought to occur by ingesting uncooked poultry products (including raw blood) from H5N1 infected poultry.[9]

Person-to-person

The spread of AI viruses from one ill person to another through prolonged, unprotected, close contact has been reported very rarely, and has been limited, inefficient and not sustained.[10-11]

Incubation period

The incubation period for AI in humans may be longer than that for normal seasonal influenza, which is around two to three days. Current data indicate an incubation period will typically (and for public health purposes should be considered to) range from one to

ten days.[11-13] This may vary depending on the AI strain.

Infectious period

No detailed studies have been conducted of infectivity of AI viruses in humans. Viral shedding of H5N1 has been detected in some patients up to 21 days after symptoms begin,[14,15] and up to 20 days after symptoms begin for H7N9 patients,[16] however the low number of secondary cases detected indicates that viral shedding is not an accurate reflection of AI infectivity in humans.

Based on data on human influenza subtypes:

- Adults and children older than 12 years of age are thought to be infectious typically from the day before[17] (and up to a maximum of 5 days before)[18] symptoms begin until usually 7 days after[19] (and up to a maximum of 14 days after)[20] symptoms begin. For practical public health purposes, adults and children older than 12 years of age should be considered infectious from 1 day before symptoms begin until 7 days after symptoms begin.
- Children up to 12 years of age are thought to be infectious typically from the day before (and up to a maximum of 6 days before) [19] symptoms begin until usually 7 days after[19,22] (and up to a maximum of 27 days after) [19,23-24] symptoms begin. For practical public health purposes, children up to 12 years of age should be considered infectious from 1 day before symptoms begin until 7 days after symptoms begin.
- Severely immunocompromised persons can shed virus for weeks or months,[25-27] and should be considered on a case-by-case basis.

Clinical presentation and outcome

The clinical presentation of AI in humans may be highly variable both between and within haemagglutinin subtypes. As with seasonal human influenza, a person infected with AI may have no symptoms, mild upper respiratory symptoms, or symptoms typical of influenza (fever, cough, fatigue, myalgia, sore throat, shortness of breath, runny nose, headache); diarrhoea may also occur.[5]

Mild symptoms, including conjunctivitis and gastrointestinal symptoms, have been typically associated with several AI subtypes and should be considered in any person who has had close exposure to birds infected with any subtype of AI.[8] An outbreak of LPAI H10N7 on a chicken farm in Australia was associated with conjunctivitis and mild respiratory symptoms in seven abattoir workers processing birds from this farm. H10 influenza subtype was laboratory confirmed in two of the cases.[12] A large outbreak of HPAI H7N7 in the Netherlands in 2004 was reported to have resulted in a rate of conjunctivitis of 8%, influenza like illness in 2%, and one death associated with respiratory failure in those exposed.[28]

The H5N1 subtype has caused viral pneumonia with a high case fatality rate, and in a small number of cases, diarrhoea, vomiting, abdominal pain, chest pain, and bleeding from the nose and gums have also been reported as early symptoms.[5] Initial data on the H7N9 subtype which emerged in eastern China in February 2013 indicates that human illness is characterised by rapidly progressive pneumonia, respiratory failure and acute respiratory distress syndrome (ARDS) with a high case fatality. However some confirmed cases, particularly young children, have been asymptomatic or associated with clinically mild upper respiratory illness.[6,11]

Persons at increased risk of disease

The likely scenarios in which a human infection with avian influenza could occur in Australia are:

- a person is infected overseas after close contact with infectious material from birds or a human case and travels to Australia during the incubation or infectious periods.
- a laboratory worker is infected while working with human or animal specimens that contain avian influenza.
- a person is infected in Australia after close contact with infectious material from infected local birds. Those at highest risk of these exposures are commercial poultry workers who work directly with potentially infected poultry.

Disease occurrence and public health significance

As of June 2015 there have been no known bird or human cases in Australia associated with the H5N1 or H7N9 viruses which have caused human illness and death overseas. Recent poultry outbreaks of HPAI H7 (2012 and 2013),[29-30] LPAI H4 and LPAI H9 (2012)[31] and LPAI H10 (2010)[12] subtypes have been recorded in New South Wales; only the H10 subtype was associated with recognised likely transmission of mild illness to humans. An LPAI H5 outbreak also occurred in a Victorian duck farm in 2012.[32]

3. Routine prevention activities

The prevention of AI in Australians principally relies on:

1. Advice to travellers to practice good hand hygiene and avoid close contacts with birds in wet markets or on farms, in countries where AI is endemic in domestic poultry.[33]
2. Good occupational health and safety practices including use of appropriate personal protective equipment (PPE) and hygiene measures for anyone working with potentially infected birds.[2]
3. Communication and collaboration between the jurisdictional agencies responsible for human and animal health. In this document, jurisdictional agencies responsible for animal health, including the surveillance and control of AI in birds, are referred to collectively as animal health agencies. Animal health agencies should involve human health authorities in human risk assessment and control. Jurisdictional Communicable Disease Branches (CDBs) must also notify the jurisdictional animal health agencies of any human cases for investigation of possible bird sources or risk to poultry.

Threat and vulnerability

Various strains of AI are enzootic in bird populations around the world. Outbreaks in Australian domestic poultry have been associated with poor biosecurity, confirmed or circumstantial evidence of contact with waterbirds, or inadequately treated surface water potentially contaminated by waterbirds or domestic ducks.[34] AI-contaminated materials carried by humans or material brought into Australia from AI-infected countries may also pose a risk of infecting poultry or humans.

Risk mitigation

Biosecurity measures have been put in place in many commercial bird facilities to minimise the risk of future AI infections in birds. However, many facilities (notably free range farms) may present opportunities for exposure of domestic poultry to waterbirds and/or their excretions. Strict quarantine and inspection measures at Australian airports and seaports are designed to prevent the importation of bird products into Australia.

[NSW Department of Primary Industries (DPI)] have contingency plans in place to minimise the impact of an outbreak of AI in Australia. These procedures are outlined in the Australian Veterinary Emergency Plan (AUSVETPLAN).[2]

People co-infected with avian influenza and human influenza infections are thought to provide the potential for re-assortment of genes from the two strains of influenza that could result in a new human pandemic influenza strain. Therefore, if human influenza is currently circulating in the community, poultry workers and other people directly involved in culling AI infected poultry should be vaccinated with the current recommended seasonal influenza vaccine. While vaccination will not prevent AI, it will help reduce the risk of co-infection, re-assortment and a pandemic.[35]

4. Surveillance objectives

1. Rapidly identify, isolate, and treat human cases and prevent transmission to their contacts.
2. Assess the risk to humans from AI infected birds, and identify, counsel and provide prevention advice to those at risk.
3. Understand the epidemiology of AI in humans in Australia, in order to identify risk factors and prevent transmission.

5. Data management

Within 1 working day of confirmation, enter confirmed case on [the Notifiable Conditions Information Management System (NCIMS) database.]

6. Communications

Immediately report suspected and confirmed cases of AI in humans to [CDB] by telephone with the patient's age, sex, date of onset, laboratory status, possible sources of infection, other people thought to be at risk and follow up action taken. Any suspect or confirmed AI infected bird(s) should also be reported to [CDB] to assess the risk of infection in human contacts.

The [NSW CDB] should immediately notify confirmed human AI cases to the National Incident Room, and the [NSW DPI].

7. Case definition

Avian Influenza in Humans (AIH) Case Definition

Reporting

Both confirmed cases and probable cases should be notified. Suspected cases should not be notified.

Confirmed case

A confirmed case requires laboratory definitive evidence AND clinical evidence

Laboratory definitive evidence

- Isolation of an AI virus

OR

- Detection of AI by nucleic acid testing using two different targets, e.g. primers

specific for influenza A and AI haemagglutinin (genetic sequencing should be employed to confirm diagnosis);

OR

- A fourfold or greater rise in antibody titre to the AI virus detected in the outbreak (or AI virus suspected of causing the human infection), based on testing of an acute serum specimen (collected 7 days or less after symptom onset) and a convalescent serum specimen. The convalescent neutralizing antibody titre must also be 80 or higher.

OR

- An antibody titre to the AI virus detected in the outbreak (or AI virus suspected of causing the human infection) of 80 or greater in a single serum specimen collected at day 14 or later after symptom onset. The result should be confirmed in at least two different serological assays (i.e. haemagglutinin-inhibition, microneutralisation, positive Western blot, etc.).

Note: Tests must be conducted in a national, regional or international influenza laboratory whose AIH test results are accepted by WHO as confirmatory

Clinical evidence

An acute illness characterised by:

a. Fever (>38ºC) or history of fever AND one or more of; cough OR rhinorrhoea OR myalgia OR headache OR dyspnoea OR diarrhoea;

OR

b. Conjunctivitis

OR

c. infiltrates or evidence of an acute pneumonia on chest radiograph plus evidence of acute respiratory insufficiency (hypoxaemia, severe tachypnoea).

Probable case

A probable case requires laboratory suggestive evidence **AND** Clinical evidence **AND** Epidemiological evidence

Laboratory suggestive evidence

Confirmation of an influenza A infection but insufficient laboratory evidence for AIH infection.

Clinical evidence

As with confirmed case

Epidemiological evidence

One or more of the following exposures in the 10 days prior to symptom onset:

a. Close contact (within 1 metre) with a person (e.g. caring for, speaking with, or touching) who is a probable, or confirmed AIH case;
b. Exposure (e.g. handling, slaughtering, de-feathering, butchering, preparation for consumption) to poultry or wild birds or their remains or to environments contaminated by their faeces in an area where AI infections in animals or humans have been suspected or confirmed in the last month;
c. Consumption of raw or undercooked poultry products in an area where AI infections in animals or humans have been suspected or confirmed in the last month;
d. Close contact with a confirmed AI infected animal other than poultry or wild birds (e.g. cat or pig);
e. Handling samples (animal or human) suspected of containing AI virus in a laboratory

or other setting.

Suspected case
A suspected case requires clinical evidence **AND** epidemiological evidence

Clinical evidence for suspected case
As with confirmed case

Epidemiological evidence
As with probable case

Note: For overseas exposures, an AI-affected area is defined as a region within a country with confirmed outbreaks of AI strains in birds or detected in humans in the last month (seek advice from the National Incident Room when in doubt). With respect to the H5N1 AI outbreak that commenced in Asia in 2003, information regarding H5-affected countries is available at: http://gamapserver.who.int/mapLibrary/. With respect to the H7N9 outbreak that commenced in eastern China in 2013, information regarding H7-affected countries is available at http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/

8. Laboratory testing

Specimen collection
Laboratory confirmation should be urgently sought to confirm all suspected cases. Consult with the virologist, but nose AND throat swabs (usually for adults) and conjunctival swabs (even in the absence of conjunctivitis) are recommended. Sputum specimens may be more effective for detecting H7N9 and are recommended wherever possible.[37]

Collect baseline and convalescent sera for symptomatic cases. Do not collect sera for asymptomatic contacts.

Viral swabs should be collected and transported using viral transport medium (VTM) or universal transport medium (UTM).

Samples should be tested at a reference laboratory using:
- PCR for AI
- Viral culture and PCR for influenza.

Nasopharyngeal and throat swabs may induce coughing and should preferably be collected in a negative pressure room, if available, by health care workers (HCWs) wearing full PPE.[38] Write on specimen forms and containers before entering the patient's room to collect the specimens.

The laboratory should be notified in advance by telephone that the specimens will be sent, and specimens should be clearly marked URGENT: SUSPECTED AVIAN INFLUENZA to ensure prioritisation by the laboratory.

Specimens should be packaged and transported according to the National Pathology Accreditation Advisory Council (NPAAC) requirements.[39] Diagnostic specimens for AI testing are classified as Biological Substances, Category B. Amplified viable material including viral cultures are classified as Infectious Substances, Category A. The Public

Health Laboratory Network may advise on packaging and transport of these specimens.

As AI is often an unlikely diagnosis in most suspected cases, other relevant tests should be done concurrently to identify an alternative diagnosis.

9. Case management

Response times
Immediately on notification of a suspected case, begin follow up investigation and notify the [CDB]. For confirmed and probable cases, the "Avian Influenza (AI) in humans - Investigation Form" (see appendices) should be completed and data transferred to the [CDB] the same day.

Response procedure

Case investigation
The response to a notification will normally be carried out in collaboration with the case's health carers. Regardless of who does the follow-up, for confirmed cases, PHU staff should ensure that action has been taken to:

- Confirm the onset date and symptoms of the illness
- Confirm results of relevant pathology tests, or recommend that tests be done (the laboratory should be advised before sending the specimens)
- Find out if the case or relevant care-giver has been told what the diagnosis is before beginning the interview
- Seek the doctor's permission to contact the case or relevant care-giver
- Review case and contact management
- Ensure appropriate infection control professionals are notified and infection control policies are available to those caring for the case
- Identify the likely source of infection
- Obtain a travel, occupational and recreational history, and follow up clinical results and case details.

Note. If interviews with suspected cases are conducted face-to-face, the person conducting the interview must have a thorough understanding of infection control practices, be competent in using appropriate personal protective equipment (PPE),[39-40] and ideally have been vaccinated with the current (human) influenza vaccine.

Case treatment
Treatment of a case is the responsibility of the clinician in consultation with an expert virologist. Neuraminidase inhibitors (e.g. oseltamivir or zanamivir) have been shown to attenuate disease in cases of human influenza if started within 5 days of the onset of illness (ideally within 48 hours).[1] They may also be effective for treating AI.

Education
Provide the [*NSW Health Avian Influenza ("Bird Flu") Fact Sheet]* to cases. Ensure that they are aware of the signs and symptoms of AI, the requirements of isolation, contact details of the PHU and the infection control practices and precautions that can prevent the transmission of AI.

Isolation and restriction
Infectious cases must be isolated until no longer infectious (see *Section 2*). Advice from the facility's infection control professional should be sought.
Health care workers and others who come into contact with the case must use airborne,

droplet, contact and standard infection control precautions including appropriate PPE (gown, gloves, protective eyewear and P2 respirator).[40-41]

The mode of transmission is unclear, but postulated to be mainly droplet and direct contact. However, the possibility of airborne transmission remains, and airborne precautions must be used.

Patients should be managed in a single room with airborne, droplet, contact and standard precautions and if available, a negative pressure room.
Similarly, in a primary care setting such as a GP surgery, patient isolation and, droplet, contact and standard infection control precautions should be employed.[39-40] Acute cases should be managed in hospital. When discharged home, a comprehensive discharge plan must be made by the treating hospital.

Active case finding

Where transmission has been identified from poultry to humans, Public Health Units should actively search for other cases in people who were exposed to the infected poultry and initiate active surveillance in these people for the duration of the infectious period.

10. Environmental evaluation

Where local transmission of AI is thought possible, a thorough review of contributing environmental factors should be performed. If transmission is thought to be poultry-related, the environmental assessment should include a review of opportunities for exposure to infected birds, in collaboration with [NSW DPI] and the [SafeWork NSW]. If health care-associated infection is suspected, the adequacy of infection control procedures must be reviewed.

Staff conducting the environmental evaluation must have a thorough understanding of infection control practices, be competent in using personal protective equipment (PPE), and have been vaccinated with the current (human) influenza vaccine. They must follow airborne, droplet, contact and standard infection control precautions, including appropriate PPE (gown, gloves, protective eyewear and P2 respirator).[33]

11. Contact management

Identification of contacts

AI is not easily transmitted between humans, and probably requires close and prolonged contact. Public health interventions need careful consideration on a case-by-case basis. Following a report of a confirmed case, an expert panel should be convened by [CDB] to help plan the public health response. The expert panel may include experts in human influenza and poultry influenza, animal health agencies, virologists, infection control, infectious disease physicians and PHUs. [The panel should include a local PHU Director where the case is associated with a certain geographical area.]

Contact definition

The evidence base for defining what constitutes “contact” with a case is limited. For the purposes of the contact definition, it is taken to mean being within one metre (e.g. caring for, speaking with, or touching) of an infectious case within the previous 10 days, in the absence of appropriate infection control. The expert panel will advise on a more specific contact definition as required. Where a case has travelled on an aeroplane, contacts are defined as persons sitting in the seats immediately beside the case, due to the lower rate

of person-to-person transmission of AI viruses. However, the expert panel should advise on contacts to be traced.

Post-exposure Prophylaxis

Antiviral medications may be effective in preventing disease in contacts. Unless the available evidence clearly shows a lack of efficacy, close contacts of confirmed cases will generally be offered neuraminidase inhibitors (e.g. oseltamivir or zanamivir) to prevent infection. The expert panel will provide more specific advice as needed.

Education

Contacts should be counselled about their risk and the symptoms of AI and placed under surveillance (see **Error! Reference source not found.** "Avian influenza ("bird flu") advice for people under surveillance" in appendices).

Isolation and restriction

Contacts are not required to isolate themselves from the community but must adhere to advice regarding self-monitoring until the incubation period expires (see *section 2*).

The PHU should ensure that contacts are communicated with daily for 10 days after the last exposure to determine if symptoms of AI have developed. If symptoms develop, the contact must be rapidly isolated until AI is excluded. The PHU should arrange assessment by an appropriately skilled medical practitioner. This must take place in a setting where risk is managed through the use of appropriate infection control precautions. If this occurs at an emergency department, arrangements should be made to ensure that the patient does not wait in any common areas and will be placed immediately in a single room, ideally with negative pressure for assessment.

12. Special situations

AI in birds in Australia

Where the [NSW DPI] reports any outbreak of AI in birds in Australia, the PHU is responsible for ensuring that the risk of human infection is minimised. The public health actions should be guided by the expert panel convened by the [CDB].

Issues to be addressed include:

- Working with the [NSW DPI] and [SafeWork NSW] to ensure that people entering the area deemed by the [NSW DPI]to harbour infection have been trained in the use of PPE, and use it where the potential for exposure to infected birds, their faeces, eggs, or the dust from infected birds is present.
- Providing oral and written information to people who were exposed to the infectious birds about the risk of infection, the methods of minimising the risk, symptoms to be alert for, and to report to the PHU immediately, should symptoms occur.
- Assessing whether people who were exposed to infectious birds require anti-viral medicine, and if so arranging supply (via [CDB]) and administration of the medicine. Ordinarily anti-viral medicines will be limited to persons with direct exposure to infected birds in the absence of effective PPE.
- Placing exposed people under surveillance for ten days. Should symptoms develop, the PHU should arrange for a medical assessment and diagnosis of the person.
- People co-infected with avian influenza and human influenza infections are thought to provide the potential for re-assortment of genes from the two strains of influenza that could result in a new human pandemic influenza strain. Therefore, if human influenza

is currently circulating in the community, poultry workers and other people directly involved in culling AI infected poultry should be vaccinated with the current recommended seasonal influenza vaccine. While vaccination will not prevent AI, it will help reduce the risk of co-infection, re-assortment and a pandemic.[35]

- Processing (slaughter, evisceration and de-feathering) of infected birds have the potential to release large amounts of the virus. Workers should wear appropriate PPE including goggles and P2 respirators during processing and monitor for symptoms for 10 days from the last contact.[2]
- [NSW DPI] staff should advise on biosecurity measures during transport of affected birds; and restrictions on the use of feathers and waste from processing plants.[2]
- Egg and poultry products from birds affected by LPAI are not considered to pose a risk to human health, provided they are cooked appropriately, as is currently advised to avoid other pathogens associated with poultry.[42-44]

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14. Appendices

The following documents are included in the appendices:

- Appendix 1: Avian Influenza ("Bird Flu") in Humans - Factsheet
- Appendix 2: Avian influenza in humans - Information for Contacts
- Appendix 3: Avian Influenza in humans - Advice for People Under Surveillance.
- Appendix 4: Avian Influenza in humans - PHU Checklist
- Appendix 5: Avian Influenza in humans - Investigation Form

15. Jurisdiction specific issues

Links to State and Territory Public Health Legislation, the Quarantine Act and the National Health Security Act 2007.

[Note that human influenza with pandemic potential is a listed disease under the Biosecurity Act and that highly pathogenic avian influenza (human) is a nationally notifiable disease under the National Health Security Act. Avian influenza is a notifiable disease in NSW under the NSW Public Health Act (2010)]