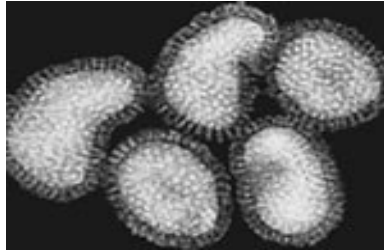


Bird Flu



Influenza virus. Photo: Linda Stannard, 1995

What is Avian influenza (bird flu)?

Avian influenza is an infectious disease of birds. Usually the virus circulates in wild bird populations causing no disease or only mild disease. Infection of domestic poultry, such as chickens, can cause severe disease in these birds. There are a number of different strains of avian influenza, only a few of which can cause disease in humans.

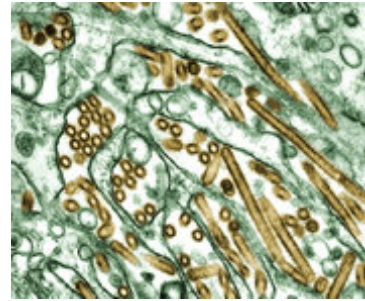
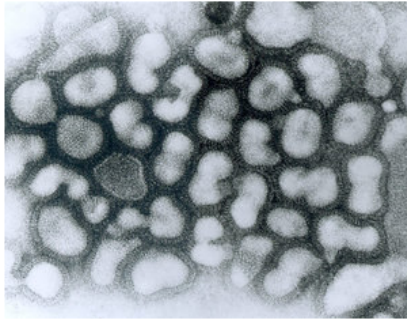
A new type of avian influenza, called influenza A H5N1, was first recognized in 1997 in Hong Kong. This strain reappeared in late 2003 and rapidly spread to several Asian countries causing severe infection in many domestic poultry flocks. There is no evidence that avian influenza is currently infecting birds in Australia.

This virus has also infected a number of people who had close contact with sick poultry or with poultry droppings. Since 28 December 2003, over 110 confirmed cases of avian influenza in humans have been reported in Thailand, Vietnam, Cambodia and Indonesia, and many of these people have died.

At this stage, humans infected with the H5N1 virus do not appear to be able to easily infect others. Exposure to infected poultry and their faeces (or dust or soil contaminated with poultry faeces) can result in human infection. Eating cooked poultry products including chicken or eggs does not result in infection.

H5N1 is a type of [avian influenza](#) virus (bird flu virus) that has [mutated](#) through [antigenic drift](#) into [dozens](#) of highly [pathogenic](#) varieties. The first of these appeared in [China](#) in [1996](#) in [birds](#) and in [Hong Kong](#) in [1997](#) in [humans](#). ([see Timeline](#))

This infection of humans coincided with an [epizootic](#) (an [epidemic](#) in nonhumans) of H5N1 influenza in Hong Kong's poultry population. This panzootic (a disease affecting animals of many species esp. over a wide area [\[1\]](#)) outbreak was stopped by the killing of the entire domestic poultry population within the territory. The name *H5N1* refers to the subtypes of surface [antigens](#) present on the [virus](#): [hemagglutinin](#) type 5 and [neuraminidase](#) type 1.



Influenza A virus, the virus that causes Avian flu. Transmission electron micrograph of negatively stained virus particles in late passage.

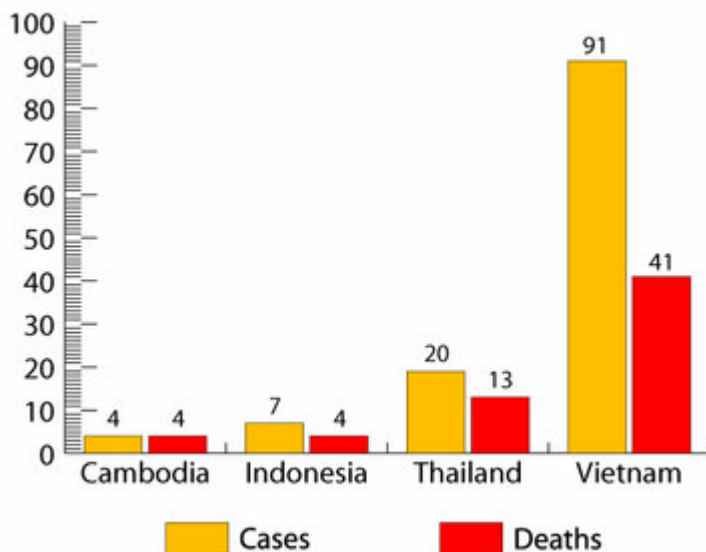
Colorized transmission electron micrograph of H5N1 (golden) grown in Madin-Darby canine kidney cells (green).

A large-scale, worldwide influenza epidemic is called a pandemic. Pandemics occur when a new virus emerges to which people have little or no immunity. Previous influenza pandemics occurred in 1918-19, 1957-58 and 1968-69. In the 1918-19 pandemic, between 20 and 40 million people died. Many scientists are concerned that the recent H5N1 outbreak in birds could mutate to produce a new strain of influenza virus that is easily spread among people, resulting in a pandemic.

Human Cases of Avian Influenza				
Year	Subtype	No. of Cases	Location	Comments
1997	H5N1	18 (6 deaths)	Hong Kong	Cases were linked to an outbreak of H5N1 in poultry. Sustained person-to-person transmission did not occur and the outbreak stopped when all birds in the Hong Kong commercial poultry industry (about 1.4 million) were slaughtered (see References : Yuen 1998).

1999	H9N2	2 (children ages 4 yr, 13 mo)	Hong Kong	Both case-patients had been hospitalized with influenza-like illness and both recovered uneventfully (see References : Peiris 1999, Uyeki 2002). No additional cases of person-to-person transmission occurred. Further investigation demonstrated that H9N2 strains were circulating in poultry in Hong Kong and China, although the viruses were not highly pathogenic for birds.
2002	H7N2	1	United States (Virginia)	Evidence of infection was found in one person in Virginia following a poultry outbreak.
2003	H5N1	2 (1 death)	Hong Kong	The 2 case-patients were family members who had recently traveled to China (see References : CDC: Basic information about avian influenza). A third family member died while in China of an undiagnosed respiratory illness). No direct link between these cases and H5N1 infection in poultry was identified.
2003	H7N7	89 (1 death)	The Netherlands	During an outbreak of H7N7 avian influenza in poultry, infection spread to poultry workers and their families in the area (see References : Fouchier 2004; Koopmans 2004). Most patients had conjunctivitis and several complained of influenza-like illness. The death occurred in a 57-year-old veterinarian. Subsequent serologic testing demonstrated that additional case-patients had asymptomatic infection.
2003	H7N2	1	New York	The source of exposure was not determined (see References : NIAID: Significant dates in influenza history).

2003-2005 (ongoing)	H5N1	130 (67 deaths), according to official WHO numbers	Vietnam, Thailand, Cambodia, Indonesia, and China	Human cases are associated with an ongoing extensive outbreak of avian influenza in poultry (see References : WHO: Cumulative number of confirmed human cases of avian influenza A (H5N1) since 28 January 2004; WHO: Avian influenza: situation in Viet Nam, Mar 7, 2005). To date, human-to-human transmission has been limited. More information on this situation can be found in the section below.
2004	H7N3	2	Canada (British Columbia)	Poultry workers became ill during an outbreak of H7N3 avian influenza in poultry (see References : Health Canada 2004).
2004	H9N2	1 (child)	Hong Kong	The source of infection remains unknown (see References : National Institute of Allergy and Infectious Diseases: Focus on the Flu).
2004	H10N7	2 (infants)	Egypt	One child's father was a poultry merchant (see References : NIAID: Significant dates in influenza history).



Cumulative number of confirmed human cases of H5N1 avian influenza infection

Transmission and infection

Infected birds pass on H5N1 through their [saliva](#), [nasal secretions](#), and [feces](#). Other birds may pick up the virus through direct contact with these excretions or when they have contact with surfaces contaminated with this material. Because migratory birds are among the carriers of the H5N1 virus it may spread to all parts of the world. Past outbreaks of avian flu have often originated in crowded conditions in [southeast](#) and [east Asia](#), where humans, [pigs](#), and poultry live in close quarters. In these conditions a virus can [mutate](#) into a form that more easily infects humans.

How can bird flu infect people?

People are rarely infected with bird flu viruses. Those who have become infected have had close direct contact with infected birds. Historically, human infection with avian influenza viruses has usually caused mild conditions such as conjunctivitis (eye infection) and mild flu like symptoms. More severe infections can lead to pneumonia, acute respiratory distress, viral pneumonia, and other severe and life-threatening complications.

The first documented cases of bird flu infecting people occurred in Hong Kong in 1997 and this was also the H5N1 strain of virus. Investigation showed that close contact with live infected poultry was the source of the infection.

H5N1 is able to infect people because it is able to cross the species-barrier. In human populations, where domestic pigs and wild and domestic birds live in close proximity with people, the mingling and exchange of human and animal viruses can more easily occur.

There is no firm evidence that the H5N1 strain causing the outbreaks in SE Asia has acquired the ability to pass easily from person to person or to sustain transmission.

So far, while some instances of spread from one person directly to another have been reported, these have been isolated one-off occurrences with no further spread to people, and the route of transmission remains unconfirmed.

What are the symptoms?

Different strains of avian influenza can lead to different symptoms in people. All strains can cause symptoms typical of human influenza (fever, cough, tiredness, muscle aches, sore throat, shortness of breath, runny nose, headache). In some cases the H5N1 strain has caused a severe pneumonia and, in a small number of cases, the patient has had encephalitis (inflammation of the brain) or diarrhoea. The most common symptom of humans infected with H7 strains is conjunctivitis (inflammation of the lining of the eye). Symptoms generally appear between two to four days following exposure.

Who is at risk?

Most people are not at risk of this disease. People at risk of becoming infected with H5N1 are those who come into contact with sick birds or their faeces while living or travelling in areas where the virus is circulating, or (rarely) people who have had close contact with a person with the human form of the disease in the affected areas.

Symptoms

Since H5N1 is an influenza virus, [symptoms](#) similar to those of the common flu, such as [fever](#), cough, sore throat, and sore muscles, can develop in infected humans. However, in more severe cases, [pneumonia](#) and [respiratory failure](#) can develop and eventually cause death. Patients with H5N1 avian influenza have rarely had [conjunctivitis](#)^[4], unlike human cases of infection by the H7 virus.

Prevention

The current method of prevention in animal populations is to destroy infected animals as well as animals suspected of being infected. In southeast Asia, millions of domestic birds have been slaughtered to prevent the spread of the virus.

The probability of a "humanized" form of H5N1 emerging through recombination in the body of a human co-infected with H5N1 and another influenza could be reduced by influenza vaccination of at-risk workers. It is not clear at this point whether vaccine production could be stepped up sufficiently to meet this demand.

If an outbreak of pandemic flu does occur, its spread might be slowed by increasing hygiene in aircraft, and by examining airline cabin air filters for presence of H5N1 virus.

What can I do?

You can reduce, but not eliminate, the risk of catching or spreading influenza during a pandemic by:

- covering your nose and mouth when coughing or sneezing, using a tissue when possible;
- disposing of dirty tissues promptly and carefully – bag and bin them;
- avoiding non-essential travel and large crowds whenever possible;
- maintaining good basic hygiene, for example washing your hands frequently with soap and water to reduce the spread of the virus from your hands to your face, or to other people;
- cleaning hard surfaces (e.g. kitchen worktops, door handles) frequently, using a normal cleaning product;
- making sure your children follow this advice.

If you do catch flu:

- stay at home and rest;
- take medicines such as aspirin, ibuprofen or paracetamol to relieve the symptoms (following the instructions with the medicines). Please note: Children under 16 must not be given aspirin or ready made flu remedies containing aspirin; drink plenty of fluids.

What is the public health response?

Outbreaks of different strains of avian influenza have occurred previously in Australia. However, there have been no recent reports of avian influenza in Australian birds and there are no reports of Australian people with H5N1 virus infection. Australia does not import live poultry or uncooked poultry products from Asia and there is surveillance for the illegal importation of birds or bird products at Australian borders. Should suspected human cases occur in NSW, NSW Health would work with the patient, the treating doctors and the laboratory to confirm the diagnosis. Suspected cases would be isolated from others to prevent further infections. Close contacts of these cases who may be exposed to the virus will be given information about the risk of infection. Should these people also develop symptoms, they would also be isolated and tested for avian influenza.

Areas affected by H5N1 avian influenza in poultry include:

- Cambodia
- China
- Hong Kong
- Indonesia
- Japan
- Laos
- Malaysia
- South Korea
- Thailand
- Vietnam
- Russia
- Kazakhstan
- Mongolia
- Turkey
- Romania
- Croatia

WHO and CDC Travel Recommendations

As of November 2005, WHO has released the following advice to international travelers regarding H5N1 influenza (see [References](#): WHO: WHO recommendations relating to

travellers coming from and going to countries experiencing outbreaks of highly pathogenic H5N1 avian influenza):

- No restrictions on travel to areas affected by H5N1 are currently recommended.
- Travelers to areas that are experiencing outbreaks of H5N1 in poultry should avoid contact with live animal markets and poultry farms as well as contact with feathers, poultry feces, and undercooked poultry meat and egg products.

CDC issued a similar advisory to travelers to Asia in September 2005 that is updated frequently [see [References](#): CDC: Update: Human infection with avian influenza A (H5N1) virus in Asia]. The advisory recommends the following:

Before You Leave

- Educate yourself and others who may be traveling with you about avian influenza A (H5N1).
- Be sure you are up-to-date with all your shots, and see your doctor or healthcare provider at least 4 to 6 weeks before travel to get any additional shots or information you may need.
- Assemble a travel health kit containing basic first-aid and medical supplies. Be sure to include a thermometer and alcohol-based hand rub for hand hygiene. Additional information is available from CDC on putting together a kit (see [References](#): CDC: Traveler's Health Kit).
- Identify in-country health-care resources in advance of your trip.
- Check your health insurance plan or get additional insurance that covers medical evacuation in case you become sick. Information about medical evacuation services is provided on the US Department of State website (see [References](#): US Department of State).

During Travel

- Avoid places all contact with poultry, including even well-appearing birds. Also avoid places such as poultry farms and bird markets and avoid touching surfaces that could be contaminated with bird feces or secretions.
- As with other infectious illnesses, one of the most important preventive practices is careful and frequent handwashing. Cleaning your hands often, using either soap and water or waterless alcohol-based hand rubs, removes potentially infectious materials from your skin and helps prevent disease transmission.
- Influenza viruses are destroyed by heat; therefore, as a precaution, all foods from poultry, including eggs and poultry blood, should be thoroughly cooked.
- If you become sick with symptoms such as a fever, difficulty breathing, cough, or any illness that requires prompt medical attention, a US consular officer can assist you in locating medical services and informing your family or friends (see [References](#): Traveler's Health: Illness Abroad).
- It is advisable that you defer further travel until you are free of symptoms.

After Your Return

- Monitor your health for 10 days.
- If you become ill with fever, difficulty breathing, cough, or any illness during this period, consult a healthcare provider. Before you visit a healthcare setting, tell the provider about your symptoms and recent travel so that he or she can be aware you have traveled to an area reporting avian influenza.
- Do not travel while ill unless you are seeking medical care and, as with other infectious diseases, limit contact with others as much as possible if you are ill.

Clinical and Treatment Considerations

A recent report of avian influenza A (H5N1) in 10 patients in Vietnam (see [References: Hien 2004](#)) demonstrated the following clinical features of the illness:

- For eight of nine patients in whom a history of exposure to infected birds could be ascertained, the median time of exposure to onset of illness was 3 days (range, 2 to 4 days).
- All patients presented with fever, shortness of breath, and cough; median time from onset of illness to hospitalization was 5.9 days (range, 3 to 8 days).
- Five patients (50%) reported sputum production and in three of these patients, the sputum was blood-tinged.
- Seven patients (70%) reported diarrhea.
- None of the patients complained of sore throat, conjunctivitis, rash, or a runny nose.
- All patients had abnormal chest radiographs at the time of admission (including extensive bilateral infiltration, lobar collapse, focal consolidation, and air bronchograms).
- All of the patients had lymphopenia at the time of presentation; the median lymphocyte count was 700 per cubic millimeter (range, 250 to 1,100 with the lower limit of normal being 1500).
- Nine of the patients also had thrombocytopenia; the median platelet count was 75,500 per cubic millimeter (range, 45,000 to 174,000 with the lower limit of normal being 150,000).
- Eight patients (80%) died.
- All patients received broad-spectrum antibiotics and five were treated with oseltamivir (four of whom died).

Use of Seasonal Influenza Vaccine in Humans at Risk for H5N1 Infections

On January 30, 2004, WHO released guidelines for the use of seasonal influenza vaccine among persons at risk for H5N1 influenza (see [References: WHO: Guidelines for the use of seasonal influenza vaccine in humans at risk of H5N1 infection](#)). WHO is recommending targeted use of seasonal influenza vaccine to reduce the potential for

humans to be infected with H5N1 at the same time that they are harboring a human influenza strain. This will decrease the opportunity for genetic reassortment of the avian H5N1 strain with genes from a human (H1 or H3) strain and thereby reduce the likelihood that a novel pandemic strain will emerge from the current situation in Asia.

Groups recommended for vaccination include:

- All persons who expected to be in contact with poultry or poultry farms suspected or known to be affected with avian influenza (H5N1), especially:
 - Cullers involved in destruction of poultry
 - People living and working on poultry farms where H5N1 has been reported or is suspected or where culling takes place
- Healthcare workers involved in the daily care of known or confirmed human cases of influenza H5N1
- Healthcare workers in emergency care facilities in areas where there is confirmed occurrence of influenza H5N1 in birds (provided that sufficient supplies of vaccine are available)

Infection Control

Recently, WHO developed guidelines on infection control for management of patients with H5N1 avian influenza (see [References](#): WHO: Influenza A [H5N1]: WHO interim infection control guidelines for health care facilities). The WHO infection control guidelines recommend that the following precautions be implemented for patients with H5N1 influenza:

- Standard precautions
- Droplet precautions
- Contact precautions
- Airborne precautions (including use of high-efficiency masks and negative-pressure rooms if available)

For adults and children over 12 years of age, these precautions should be implemented at the time of admission and maintained until 7 days after resolution of fever. For children 12 and under, precautions should be continued until 21 days have lapsed from onset of illness.

The WHO guidelines also recommend that all healthcare workers who may come into contact with the H5N1 virus or with infected patients should be vaccinated with the current WHO-recommended vaccine. Although this will not protect against H5N1 influenza A, it will help avoid simultaneous infection with other influenza strains and may thereby decrease the risk of genetic reassortment.

Discussion and Conclusions

- It can be concluded that Nobilis Influenza H5 has the potency to induce a significant antibody response in ducks to the H5 subtype of Avian Influenza.
- Because ducks are more resistant to avian influenza than chickens it was anticipated that a higher vaccine dose would be required to induce antibody titres comparable to those induced in chickens. For this reason in this experiment ducks were vaccinated with 1 ml vaccine (double recommended chicken dose).
- Nobilis Influenza H5 induces H5 specific antibodies in ducks as from 3 weeks post-vaccination. (In 2 of the ducks titers were only demonstrated 5 weeks post-vaccination.) The level of antibody titer demonstrated in ducks exceeds the antibody titer level known to be protective in chickens when challenged with highly virulent Avian Influenzavirus of H5 subtype.
- Further challenge experiments are required to confirm the ability of the vaccine to reduce virus shedding after infection and the minimum protective antibody titer in ducks.