



# **Guidelines for Prevention and Control of Human Cases of Avian Influenza Disease (Bird Flu)**

**Developed with joint collaboration of  
the Public Health Laboratories Division (PHLD),  
National Institute of Health, Islamabad (NIH and  
World Health Organization (WHO)**

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**Epidemic Investigation Cell (EIC),  
Public Health Laboratories Division  
National Institute of Health, Islamabad  
Tel: 051- 9255237, 9255117, Fax: 051-9255099  
E-mail: [edoffice@apollo.net.pk](mailto:edoffice@apollo.net.pk)**

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## 1. Introduction

Avian Influenza, a contagious poultry disease caused by type A strains of the influenza virus, may result in rapid systemic illness and death to susceptible birds. Domestic chickens and turkeys are most severely affected; mortality in these birds often exceeds 50%.<sup>1</sup> Outbreaks of a highly pathogenic strain of the subtype H5N1 have been reported in South-east Asia since 2003, causing the unprecedented loss of about 150 million birds, and the disease is now considered “entrenched” in areas of Viet Nam, Indonesia, Cambodia, China, Thailand and Laos.<sup>2</sup>

As of 3<sup>rd</sup> January 2008

S#	Country	2003		2004		2005		2006		2007		2008		Total	
		Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
1.	Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	8	5
2.	Cambodia	0	0	0	0	4	4	2	2	1	1	0	0	7	7
3.	China	1	1	0	0	8	5	13	8	5	3	0	0	27	17
4.	Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	1	0
5.	Egypt	0	0	0	0	0	0	18	10	25	9	0	0	43	19
6.	Indonesia	0	0	0	0	20	13	55	45	41	36	0	0	116	94
7.	Iraq	0	0	0	0	0	0	3	2	0	0	0	0	3	2
8.	Lao PDR	0	0	0	0	0	0	0	0	2	2	0	0	2	2
9.	Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	1	0
9.	Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	1	1
10.	Thailand	0	0	17	12	5	2	3	3	0	0	0	0	25	17
11.	Turkey	0	0	0	0	0	0	12	4	0	0	0	0	12	4
12.	Viet Nam	3	3	29	20	61	19	0	0	8	5	0	0	101	47
13.	Pakistan	0	0	0	0	0	0	0	0	1	1	0	0	1	1
<b>Total</b>		<b>4</b>	<b>4</b>	<b>46</b>	<b>32</b>	<b>98</b>	<b>43</b>	<b>115</b>	<b>79</b>	<b>85</b>	<b>58</b>	<b>0</b>	<b>0</b>	<b>348</b>	<b>216</b>

Avian influenza does not usually infect humans, however, once transmitted; the infection may lead to development of disease with symptoms ranging from typical influenza-like symptoms (e.g., fever, cough, sore throat and muscle aches) to eye infections, pneumonia, acute respiratory distress, viral pneumonia, and other severe and life-threatening complications.<sup>3</sup> In the current outbreak, 348 confirmed cases of avian influenza viruses infecting humans, including 216 deaths, have been reported from twelve countries: as shown in table above.<sup>4</sup> So far, all genes are of avian origin, indicating that the virus has not acquired human genes. The acquisition of human genes is known to increase the likelihood that a virus of avian origin can be readily transmitted from one human to another.

## 2. Description and Epidemiology

<b>Infectious agent</b>	H5N1 strain of Type A Influenza virus or other pathogenic avian influenza virus
<b>Occurrence</b>	<ul style="list-style-type: none"> <li>Since October 2003, H5N1 has been reported in poultry in Viet Nam, Thailand, Cambodia, China, Indonesia, Turkey, Lao People’s Republic, Republic of Korea, and Japan, and in migratory birds in Siberia / Russia, Kazakhstan, and Mongolia. Cases of avian to human virus transmission have occurred in the first six countries.<sup>2</sup></li> </ul>

	<ul style="list-style-type: none"> <li>H7 in poultry in USA and Canada in 2004; H7N7 in Holland caused 83 human cases, mostly conjunctivitis, and one death in 2003.<sup>1</sup></li> <li>H7N3, H9N2 subtypes reported in poultry in Pakistan 2003-2005.<sup>5</sup></li> </ul>
<b>Reservoir</b>	Migratory waterfowl and ducks are historically the host reservoir of all influenza A viruses. Domestic ducks have been shown to excrete large quantities of highly pathogenic virus without showing signs of illness. <sup>1</sup>
<b>Mode of transmission</b>	Route and mode of spread according to current evidences includes: <ul style="list-style-type: none"> <li>Bird to bird – within species and across species such as migratory birds to chickens, chickens to turkeys and other chickens.<sup>1</sup></li> <li>Bird to person contact – about 100 reported cases and 63 deaths</li> <li>Four cases of human to human transmission of the H5N1 strain have been reported.<sup>2</sup></li> </ul>
<b>Seasonality</b>	Cases among bird populations can occur year round. However cases and outbreaks in poultry chickens are known to occur more commonly during winter months.
<b>Incubation period</b>	The incubation period for human influenza viruses is short – 2 to 3 days (range 1 to 7 days). However with influenza A (H5N1) the median time between exposure and onset of illness is 3 days (range 2 to 4 days). <sup>6</sup>
<b>Period of communicability</b>	<p>The infectious period is 7 days after resolution of fever in adults and 21 days after onset of illness in children. Communicability increases with the severity of disease and degree of direct exposure.<sup>5</sup></p> <p>The virus is known to survive in cold temperatures and in contaminated manure of birds for up to three months. In water it may survive up to 4 days at 22 degrees C and more than 30 days at zero degrees C. The virus can be killed by heat, i.e. meat cooked to internal temperature of 70 deg C is not infective.<sup>3</sup></p>
<b>Portal of entry</b>	<ul style="list-style-type: none"> <li>Orally among humans or birds</li> <li>Upper respiratory tract among humans</li> </ul>
<b>Portal of exit</b>	<ul style="list-style-type: none"> <li>Faeces, saliva and nasal secretions of infected birds</li> <li>Mainly upper respiratory tract among humans</li> </ul>
<b>Source of infection</b>	<ul style="list-style-type: none"> <li>Faeces among birds</li> <li>Respiratory discharge among humans</li> </ul> <p>This virus can be transmitted from farm to farm by mechanical means such as contaminated equipment, vehicles, feed, cages or clothing.</p>
<b>Susceptibility and resistance</b>	<p>All age and sex groups are susceptible. Most of the cases have occurred among those exposed to infected poultry.</p> <p>Experts express growing concern that there may be a possibility of reassortment of the H5N1 strain with an existing human influenza strain which may lead to a new influenza virus for which currently no vaccine has been developed and which may carry high transmission properties and may lead to higher case fatality rates than the usual influenza.</p> <p>Analysis of viruses isolated from the fatal cases in Vietnam indicates that the viruses are resistant to the anti-viral drugs like M2 inhibitors rimantidine and amantadine but susceptible to oseltamivir or Tamiflu.<sup>2</sup></p>
<b>Case definition</b>	<p><b>Possible Case</b></p> <p>Person with acute respiratory illness, characterized by fever (temperature &gt;38 degrees C) and cough and/or sore throat and either</p> <ul style="list-style-type: none"> <li>contact with a confirmed case of influenza A (H5N1) during the infectious period</li> <li>OR recent (less than 1 week) visit to a poultry farm in an area known to have outbreaks of highly pathogenic avian influenza (HPAI)</li> <li>OR worked in a laboratory that is processing samples from persons or</li> </ul>

	<p>animals that are suspected for HPAI virus infection.</p> <p><b>Probable Case</b> Possible case AND limited laboratory evidence for Influenza A (H5N1) (such as IFA + using HF5 monoclonal antibodies) OR no evidence for another cause of disease.</p> <p><b>Confirmed Case<sup>5</sup></b> A confirmed case of influenza A/H5 infection is an individual with an acute respiratory febrile illness for whom laboratory testing demonstrates one or more of the following:</p> <ul style="list-style-type: none"> <li>• positive viral culture for influenza A/H5;</li> <li>• positive polymerase chain reaction (PCR) for influenza A/H5;</li> <li>• positive immunofluorescence antibody (IFA) test to H5 antigen using H5 monoclonal antibodies;</li> </ul> <p>4-fold rise in H5 specific antibody titre in paired serum samples.</p>
<b>Exclusion criteria</b>	A case should be excluded if an alternative diagnosis can fully explain the illness
<b>Alert threshold</b>	Even a single case must lead to an alert and adequate response.

### 3. Clinical management of human cases of avian influenza

<b>Clinical picture</b>	Initially flu-like symptoms: rapid onset of high grade fever (> 38.5 deg C) followed by muscle aches, headache, sore throat. In some cases there may be unilateral or bilateral pneumonia, progressing to acute respiratory distress requiring assisted breathing on respirator.
<b>Case Fatality Rate (CFR)</b>	In the current outbreak, the case fatality rate ranges from 50 - 70 % among the reported human cases in Vietnam and Thailand. <sup>1</sup>
<b>Diagnosis</b>	Hemagglutinin inhibition (HAI), ELISA, IFA with HF5 monoclonal antibodies and RT-PCR have been developed. Virus isolation is the key factor in confirming the sub-type of the influenza virus. <sup>6</sup>
<b>Treatment Guidelines</b>	<p>The patient may present with rapid onset of Flu symptoms like severe nasal and oral irritation with profuse watery secretions followed by immediate high-grade fever with throbbing headache and generalized muscular aches. The syndrome if not controlled with medical treatment and nursing care is liable to progress in the subsequent complications e.g. wide spread pneumonia which can lead to acute respiratory failure in a short span of time.</p> <ol style="list-style-type: none"> <li>a) Isolation ward: gowns, masks, gloves, goggles, for aerosol producing procedures</li> <li>b) Immediate maintenance of IV line for Infusion / Antibiotics</li> <li>c) Immediate commencement of Oral Capsules of Oseltamivir 75mg BD up to 5 days.</li> <li>d) Analgesics / antipyretic (Paracetamol-Tablet / Syrup or Broufen Tablet / Syrup or Injection diclofenac 75-150mg IM which ever is clinically necessary.</li> <li>e) Antibiotics (Quinolone Tablets / Injection / Infusion Ciprofloxacin BD) for 7-10 days in case of complication like Pneumonia.</li> <li>f) Putting patient on ventilator if patient develops respiratory failure.</li> </ol> <p><b>Dosage of Oseltamivir Antiviral Medication</b> The currently recommended doses of Oseltamivir (Tamiflu®) for treatment of influenza are:</p> <ul style="list-style-type: none"> <li>• Adults: 75 milligrams (mg) two times a day for five days.</li> <li>• Children 1 year of age or older: weight adjusted doses <ul style="list-style-type: none"> <li>➢ 30mg twice daily for ≤ 15 kg</li> </ul> </li> </ul>

	<ul style="list-style-type: none"> <li>➤ 45mg twice daily for &gt;15 to 23 kg</li> <li>➤ 60mg twice daily for &gt;23 to 40kg</li> <li>➤ 75mg twice daily for &gt;40kg</li> <li>• Children up to 1 year of age: not recommended</li> </ul>
	<p><b><i>Once started the patient must complete the whole course of Oseltamivir.</i></b></p>
	<p><b>Evidence for effectiveness of treatment</b>  The evidence for effectiveness of oseltamivir in human H5N1 disease is based on virological data from in vitro, animal models, and limited human studies and extrapolation from the results of trials in patients with ordinary human influenza. The clinical course and, presumably, some aspects of the immunopathogenesis, of human H5N1 disease (in particular the severe form) may be different from normal seasonal influenza requiring a different dosing approach.</p>
<p><b>Collection of clinical specimens<sup>7</sup></b></p>	<p>Specimens for transport must be surrounded by absorbable material such as cotton, placed in leak-proof specimen bag, and sealed in another bag or container to further isolate and prevent breakage. Specimens must be kept at 4°C with icepacks inside a cold box and transported to the laboratory within 2 days. Repeated freezing and thawing must be avoided to prevent loss of infectivity. Icepacks and cold boxes can be provided by the Polio Program focal point.</p> <p>Investigation forms should be also kept in the cold box with the specimen so they are not misplaced. When samples have been collected, the officer would call the specified courier and hand over a cold box lined with four fresh ice packs and containing the specimens along with the investigation form for each specimen.</p> <p>Personnel who transport specimens should be trained in safe handling practices and decontamination procedures in case of a spill. A register should be kept of all those who have handled specimens of patients being investigated for influenza.</p>
	<p><b>Procedure for specimen collection among humans:</b></p>
	<p>Standard precautions should always be followed, and barrier protections applied whenever samples are obtained from patients.</p> <p><b>Throat swab</b></p> <ul style="list-style-type: none"> <li>• Both tonsils and the posterior pharynx are swabbed vigorously.</li> <li>• The tip of the swab is put into a plastic vial containing 2–3 ml of virus transport medium and the applicator stick is broken off.</li> </ul> <p><b>Nasal swab</b></p> <ul style="list-style-type: none"> <li>• A dry polyester swab is inserted into the nostril, parallel to the palate, and left in place for a few seconds. It is then slowly withdrawn with a rotating motion.</li> <li>• Specimens from both nostrils are obtained with the same swab.</li> <li>• The swab is placed in transport medium as described above.</li> </ul> <p><b>Nasopharyngeal swab</b></p> <ul style="list-style-type: none"> <li>• A flexible, fine-shafted polyester swab is inserted into the nostril and back to the nasopharynx and left in place for a few seconds. It is then slowly withdrawn with a rotating motion.</li> <li>• A second swab should be used for the second nostril.</li> <li>• The tip of the swab is put into a vial containing 2–3 ml of virus transport medium and the shaft cut.</li> </ul> <p><b>Nasopharyngeal aspirate</b></p> <ul style="list-style-type: none"> <li>• Nasopharyngeal secretions are aspirated through a catheter connected to a mucus trap and fitted to a vacuum source. The catheter is inserted into the nostril parallel to the palate. The vacuum is applied and the catheter is slowly withdrawn with a rotating motion.</li> <li>• Mucus from the other nostril is collected with the same catheter in a similar manner.</li> </ul>

	<ul style="list-style-type: none"> <li>• After mucus has been collected from both nostrils, the catheter is flushed with 3 ml of transport medium.</li> </ul> <p><b>Nasal wash</b></p> <ul style="list-style-type: none"> <li>• The patient sits in a comfortable position with the head slightly tilted backward and is advised to keep the pharynx closed by saying "K" while the washing fluid (usually physiological saline) is applied to the nostril.</li> <li>• With a transfer pipette, 1–1.5 ml of washing fluid is instilled into one nostril at a time. The patient then tilts the head forward and lets the washing fluid flow into a specimen cup or a Petri dish.</li> <li>• The process is repeated with alternate nostrils until a total of 10–15 ml of washing fluid has been used.</li> <li>• Dilute approximately 3 ml of washing fluid 1:2 in transport medium.</li> </ul> <p><b>Sera collection for influenza diagnosis</b></p> <ul style="list-style-type: none"> <li>• An acute-phase serum specimen (3–5 ml of whole blood) should be taken soon after onset of clinical symptoms and not later than 7 days after onset.</li> <li>• A convalescent-phase serum specimen should be collected 14 days after the onset of symptoms. Where patients are near death, a second ante-mortem specimen should be collected.</li> <li>• Although single serum specimens may not provide conclusive evidence in support of an individual diagnosis, when taken more than 2 weeks after the onset of symptoms they can be useful for detecting antibodies against avian influenza viruses in a neutralization test.</li> </ul> <p><b>Postmortem specimens</b></p> <ul style="list-style-type: none"> <li>• Collect tissue and heart blood in fatal cases.</li> <li>• Divide lung tissue into two, place half portion in 10% formalin or formalin-saline and the remaining half collect as fresh.</li> </ul> <p><b>Procedure for specimen collection among poultry birds</b></p> <p>In liaison with designated laboratories, blood and post mortem specimens (intestinal contents, anal and oro-nasal swabs, trachea, lung, intestine, spleen, kidney, brain, liver and heart) may be collected for identification of virus through similar diagnostic techniques as for humans.</p>
<p><b>Storage and transportation of clinical specimens<sup>8</sup></b></p>	<ul style="list-style-type: none"> <li>• Standard precautions should always be followed, and barrier protections applied whenever samples are obtained from patients.</li> <li>• Specimens in viral transport medium for viral isolation should be kept at 4 °C and transported to the laboratory promptly on ice or in liquid nitrogen.</li> <li>• If specimens are transported to the laboratory within 2 days, they may be kept at 4 °C; otherwise they should be frozen at or below –70 °C until they can be transported to the laboratory.</li> <li>• Repeated freezing and thawing must be avoided to prevent loss of infectivity. Sera may be stored at 4 °C for approximately one week, but thereafter should be frozen at –20 °C.</li> <li>• Specimens for influenza should not be stored or shipped in dry ice (solid carbon dioxide) unless they are sealed in glass or sealed, taped and double plastic-bagged. Carbon dioxide can rapidly inactivate influenza viruses if it gains access to the specimens through shrinkage of tubes during freezing.</li> </ul>
<p><b>Care and management of human cases<sup>6</sup></b></p>	<ul style="list-style-type: none"> <li>• Patients meeting case definition for suspected avian influenza should be hospitalized under isolation or cohorted with other avian influenza patients and cared for using barrier-nursing techniques.</li> <li>• Detailed clinical, contact and travel history is needed including contact with acute respiratory diseases over last 10 days.</li> <li>• Lab investigation, in laboratories with proper containment facilities, to exclude known causes of pneumonia: Complete blood picture</li> </ul>

	<p>Serology from blood samples Throat and/or nasopharyngeal swabs and cold agglutinin</p> <ul style="list-style-type: none"> <li>• Chest x-ray as clinically indicated.</li> <li>• Good supportive care including intensive therapy has been shown to improve the prognosis.</li> <li>• The drug oseltamivir (Tamiflu) has been shown to be effective in human cases of H5N1.</li> </ul>
<p><b>Hospital infection control guidance<sup>6</sup></b></p>	<ul style="list-style-type: none"> <li>• Strict adherence with barrier nursing of avian influenza patient</li> <li>• Use precautions for airborne, droplet and contact transmissions</li> <li>• Rapidly divert the patient reporting to health care facility with flu-like symptoms to a separate area to minimize transmission to others.</li> <li>• Suspect case should wear surgical masks until avian influenza is excluded</li> <li>• Isolate the patient and accommodate as follows: <ul style="list-style-type: none"> <li>○ Single room with their own bathroom facilities or cohorted placement in an area with an independent air supply and exhaust system; Patients under investigation for avian influenza should be separated from those diagnosed with the disease.</li> <li>○ Disposable equipments should be used. If devices are to be reused, they should be sterilized with broad-spectrum disinfectants of proven efficacy.</li> <li>○ Restrict movement of patient as much as possible, or patient should wear surgical mask to minimize dispersal of droplets.</li> <li>○ Visitors, staff, students and volunteers should wear N95 masks on entering the room of the patient</li> </ul> </li> <li>• Hand washing before and after contact with any patient is the most important hygienic measure in preventing the spread of infection.</li> <li>• Health Care Workers (HCWs) should wear gloves for all patient handling, and gloves should be changed after any contact with the items likely to be contaminated with respiratory secretions.</li> <li>• HCWs must wear protective eyewear or face shields or masks during procedures where there is potential splashing, splattering or spraying of blood or other body substances of the patients suspected, probable or confirmed avian influenza.</li> <li>• Standard precautions should be applied when handling any clinical wastes. Gloves and protective clothing should be worn while handling clinical waste bags and containers. Manual handling should be avoided and clinical waste should be placed in leak-resistant biohazard bags or containers labeled and disposed of safely.</li> </ul>

**4. Prevention and control measures**

<p><b>Management of viral disease among poultry<sup>9</sup></b></p>	<ul style="list-style-type: none"> <li>• World Health Organization recommends culling of poultry (burn or burial) with decontamination of yard or chicken pen and at the site of the burial; as a measure to prevent the transmission of this form of influenza into human populations.</li> </ul> <p><b>Safety measures for poultry workers, cullers and poultry transporters</b></p> <ul style="list-style-type: none"> <li>• If you need to handle dead or sick poultry, make sure you are protected. Wear protective clothing such as a mask, goggles, gown, rubber boots and gloves. If these are not available, cover your mouth with a piece of cloth, wear glasses, use plastic bags to cover hands and shoes and fix these tightly around wrists and ankles with a rubber band or string. Wear overalls that can be washed.</li> <li>• When burying dead birds or their faeces, try to avoid generating dust by spraying or sprinkling water to dampen the area first. Bury bird carcasses and faeces at a depth of at least one meter.</li> <li>• Wearing protective clothing, remove all organic matter from the chicken</li> </ul>
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	<p>pens and thoroughly clean with detergent and water.</p> <ul style="list-style-type: none"> <li>• As outdoor areas used by infected poultry can be difficult to disinfect, new poultry should be excluded from these areas for a minimum of 42 days to allow natural ultraviolet radiation to destroy any residual virus. The period of exclusion should be longer in cold weather.</li> <li>• Persons at high risk for severe complications of influenza (e.g. the immuno-compromised, people over 60 years old, or people with known chronic heart or lung disease) should avoid working with affected chickens.</li> <li>• All persons who have been in close contact with the infected poultry should wash their hands frequently with soap and water. For decontamination of protective clothing, please see below.</li> </ul>
<p><b>Decontamination of protective clothing<sup>9</sup></b></p>	<ul style="list-style-type: none"> <li>• Remove all the protective materials and wash your hands with soap and water.</li> <li>• Wash clothes in warm soapy water and hang in the sun to dry.</li> <li>• Put used gloves and other disposable materials in a plastic bag for safe disposal.</li> <li>• Clean all reusable items such as rubber boots and glasses/goggles with water and detergent, but always remember to wash your hands after handling these items.</li> <li>• Items that cannot be cleaned properly should be destroyed.</li> <li>• Shower/ wash body using soap and water. Wash your hair.</li> <li>• Most importantly, wash your hands every time after handling any contaminated items.</li> </ul>
<p><b>Advice for people living in areas affected by avian influenza<sup>9</sup></b></p>	<p>Avoid contact with chickens, ducks or other poultry unless absolutely necessary. Implement and teach children the following:</p> <ul style="list-style-type: none"> <li>• Avoid contact with any birds, their feathers, faeces and other waste.</li> <li>• Do not keep birds as pets.</li> <li>• Wash hands with soap and water after any contact.</li> <li>• Do not sleep near poultry.</li> <li>• Do not transport live or dead chickens, ducks, or other poultry from one place to another even if you think your birds are healthy.</li> <li>• Do not slaughter or prepare fresh poultry from affected areas.</li> <li>• If you unintentionally come into contact with live poultry from affected areas, including touching dead birds or feathers or walking on soil contaminated with poultry faeces: <ul style="list-style-type: none"> <li>○ Remove your shoes outside the house and clean them thoroughly with soap and water.</li> <li>○ Wash hands with soap and water.</li> <li>○ Remove your clothes and shower.</li> <li>○ Wash hands with soap and water.</li> <li>○ Check your temperature for seven days and report to the nearest health care facility if you develop a fever.</li> </ul> </li> </ul>
<p><b>Respiratory etiquette for those with flu-like illness<sup>9</sup></b></p>	<p>Anyone with flu-like illness should be careful with secretions from the nose and mouth when around other people, especially small children, in order not to spread influenza virus.</p> <ul style="list-style-type: none"> <li>• Use a tissue to cover your nose and mouth when coughing or sneezing and throw it away once used.</li> <li>• Always wash your hands with soap and water after any contact with secretions from nose or mouth as these can carry a virus. Avoid touching your face, eyes and mouth with unwashed hands.</li> <li>• Teach children to cover their coughing as above and the importance of hand washing after coughing, sneezing and touching dirty items.</li> </ul>

## References

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