

**PREVENTION AND CONTROL OF INFLUENZA
DUE TO
AVIAN INFLUENZA VIRUS A (H5N1)**

A compilation of technical information as of 30 January 2004

Version 30 January 2004



WORLD HEALTH ORGANIZATION
Regional Office for South-East Asia
New Delhi

CONTENTS

	<i>Page</i>
1. INTRODUCTION	1
2. GENESIS OF CURRENT OUTBREAK	2
3. EPIDEMIOLOGY	2
4. AETIOLOGY	4
5. PROVISIONAL CASE DEFINITIONS FOR AVIAN INFLUENZA	4
6. CLINICAL PICTURE	5
7. LABORATORY DIAGNOSIS	5
8. MANAGEMENT OF CASE	8
9. PREVENTION AND CONTROL	8
10. POTENTIAL FOR AN INFLUENZA PANDEMIC	10
11. ADVICE TO INTERNATIONAL TRAVELLERS	10
12. INFECTION CONTROL PRACTICES	10
13. PERSONAL PROTECTIVE EQUIPMENT (PPE) AND THEIR USE	11
14. PATIENT, FAMILY AND COMMUNITY EDUCATION	14
15. IEC AND ROLE OF MEDIA	14
16. COUNTRY PREPAREDNESS	14
Annex -Guidelines for Packing and Shipping of Clinical Material	16

1. INTRODUCTION

Influenza virus can infect both human beings and animals, notably pigs and birds. The subtypes of influenza virus demonstrate species specificity and those, which infect animals, do not usually cause infection and disease in human beings. Fifteen subtypes of influenza virus are known to infect birds; some of these are highly pathogenic. To date, all outbreaks of the highly pathogenic form have been caused by influenza A viruses of subtypes H5 and H7. This “highly pathogenic avian influenza” is characterized in birds by sudden onset, severe illness, and rapid death, with a mortality that can approach 100%.

Migratory waterfowl – most notably wild ducks – are the natural reservoir of avian influenza viruses, and these birds are also the most resistant to infection. Domestic poultry, including chickens and turkeys, are particularly susceptible to epidemics of rapidly fatal influenza. Direct or indirect contact of domestic flocks with wild migratory waterfowl has been implicated as a frequent cause of epidemics. Live bird markets have also played an important role in the spread of epidemics.

Avian influenza usually does not make wild birds sick, but can make domesticated birds very sick and kill them. Avian influenza A viruses do not usually infect humans; however, several instances of human infections and outbreaks have been reported since 1997. When such infections occur, public health authorities monitor the situation closely because of concerns about the potential for more widespread infection in the human population.

Avian Influenza Infections in Humans

The first documented infection of humans with an avian influenza virus occurred in Hong Kong in 1997, when the H5N1 strain caused severe respiratory disease in 18 humans, of whom 6 died. The infection of humans coincided with an epidemic of highly pathogenic avian influenza, caused by the same strain, in Hong Kong’s poultry population.

Extensive investigation of that outbreak determined that close contact with live infected poultry was the source of human infection. Studies at the genetic level further determined that the virus had jumped directly from birds to humans. Limited transmission to health care workers occurred, but did not cause severe disease.

Rapid destruction – within three days – of Hong Kong’s entire poultry population, estimated at around 1.5 million birds, reduced opportunities for further direct transmission to humans, and may have averted a pandemic.

The Hong Kong episode alarmed public health authorities, as it marked the first time that an avian influenza virus was transmitted directly to humans and caused severe illness with high mortality.

Confirmed instances of avian influenza viruses infecting humans since 1997 have been summarized in Table 1. In all these cases close contact with poultry was incriminated.

Table 1. Confirmed cases of avian influenza in human beings 1997-2003

Year	Country	Cases	Deaths	Type of Influenza A Virus
1997	Hong Kong	18	6	H5N1
1999	Hong Kong	2	0	H9N2
1999	Mainland China	Several	?	H9N2
2003	Hong Kong	2	1	H5N1
2003	Netherlands	80	1	H7N7
2003	Hong Kong	1	1	H9N2

The importance of H5N1 subtype of Influenza virus type A

Of the 15 avian influenza virus subtypes, H5N1 is of particular concern for several reasons. H5N1 mutates rapidly and has a documented propensity to acquire genes from viruses infecting other animal species. Its ability to cause severe disease in humans has now been documented on two occasions. In addition, laboratory studies have demonstrated that isolates from this virus have a high pathogenicity and can cause severe disease in humans. Birds that survive infection excrete virus for at least 10 days, orally and in faeces, thus facilitating further spread at live poultry markets and by migratory birds

2. GENESIS OF CURRENT OUTBREAK

The most recent cause for alarm occurred in January 2004, when laboratory tests confirmed the presence of H5N1 avian influenza virus in human cases of severe respiratory disease in the northern part of Viet Nam. The epidemic of highly pathogenic avian influenza caused by H5N1, is presumed to have begun in mid-December 2003 in the Republic of Korea and is now being seen in other Asian countries, is therefore of particular public health concern. H5N1 subtype has already demonstrated a capacity to directly infect humans in 1997, and has done so again in Viet Nam and Thailand in January 2004. The spread of infection in birds increases the opportunities for direct infection of humans. If more humans become infected over time, the likelihood also increases that humans, if concurrently infected with human and avian influenza strains, could serve as the "mixing vessel" for the emergence of a novel subtype with sufficient human genes to be easily transmitted from person to person. Such an event would mark the start of an influenza pandemic.

Till date, WHO reported three laboratory-confirmed cases of H5N1 avian influenza in central Thailand of whom two have died. The first case is in a 7-year-old boy from Suphanburi province who developed fever and cough on January 3; his illness progressed to acute respiratory distress syndrome on January 13. The second case is a 6-year-old boy from Kanchanaburi province who developed fever on January 6, followed a week later by severe pneumonia with acute respiratory distress syndrome.

3. EPIDEMIOLOGY

Form to accompany clinical sample for testing in laboratory

Patient name: _____

Nationality: _____

Date of birth: _____ Age: _____ Male Female

Patient's residence: _____

(Town/Province/State/City/Country)

Date of onset: _____ (DD/MM/YY)

Date of hospitalization: _____ (DD/MM/YY)

Occupation : Healthcare worker Yes No.

If yes, specify Physician Nurse/Patient Assistant Laboratory

Other Occupation (specify) _____

Signs and Symptoms:

Temperature _____ Cough Shortness of breath / difficulty breathing

Pneumonia Radiographic evidence of pneumonia

Respiratory distress syndrome (ARDS)

Other symptoms: _____

Exposure History

Indicate if the patient was one or more of the following:

Health care worker Poultry Other Unknown

Specimens for this patient being sent in this shipment (DD/MM/YY)

Nasopharyngeal wash / aspirate Date of collection _____

Nasopharyngeal / Oropharyngeal swabs Date of collection _____

Bronchoalveolar lavage, Date of collection _____

Tracheal aspirate or pleural tap Date of collection _____

Serum (DD/MM/YY)

Acute Date of collection _____

Convalescent Date of collection _____

Whole blood

Acute Date of collection _____

Convalescent Date of collection _____

Additional specimens (Please describe)

Date of collection _____ (DD/MM/YY)

Name and address of the sender:-

Viral Transport Media (VTM)

Transport media preparation

Nutrient broth (VTM) or Cell culture broth (VTM)

1. Nutrient broth

Beef extract	0.5	g
Peptone	1.5	g
NaCl	0.5	g
K ₂ HPO ₄	0.5	g
Distilled water	100	ml

Autoclave at 121°C 15 min

Add Penicillin G, Streptomycin and Fungizone at the final concentration 1000 U/ml, 1,000 ug/ml and 4 ug/ml respectively. Adjust nutrient broth at pH 7.0 ±0.2 by using 1 N NaOH or 1N HCL. Aliquot nutrient broth 2 ml into disposable sterile tube. Keep in refrigerator at 4°C.

2. Cell culture broth

Hank balance salt media 100 ml

Bovine serum albumin (BSA)	0.5	g
Add antibiotics at the concentration as follow		
Penicillin G	1000	U/ml
Streptomycin	1000	mg/ml
Fungizone	4	mg/ml

Mix the cell culture broth with magnetic stirrer. Adjust cell culture broth at pH 7.0 ±0.2 by using 1 N NaOH or 1N HCL. Then filtrate cell culture broth with membrane filter size 0.2-0.45 µm Aliquot VTM 2 ml into disposable sterile tube. Keep in refrigerator at 4°C

Influenza A viruses are found in many different animals, including ducks, chickens, pigs, whales, horses, and seals. Influenza B viruses circulate widely only among humans.

Wild birds are the primary natural reservoir for all subtypes of influenza A viruses and are thought to be the source of influenza A viruses in all other animals (not human beings). Most influenza viruses cause asymptomatic or mild infection in birds; however, the range of symptoms in birds varies greatly depending on the strain of virus. Infection with certain avian influenza A viruses (for example, some strains of H5 and H7 viruses) can cause widespread disease and death among some species of wild and especially domestic birds such as chickens and turkeys.

Pigs can be infected with both human and avian influenza viruses in addition to swine influenza viruses. Infected pigs get symptoms similar to humans, such as cough, fever, and runny nose. Because pigs are susceptible to avian, human and swine influenza viruses, they potentially may be infected with influenza viruses from different species (e.g., ducks and humans) at the same time. If this happens, it is possible for the genes of these viruses to mix and create a new virus. For example, if a pig were infected with a human influenza virus and an avian influenza virus at the same time, the viruses could mix (reassort) and produce a new virus that had most of the genes from the human virus, but a hemagglutinin and/or neuraminidase from the avian virus. The resulting new virus would likely be able to infect humans and spread from person to person, but it would have surface proteins (hemagglutinin and/or neuraminidase) not previously seen in influenza viruses that infect humans. This type of major change in the influenza A viruses is known as antigenic shift. Antigenic shift results when a new influenza A subtype to which most people have little or no immune protection infects humans. If this new virus causes illness in people and can be transmitted easily from person to person, an influenza pandemic can occur.

While it is unusual for people to get influenza infections directly from animals, sporadic human infections and outbreaks caused by certain avian influenza A viruses have been reported. The exact epidemiology of avian influenza and precise mechanisms of transmission of these viruses to human-beings need to be fully elucidated.

Once influenza virus is established in domestic poultry, it is a highly contagious disease and wild birds are no longer an essential ingredient for spread. Infected birds excrete virus in high concentration in their faeces and also in nasal and ocular discharges. Once introduced into a flock, the virus is spread from flock to flock by the usual methods involving the movement of infected birds, contaminated equipment, egg flats, feed trucks, and service crews, to mention a few. The disease generally spreads rapidly in a flock by direct contact, but on occasions spread is erratic.

In virulent (or highly pathogenic avian influenza) of the type traditionally associated with fowl plague, the disease appears suddenly in a flock and many birds die either without premonitory signs or with minimal signs of depression, loss of inappetence, ruffled feathers and fever. Other birds show weakness and a staggering gait. Hens may at first lay soft-shelled eggs, but soon stop laying. Sick birds often sit or stand in a semi-comatose state with their heads touching the ground. Combs and wattles are cyanotic and oedematous, and may have petechial or ecchymotic haemorrhages at their tips. Profuse watery diarrhoea is frequently present and birds are excessively thirsty. Respiration may be laboured. Haemorrhages may occur on unfeathered areas of skin. The mortality rate varies from 50 to 100%.

Airborne transmission may occur if birds are in close proximity and with appropriate air movement. Birds are readily infected via instillation of virus into the conjunctival sac, nares, or the

trachea. Preliminary field and laboratory evidence indicates that virus can be recovered from the yolk and albumen of eggs laid by hens at the height of the disease. The possibility of vertical transmission is unresolved; however, it is unlikely infected embryos could survive and hatch. Attempts to hatch eggs in disease isolation cabinets from a broiler breeder flock at the height of disease failed to result in any avian influenza -infected chickens. This does not mean that broken contaminated eggs could not be the source of virus to infect chicks after they hatch in the same incubator. The hatching of eggs from a diseased flock would likely be associated with considerable risk.

4. AETIOLOGY

Influenza viruses are members of the family Orthomyxoviridae. These are classified into types A, B or C based on differences between their nucleoprotein and matrix protein antigens. Influenza viruses are further categorised into subtypes according to the antigens of the haemagglutinin (H) and neuraminidase (N) projections on their surfaces. There are 15 haemagglutinin subtypes and 9 neuraminidase subtypes of influenza A viruses. While all subtypes can be found in birds, only 3 subtypes of HA (H1, H2 and H3) and two subtypes of NA (N1 and N2) are known to have circulated widely in humans.

Influenza A, B, and C viruses

Influenza types A or B viruses cause epidemics of disease in human beings almost every winter. Influenza type C infections cause a mild respiratory illness and are not thought to cause epidemics. Influenza type A viruses are divided into subtypes based on two proteins on the surface of the virus. These proteins are called hemagglutinin (H) and neuraminidase (N). The current subtypes of influenza A viruses found in people are A(H1N1) and A(H3N2). Influenza B and C viruses are not divided into subtypes. Influenza A(H1N1), A(H3N2), and influenza B strains are included in each year's influenza vaccine.

5. PROVISIONAL CASE DEFINITIONS FOR AVIAN INFLUENZA

Possible/Suspect Case of Influenza A (H5N1)

- (1) person with acute respiratory illness, characterized by fever (temperature ≥ 38 C) and cough and/ or sore throat AND EITHER
- (2) contact with a confirmed case of influenza A(H5N1) during the infectious period OR
- (3) recent (less than 1 week) visit to a poultry farm in an area known to have outbreaks of HPAI OR
- (4) worked in a laboratory that is processing samples from persons or animals that are suspected from HPAI infection

Probable Case of Influenza A (H5N1)

- (1) possible case AND

labelled specimen. The outer package should display the sender, the laboratory name with complete address and telephone numbers for the sender and the recipient, the appropriate biohazard labels, and storage temperature requirements.

Samples for laboratory processing

Type of specimen	Method	Medium/ container/ shipment	Timing	Potential use
Nasopharyngeal	Aspirate: specimen of choice for respiratory viruses	Sterile vial Ship on ice (+4°C)	Any time in course of illness Particularly useful during initial phase of disease	Viral culture PCR immunofluorescence,
Nasopharyngeal or oropharyngeal	Swab: use only sterile Dacron or rayon swab with plastic shaft	Sterile vials with viral transport media. Ship on ice (+4°C)	Any time in course of illness Particularly useful during initial phase of disease	
Serum		$\geq 200 \mu$ l preferred. Ship on ice or frozen	Acute: as soon as possible (up to 7 days) Convalescent: after 3-4 weeks	Specific antibody detection (IgM, rising IgG titers)
Blood		Standard blood culture bottle		Viral culture, PCR

RT: room temperature

Biosafety Guidelines

1. The virology work, PCR as well as preparations for transportation of infectious material should may be performed in Biosafety Level (BSL) 2 facilities using BSL-2 practices
2. The following activities require BSL-3 facilities and BSL-3 work practices :
 - Culture-based attempts to isolate the agent, including inoculation onto cell culture, and eggs.
 - Initial characterization of agents recovered in cultures of specimens.
 - Protective clothing, preferably coveralls plus impermeable apron or long cuffed sleeves surgical gowns plus impermeable apron;
 - Disposable examination gloves;
 - Masks: the minimum requirement are well-fitted surgical masks. Where available the use of N95 masks is recommended.
 - Goggles.
 - Boots or some protective foot cover that can be disinfected

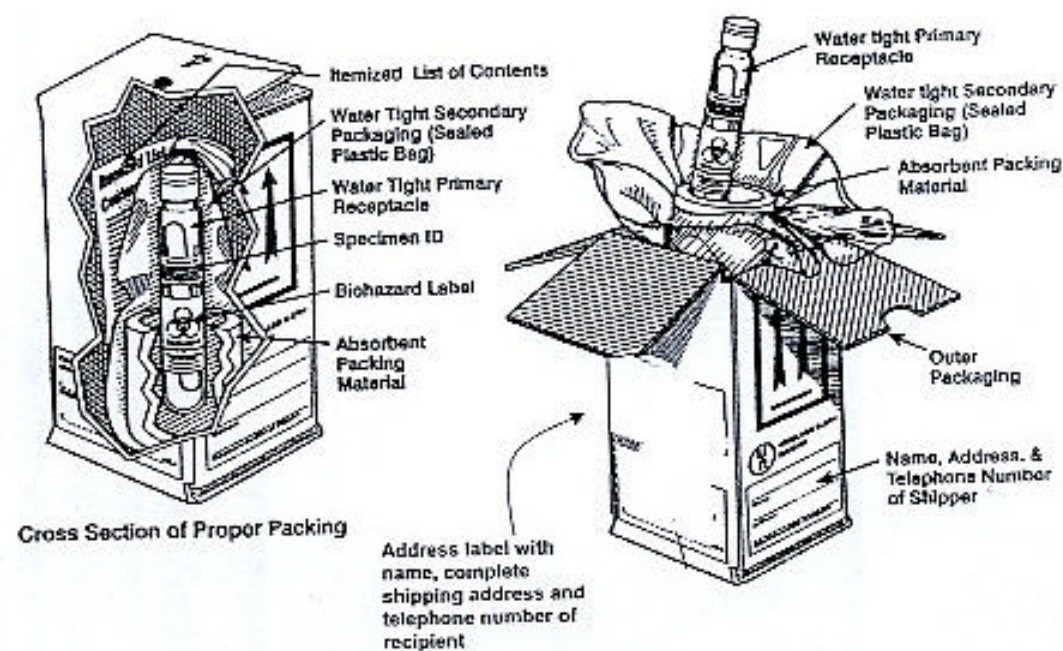
Annex 1

GUIDELINES FOR PACKING AND SHIPPING OF CLINICAL MATERIAL

Packing and shipping

- Primary receptacle(s) must be water tight, e.g., if screw cap seal with parafilm or similar.
- Multiple primary receptacles must be wrapped individually to prevent breakage.
- Use enough absorbent material to absorb the entire contents of all primary receptacles in case of leakage or damage

Proper packing and labeling of the secondary container for shipping of diagnostic



The labeling for contents should include the words:

“UN 3373 Diagnostic Specimens”

In order to minimise possible loss of usefulness in specimens for further assays during the transportation period, it is advised to ship samples packed preferably with dry ice, or alternatively with enough amount of frozen ice packs/refrigerant. Detail packing, documentation, and handling requirements for the international transport of infectious materials as contained in the regulations of the International Air Transport Association (IATA) and in documentation of the International Health Regulations (IHR).

Before transport, the collection team should notify the receiving laboratories of all shipping specimen details in advance of specimen arrival. Laboratory request form must accompany the

- (2) limited laboratory evidence for Influenza A(H5N1) (such as IFA+ using H5 monoclonal antibodies) OR c) no evidence for another cause of disease

Confirmed H5N1 Case

- (1) positive viral culture for influenza A(H5N1) OR
- (2) positive PCR for Influenza (H5) OR c) a 4-fold rise in H-5 specific Ab titer

6. CLINICAL PICTURE

The reported symptoms of avian influenza in humans have ranged 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.

Published information about the clinical course of human infection with H5N1 avian influenza is limited to studies of cases in the 1997 Hong Kong outbreak. In that outbreak, patients developed symptoms of fever, sore throat, cough and, in several of the fatal cases, severe respiratory distress secondary to viral pneumonia. Previously healthy adults and children, and some with chronic medical conditions, were affected.

7. LABORATORY DIAGNOSIS

Laboratory diagnosis depends upon the demonstration of the virus and or a rising antibody titre. Following tests are available (kits for these are being developed and may be available soon):

- (1) Virus culture
- (2) RT-PCR
- (3) Immunofluorescence using monoclonal antibody to H5N1
- (4) Serological tests (ELISA and IFAT) for detection of specific antibody

Of these, virus culture can be done in laboratories with infrastructure, skills and reagents for isolation of influenza virus and confirmation of H5N1 subtype. These facilities are available only in a limited number of laboratories.

Primers for performing RT-PCR tests are being developed and expected to be available shortly. The information on these primers shall be made available on websites of WHO, CDC, Atlanta, Ga and other institutes which may develop these.

Direct immunofluorescence test can be used to ascertain presence of virus using H5N1 specific monoclonal antibody conjugated with a fluorescing dye.

As and when reliable laboratory tools become available, greater emphasis shall be placed on the results obtained through them in defining or classifying the cases.

Clinical material

(5) Upper respiratory tract secretions

(6) Blood/serum

Among respiratory specimens for viral isolation or rapid detection, nasopharyngeal specimens are typically more effective than throat swab specimens. Upper respiratory specimens are most suitable for virus detection (isolation, immunofluorescence and RNA detection) whereas serum is needed for serological tests

Collection of nasopharyngeal wash/aspirate

This is the specimen of choice for detection of respiratory viruses and can be collected by following procedure:

- Have the patient sit with head tilted slightly backward.
- Instill 1 – 1.5 ml of nonbacteriostatic saline into one nostril.
- Flush a plastic catheter or tubing with 2-3 ml of saline.
- Insert the tubing into the nostril parallel to the palate.
- Aspirate nasopharyngeal secretions.
- Repeat this procedure for the other nostril.
- Collect specimens in sterile vials or vials with viral transport medium (Annex 1).

Collection of nasopharyngeal swab

Procedure for collection of nasopharyngeal swab is as follows:

- Insert swab into nostril parallel to the palate
- Leave in place for a few seconds to absorb secretions.
- Swab both nostrils and place in container with viral transport medium (Annex 1)

Collection of oropharyngeal swab

- Swab both posterior pharynx and tonsillar areas, avoiding tongue and place in container with viral transport medium (Annex 1)

Tubes and vials containing body specimens should be properly sealed to avoid spillage, clearly labelled with a biohazard label, as well as with identity of sample and date of sampling. For shipment, appropriate packaging for diagnostic specimens should be used and adequately labelled.

Collection of Blood

Serum: Acute serum specimens should be collected and submitted as soon as possible. When applicable, convalescent specimens should be collected and submitted in 3-4 weeks. Collect 5-10 ml of

To ensure preparedness, the country is advised to set up a response structure at the national level and set up a contingency plan including the designation of a health care facility trained and equipped to deal with avian influenza. It is urgent that this is done as soon as possible. In summary the following actions are needed:

- Establish National Task Force with senior officials of animal husbandry departments
- Designate Focal Point
- Establish Expert Committee
- Establish Surveillance Unit and forge linkages with animal husbandry departments
- Put into place a national surveillance
- Designate at least one hospital and one laboratory
- Develop an inventory of supplies and equipment
- Provide accurate and timely information to public by efficient utilization of mass media
- Establish a mechanism of monitoring and supervision

Cleaning and disinfection of hospital environment and equipment

The practices as approved by the Hospital Infection Control Committee or hospital authorities must be followed. Some of these are:

- Cleaning staff should wear full PPE
- Cleaning should be done thoroughly to be followed by disinfection
- Isolation, X-ray and changing rooms should be cleaned and disinfected
- Items and areas requiring cleaning and disinfection are: Bedside table, bed stand, accessible areas of bed and floors (Use 0.1% sodium hypochlorite as disinfectant)
- If any surface is grossly contaminated, pour 1% sodium hypochlorite first and leave it for 10-15 minutes to be followed by cleaning and usual disinfection (0.1% sod. hypochlorite).
- Basins and bedpans should be cleaned and disinfected before being used for another patient.
- Spray disinfectant is prohibited.

14. PATIENT, FAMILY AND COMMUNITY EDUCATION

Education for the patient, their family, contacts at home isolation and the community is essential for control and prevention of avian influenza.

Education should be imparted on

- What avian influenza is and how it is transmitted.
- Why isolation is required for a case/contact of influenza
- Precaution required including PPE and how to wear N-95 mask.
- Hand washing procedure

15. IEC AND ROLE OF MEDIA

Avian influenza is a disease that has raised a lot of concern and even panic in the population. The prevention and containment of avian influenza cannot be done without acting at the community level besides the steps taken in hospitals and laboratories. To be effective the prevention and control of any infectious disease is dependant upon the understanding, cooperation and partnership of the community. For this reason it is essential that effective and widespread awareness about avian influenza is propagated in the community with an explanation of the steps necessary to contain the disease. The media can be of great assistance in these objectives and also in getting cooperation without generating panic. An attitude of transparency and sharing will generally get media cooperation and help.

16. COUNTRY PREPAREDNESS

whole blood in a serum separator tube. Allow blood to clot, centrifuge briefly and collect all resulting sera in vials with external caps and internal O-ring seals. A minimum of 200 microliters of serum is preferred for each test.

EDTA blood: Collect 5-10 ml of whole blood in an EDTA (purple-top) tube. Transfer to vials with external caps and internal O-ring seals.

Storage of specimens

To preserve the viral integrity in specimens for inoculation, place specimens should be placed in appropriate viral transport medium and stored at recommended temperatures: for respiratory samples and frozen tissues -70 °C, for serum 4-8 °C for 24-48 hrs, or at -20°C for longer periods. Expert advice should be sought when in doubt about storage conditions related to the type of test to be done.

Labelling and documentation

Specimen labeling: Each specimen should be labeled with the patient ID number and date collected.

Accompanying documentation: The package should include a linelist for all specimens including patient name and ID number, date collected, samples collected, clinical contact name and phone number, and submitter contact name and phone number (Annex 1).

Tests for diagnosing all influenza strains of animals and humans are rapid and reliable. Many laboratories in the WHO global influenza network have the necessary high-security facilities and reagents for performing these tests as well as considerable experience. Rapid bedside tests for the diagnosis of human influenza are also available, but do not have the precision of the more extensive laboratory testing that is currently needed to fully understand the most recent cases and determine whether human infection is spreading, either directly from birds or from person to person

Rapid tests for diagnosis of influenza type A

Commercial rapid diagnostic tests are available that can be used by to detect influenza viruses within 30 minutes. These rapid tests provide information upto type level. Which means that by using rapid kits one can obtain a fairly reliable indication about the presence of Influenza A virus. Confirmation of H5N1 subtype can be done only in a well equipped laboratory with all facilities and adequate biocontainment measures (details given in annex 1). Since most of the rapid tests have good specificity, a negative test can give broad indication about absence of influenza virus in specimen. As of now no commercial kit is available that can diagnose infection due to H5N1 subtype. The types of specimens acceptable for use (i.e., throat swab, nasal wash, or nasal swab) also vary by test.

Despite the availability of rapid diagnostic tests, collecting clinical specimens for viral culture is critical, because only culture isolates can provide specific information regarding circulating influenza subtypes and strains. This information is needed to establish diagnosis of avian influenza.

Keeping their limitations in mind, rapid diagnostics for influenza have proven to be valuable in early diagnosis which enables treatment in a timely fashion. Anti-influenza treatments must be administered within 48 hours of onset of symptoms in order to be effective. Some of the rapid kits appear to be quite sensitive (mean of 87.4%; range of 74-100%) for detection of virus in nasopharyngeal specimens and is preferred for screening for influenza.

8. MANAGEMENT OF CASE

The management of a case with avian influenza does not differ from that of influenza due to a primarily human pathogenic virus. Antiviral drugs, some of which can be used for both treatment and prevention, should be theoretically effective against influenza A virus strains in otherwise healthy adults and children. However, preliminary studies with Hong Kong isolates of 1997 have shown resistance to amantadine and rimantadine. It is believed that oseltamivir may be an effective drug for which reliable evidence is awaited.

Aspirin and Influenza

Children or teenagers who have flu-like symptoms – and particularly fever – should not be given aspirin as it may cause a rare but serious illness called Reye syndrome. Children or teenagers with the flu should get plenty of rest, drink lots of liquids, and take medicines that contain no aspirin to relieve symptoms.

9. PREVENTION AND CONTROL

Control in poultry

- Early identification
- Destruction of the entire infected cohort as per the guidelines of FAO/OIE
- Proper disposal
- Early notification
- Close coordination with health department

Efficacy and utility of a specific vaccine to protect birds against avian flu is yet to elucidated.

Control in human beings

The essential components to control an outbreak in human beings include:

- Early identification
- Isolation of both suspect and probable cases
- Tracing and monitoring close contacts of all suspect / probable cases identified,
- Barrier nursing

Respiratory precautions

These are respiratory-based precautions as for other infectious respiratory pathogens.

Standard precautions

These are universal precautions for blood and body fluids.

Hand washing

It is the single most important and effective component for preventing the transmission of infection. Running water and soap with friction should be ideally used for 15 to 20 seconds. It is important to dry hands after washing. A 70% alcohol-based hand rub solution after hand washing can be used.

Hand washing should be done:

- After removing gloves
- Before and after patient contact
- After contact with blood and body fluids
- After taking samples
- After taking blood pressure or vital signs from patient
- After using bath room
- After blowing/wiping nose
- Before eating and preparing food.
- When leaving the isolation unit.

Linen handling

- Designated laundry staff should put patient's linen in bags and seal in the isolation room itself.
- Laundry staff should wear full PPE.
- Washing should be done in laundry with hot water and detergent, bleach may be added if compatible with the detergent being used.

Waste disposal

The practices as approved by the Hospital Infection Control Committee or hospital authorities must be followed. Some of these are:

- Puncture proof and leak proof containers should be used for sharps.
- Waste should be collected in designated colour coded plastic bags for sterilization and disposal.
- Double bag system for transport should be used.

- The use of PPE does not replace basic hygiene measures such as hand-washing, washing is still essential to prevent transmission.
- Exposure to the infected patient should be kept to an absolute minimum necessary for the level of care required.

Who should use PPE?

The staff team assigned to care for the patient should be kept to a minimum. Staff should be strictly supervised and be experienced in infection control. PPE should be used by:

- All doctors, nurses and health care workers who provide direct patient care to avian influenza cases (keep to minimum necessary for patients' condition);
- All support staff including medical aides, X-ray technicians, cleaners, transport staff, laundry staff (keep staff to the minimum necessary, designate avian influenza laundry staff, etc.);
- All laboratory staff who handle patient specimens from suspect cases (keep to the minimum the staff necessary for laboratory procedures);
- Family members who care for avian influenza patients (visits should be avoided where possible);
- The patient(s) should wear a mask (N95 preferable) when other people are in the isolation area.
- Contacts and international travellers during home isolation/quarantine must wear a mask (N95 preferable).

Personal Protective Equipment

The items included are:

- Masks (N-95; N/P/R-100, If not available N80 or surgical masks as last resort)
- Gloves
- Gloves and aprons
- Hair Covers
- Eye protective ware (goggle)
- Boots or shoe covers

Storage / positioning of the supplies

- The PPE stock should be stored where it can be readily accessed at all times (24 hours a day), and is available for despatch to a facility/transport where suspected influenza patients are involved.
- The stock must be accessible after hours and on weekends.

- Public information

Several measures can help minimize the global public health risks that could arise from large outbreaks of highly pathogenic H5N1 avian influenza in birds. An immediate priority is to halt further spread of epidemics in poultry populations. This strategy works to reduce opportunities for human exposure to the virus. Vaccination of persons at high risk of exposure to infected poultry, using existing vaccines effective against currently circulating human influenza strains, can reduce the likelihood of co-infection of humans with avian and influenza strains, and thus reduce the risk that genes will be exchanged. Workers involved in the culling of poultry flocks must be protected, by proper clothing and equipment, against infection. These workers should also receive antiviral drugs as a prophylactic measure.

When cases of avian influenza in humans occur, information on the extent of influenza infection in animals as well as humans and on circulating influenza viruses is urgently needed to aid the assessment of risks to public health and to guide the best protective measures. Thorough investigation of each case is also essential. While WHO and the members of its global influenza network, together with other international agencies, can assist with many of these activities, the successful containment of public health risks also depends on the epidemiological and laboratory capacity of affected countries and the adequacy of surveillance systems already in place.

While all these activities can reduce the likelihood that a pandemic strain will emerge, the question of whether another influenza pandemic can be averted cannot be answered with certainty.

Prevention and Control of Avian Influenza in Health-Care Facilities

In the absence of precise knowledge, it will be prudent to take all those precautions in a health care setting which were instituted for prevention of spread of SARS. Briefly these are:

- Patients with influenza should be placed on droplet precautions.
- Respiratory precautions should be incorporated into infection control practices as one component of Standard Precautions.
- Visitors who have any respiratory illness symptoms should be discouraged from visiting patients.
- Health-care workers who are ill should be restricted from working until they are healthy.
- If a suspected influenza outbreak occurs among nursing home or hospitalized patients, steps to identify influenza as the cause and to control its spread should be instituted.

Vaccination of human beings

Vaccination of human beings is possible with currently available vaccines against influenza with the objective of limiting the risk of reassortment and emergence of an influenza virus with pandemic potential that readily spreads from human to human. However, it must be made clear to the vaccinee as well as the health authorities that human vaccination with current inter-pandemic vaccine will not protect humans from infection with avian H5N1 influenza. The vaccine may be administered to cullers who are involved in destruction of poultry, people living and working on poultry farms where H5N1

infection is reported or suspected and health care workers involved in daily care of known or confirmed human cases of influenza due to H5N1 subtype.

10. POTENTIAL FOR AN INFLUENZA PANDEMIC

All influenza viruses have the potential to can change. It is possible that an avian influenza virus could change so that it could infect humans and could spread easily from person to person. Because these viruses do not commonly infect humans, there is little or no immune protection against them in the human population. If an avian virus were able to infect people and gain the ability to spread easily from person to person, an “influenza pandemic” could begin. An influenza pandemic is a global outbreak of influenza and occurs when a new influenza virus emerges, spreads, and causes disease worldwide. Past influenza pandemics have led to high levels of illness, death, social disruption and economic loss. There were 3 pandemics in the 20th century. All of them spread worldwide within 1 year of being detected. They are:

Period	Common name	Virus subtype	Deaths
1918-1919	Spanish flu	H1N1	20 million-50 million
1957-58	Asian flu	H2N2	70,000 deaths in USA alone
1968-1969	Hong Kong flu	H3N2	34,000 deaths in USA alone

11. ADVICE TO INTERNATIONAL TRAVELLERS

So far WHO has not issued any travel alerts or advisories for the region in response to the H5N1 outbreak. However, travelers to countries in Asia with documented H5N1 outbreaks are advised to avoid poultry farms, contact with animals in live food markets and any surfaces that appear to be contaminated with feces from poultry or other animals.

12. INFECTION CONTROL PRACTICES

These are similar to those required for infectious respiratory pathogens and were practised for SARS containment during 2002-2003. Management of avian influenza cases will depend on assigning proper isolation areas in the hospital, barrier nursing and stocking PPE and availability of other essential supplies and materials. This will require advance planning.

Isolation facility

This consists of:

- Isolation room with no air-flow into other rooms.
- Changing room for storage of outside clothes and removal of PPE.
- General access area (i.e., rest of hospital).
- **Isolation room:** There should be good ventilation. The movement of air should be from general access area to changing room to isolation room to outdoors. If independent air supply not feasible, open windows to areas with no public access and have a fan to blow out air. The

room to have sink, running water and alcohol based disinfectant and 0.1% and 1% freshly made sod. hypochlorite solutions. The doors are kept closed.

- **Changing room:** It should have sink with running water, soap, alcohol based disinfectant sodium hypochlorite solutions (0.1% and 1%), biohazard bags for PPE disposal, storage area for general ward clothes, new PPE and containers for disinfection of reusable items e.g., goggles.

Principles for isolation of patient with avian influenza

- The suspect and probable cases should be in separate rooms. It is ideal to have single rooms. If not feasible cohort isolation may be done. Cohort of suspect and probable cases should be done in separate rooms.
- Central air-conditioning should be turned off.
- Entry to the room should be restricted. It is preferable to forbid entry to visitors and non-essential staff.
- Patient’s travel/transport outside the room should be limited. If unavoidable patient should wear N-95 mask.
- Limit the Number of staff providing care to the patient should be limited.
- The patient should be as self-caring as possible. The exposure of health care worker to influenza patients be kept to an absolute minimum necessary for the level of care required.
- Designated laundry staff and cleaning staff should be assigned.
- All patient care devices should be restricted to the patient and disposed of or cleaned and disinfected by staff using PPE.
- Separate eating utensils should be provided to the patient.

Strict barrier nursing

All those coming in contact with a case or their body fluids/tissues and contaminated material must wear PPE.

13. PERSONAL PROTECTIVE EQUIPMENT (PPE) AND THEIR USE

In all cases, following principles apply:

- PPE reduces but does not completely eliminate the possibility of infection.
- PPE is only effective if used correctly and at all times where contact may occur.
- Any contact between contaminated (used) PPE and surfaces / clothing / people outside the isolation area must be avoided.
- Used PPE must be sealed in appropriate disposal bags and sterilized or decontaminated. If staff temporarily leave the isolation area, a complete change of PPE and hand washing required.