NJHealth New Jersey Department of Health Communicable Disease Service

Highly Pathogenic Avian Influenza (HPAI) A(H5N1) in Humans

Recommendations for Public Health Investigations

Background

Novel influenza virus A infection is defined as any human infection with an influenza A strain that differs from the currently circulating seasonal H1 and H3 strains. Over the past decade, the epidemiology of novel influenza A infections in humans has evolved. Highly pathogenic avian influenza (HPAI) A(H5N1) viruses now routinely circulate among wild birds in the United States, leading to outbreaks in domestic poultry and other animals, thereby increasing human exposure to these viruses. Human infections with novel influenza A viruses capable of person-to-person transmission could signal the onset of an influenza pandemic. Rapid detection and reporting of these infections, caused by viruses against which there is little to no pre-existing immunity, are crucial for promptly identifying and assessing influenza A viruses with pandemic potential and for implementing effective public health measures.

The panzootic of HPAI A(H5N1) viruses in wild birds has resulted in outbreaks among commercial poultry and backyard bird flocks and has spread to infect wild and domesticated animals. Sporadic human infections with H5N1 virus have been reported in multiple countries since 1997, and most human infections have occurred after unprotected exposures to sick/dead infected poultry. Available data suggest that the estimated incubation period for human infection with avian influenza A(H5N1) and A(H7N9) viruses is generally 3 to 5 days but has been reported to be 7-10 days. Currently there is no evidence of sustained human-to-human transmission.

Epidemiologic, Clinical, and Public Health Response Criteria

Rapid detection and characterization of novel influenza A viruses in humans remain critical components in preventing further cases. People exposed to H5N1 (as defined in the epidemiologic criteria), including people wearing recommended PPE, should monitor for signs and symptoms of acute respiratory illness beginning after first exposure and for 10 days after last exposure. Testing should be performed on persons who meet epidemiologic criteria **AND** either clinical OR public health response criteria.

Epidemiologic Criteria

Persons with recent exposure (within 10 days) to HPAI A(H5N1) virus through one of the following:

- **Exposure to HPAI A(H5N1) virus infected birds or other animals defined as follows:**
  - Close exposure (within six feet) to birds or other animals, with confirmed avian influenza A(H5N1) virus infection. Bird or other animal exposures can include, but are not limited to handling, slaughtering, defeathering, butchering, culling, or preparing birds or other animals for consumption, or consuming uncooked or undercooked food or related uncooked food products, including unpasteurized (raw) milk, **OR**
  - Direct contact with surfaces contaminated with feces, unpasteurized (raw) milk or other unpasteurized dairy products, or bird or animal parts (e.g., carcasses, internal organs) from infected birds or other animals, **OR**
  - Visiting a live bird market with confirmed HPAI A(H5N1) virus infections in birds or associated with a case of human infection with HPAI A(H5N1) virus.
- **Exposure to an infected person**
  - Close (within six feet) unprotected (without use of respiratory and eye protection) exposure to a person who is a confirmed, probable, or symptomatic suspected case of human infection with HPAI A(H5N1) virus (e.g., in a household or healthcare facility).
- **Laboratory exposure**
  - Unprotected exposure to HPAI A(H5N1) virus in a laboratory

Clinical Criteria

Persons with signs and symptoms consistent with acute or lower respiratory tract infection, conjunctivitis or complications of acute respiratory illness without an identified cause. In addition, gastrointestinal symptoms such as diarrhea are often reported with HPAI A(H5N1) virus infection. Examples include but are not limited to:

- Mild illness: cough, sore throat, eye redness or eye discharge such as conjunctivitis, fever or feeling feverish, rhinorrhea, fatigue, myalgia, arthralgia, headache
- Moderate to severe illness: shortness of breath or difficulty breathing, altered mental status, seizures
- Complications: pneumonia, respiratory failure, acute respiratory distress syndrome, multi-organ failure (respiratory and kidney failure), sepsis, meningoencephalitis

Public Health Response Criteria

Testing of asymptomatic persons for HPAI A(H5N1) virus infection is not routinely recommended. As part of investigations, asymptomatic persons who are close contacts of a confirmed case of HPAI A(H5N1) virus infection, may be tested after consultation with the state health department.

Case Definitions

NJDOH adheres to the Centers for Disease Control and Prevention (CDC) and the Council of State and Territorial Epidemiologists (CSTE) case definitions.

- **Confirmed:**
  Avian influenza A virus infection in a person that is confirmed by CDC's Influenza Division Laboratory or a CDC designated laboratory using methods mutually agreed upon by CDC and CSTE.
- **Suspect:**
  A person meeting criteria for avian influenza A virus infection and for whom confirmatory laboratory test results are unknown or pending.
- **Probable:**
  A person meeting criteria for avian influenza A virus infection and for whom laboratory test results do not provide a sufficient level of detail to confirm HPAI A H5 virus infection.

Reporting

Healthcare Providers

Clinicians should consider the possibility of HPAI A(H5N1) infection in persons showing signs or symptoms of acute respiratory illness who have relevant exposure history. More information is available at Brief Summary for Clinicians. Additional respiratory pathogen testing should be considered based on circulating respiratory viruses.

Cases meeting any of the above criteria should be reported **IMMEDIATELY** to the local health department (LHD) where the patient resides. If patient residence is unknown, report to your own local health department. Contact information for local health departments is available here.

If LHD personnel are unavailable, healthcare providers should report the suspected case to NJDOH Communicable Disease Service (CDS) at (609) 826-5964 during business hours or at (609) 392-2020 after-hours.

Local Health Departments

LHDs should report possible cases H5N1 cases **IMMEDIATELY** to NJDOH CDS at (609) 826-5964 during business hours or at (609) 392-2020 after-hours.

The LHD should also complete or work with the reporting healthcare provider to complete the Novel Influenza Worksheet and send to CDS via encrypted email to cdsfluteam@doh.nj.gov or fax to (609) 826-5972.

Testing

The submitted Novel Influenza Worksheet will be reviewed by CDS who will make the final determination if the case meets criteria and if a specimen is required for testing. The NJ Public Health and Environmental Laboratories (PHEL) conducts Real-Time RT-PCR (rRT-PCR) testing for Novel Influenza A. Positive results will be confirmed at CDC and may take several days. Testing will be performed on persons who meet the epidemiologic **AND** either clinical or public health response criteria and must be pre-approved by CDS. Any specimens that are "unsubtypeable" with a molecular influenza assay that can detect currently circulating influenza A virus subtypes (i.e., "seasonal influenza" subtypes) should also be submitted to PHEL for testing.

Staff collecting specimens should follow Interim Guidance on Testing and Specimen Collection. Specimens should be obtained for testing as soon as possible after illness onset and ideally within seven days of illness onset. Submitters should review PHEL guidance on testing criteria for HPAI A(H5N1) and preferred respiratory specimens, storing and shipping. CDS will consult with LHDs and/or hospitals to determine specimen shipping method/timeframe. If commercial carriers are used, specimens should be handled as Biologic Substance, Category B. Information on shipping regulations for these carriers can be found here. For questions regarding specimen collection and submission contact phel.influenza@doh.nj.gov.

Any exposed person who tested positive for A(H5) virus while asymptomatic and who develops signs or symptoms of acute respiratory illness or conjunctivitis while receiving oseltamivir for treatment or post-exposure prophylaxis, should be isolated, and tested again for influenza A(H5) virus. Repeat testing is recommended to rule out initial A(H5) test positivity as a result of viral contamination, such as from an environmental exposure, that did not progress to infection (i.e., repeat testing yields a negative A(H5) result) and to allow for evaluation of development of antiviral resistance during treatment/prophylaxis if repeat testing is still positive for A(H5).

Infection Prevention and Control

Standard, contact, and airborne precautions are recommended for management of patients presenting for medical care or evaluation who have illness consistent with influenza and recent exposure to birds or other animals potentially infected with HPAI A(H5N1) virus, which is different from that outlined for patients with seasonal influenza. For additional guidance refer to the Interim Guidance for Infection Control Within Healthcare Settings. Based on currently available information, non-hospitalized confirmed, probable, or suspected cases of HPAI A(H5N1) should isolate at home away from household members and not go to work or school until it is determined they do not have avian influenza A virus infection.

Exposed asymptomatic persons who test positive for influenza A(H5) virus should wear a facemask when in close contact with others and should continue to be actively monitored for signs and symptoms of acute respiratory illness or conjunctivitis for 10 days after testing A(H5) positive.

Antiviral Treatment

Antiviral treatment may be warranted for symptomatic and asymptomatic individuals exposed to HPAI A(H5N1). Detailed guidance on dosing and treatment duration is available at Interim Guidance of the Use of Antiviral Medications for the Treatment of Human Infection with Novel Influenza A Viruses Associated with Severe Human Disease.

Symptomatic Persons with Animal Exposures Who Test Positive for Influenza A(H5)

Outpatients meeting epidemiologic exposure criteria who develop signs and symptoms compatible with influenza should be referred for prompt medical evaluation, testing, and empiric initiation of antiviral treatment with oseltamivir as soon as possible. Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of illness onset.

Hospitalized patients who are confirmed, probable, or suspected cases of human infection with HPAI A(H5N1) virus, regardless of time since illness onset are recommended to initiate antiviral treatment with oral or enterically administered oseltamivir as soon as possible. Antiviral treatment should not be delayed while waiting for laboratory testing results.

Asymptomatic Persons with Animal Exposures Who Test Positive for Influenza A(H5)

Asymptomatic persons exposed to animals infected with HPAI A(H5N1) virus, who reported not wearing recommended PPE or who experienced a PPE breach in recommended PPE, and who tested positive for influenza A(H5) virus should be offered oseltamivir treatment (unless already receiving oseltamivir post-exposure prophylaxis).

Antiviral Post-Exposure Chemoprophylaxis

Persons Meeting Epidemiologic Exposure Criteria

Antiviral chemoprophylaxis is not routinely recommended for persons who properly used (including when taking off) recommended PPE and experienced no breaches while handling sick or potentially infected birds or other sick or dead animals or decontaminating infected environments (including animal disposal).

Chemoprophylaxis with influenza antiviral medications can be considered for any person meeting epidemiologic exposure criteria. Decisions to initiate post-exposure antiviral chemoprophylaxis should be based on clinical judgment, with consideration given to the type of exposure, duration of exposure, time since exposure, known infection status of the birds or animals the person was exposed to, and whether the exposed person is at higher risk for complications from seasonal influenza. Antiviral chemoprophylaxis is not an alternative for use of appropriate PPE and engineering and administrative controls, and receipt of PEP should not be contingent upon acceptance of and participation in influenza testing.

If antiviral chemoprophylaxis is initiated, oseltamivir treatment dosing (one dose twice daily) is recommended instead of the antiviral chemoprophylaxis regimen for seasonal influenza. If exposure was time-limited and not ongoing, five days of medication (one dose twice daily) from the last known exposure is recommended. Longer duration of oseltamivir post-exposure prophylaxis (e.g., twice daily for 10 days) can be given for ongoing high risk of exposure (e.g., inadequate PPE) to infected animals. Detailed guidance on dosing and treatment duration is available at Interim Guidance on Influenza

Antiviral Post-exposure Prophylaxis of Persons Exposed to Birds or Other Animals with Novel Influenza A Viruses Associated with Severe Human Disease or with the Potential to Cause Severe Human Disease.

Close Contacts

Close contacts are defined as persons within approximately six feet in a room, care area or other enclosed space (e.g., vehicle), who had unprotected (without use of recommended personal protective equipment) exposure to a person who is a symptomatic confirmed or probable human case of novel influenza A virus infection for a prolonged period of time, or who had direct contact with infectious secretions while the case-patient was likely to be infectious (beginning one day prior to illness onset and continuing until resolution of illness). Antiviral post-exposure prophylaxis should be guided by the Risk Assessment Tool for Healthcare Providers and Local Health Departments.
Identified close contacts should be monitored daily for 10 days after the last known exposure to a symptomatic confirmed or probable case. Measured temperature and presence of acute respiratory symptoms should be assessed daily during this period. Any close contacts of a confirmed, probable, or suspected case who develop any new illness signs or symptoms listed under clinical criteria should be referred for prompt medical evaluation and testing.

For additional guidance on healthcare personnel (HCP) who develop any respiratory symptoms or asymptomatic HCP who have been determined to have unprotected exposures refer to the Interim Guidance for Infection Control Within Healthcare Settings for exclusion, testing, treatment, and chemoprophylaxis details.

Resources

- NJDOH Novel Influenza
- Public Health and Environmental Laboratories (PHEL)
- CDC Avian Influenza Current Situation
- CDC HPAI A(H5N1) Interim Recommendations
- USDA: Detections of Highly Pathogenic Avian Influenza in Livestock