Novel Influenza A

Investigative Guidelines

December 2024

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

- To identify cases of novel influenza A
- To provide education, testing, and treatment to people exposed to and infected with novel influenza A
- To prevent the spread of novel influenza A
- To characterize the epidemiology of novel influenza A in Oregon

1.2 Laboratory and Clinician Reporting Requirements

Clinicians and laboratories are required to report any novel influenza A virus by phone immediately, day or night. Novel influenza A virus is defined as influenza A virus that cannot be subtyped by commercially distributed assays.[1] Clinical laboratories must forward these specimens to the Oregon State Public Health Laboratory for additional characterization.

1.3 Local Public Health Authority (LPHA) Reporting and Follow-Up Responsibilities

- Report all confirmed, probable, and suspect cases to the Acute and Communicable Disease Prevention Program immediately
- Conduct a case investigation
- Facilitate specimen collection for all probable and suspect cases
- Facilitate prompt access to oseltamivir treatment for all confirmed, probable, and suspect cases
- Facilitate prompt access to oseltamivir chemoprophylaxis when indicated
- Monitor exposed persons for signs and symptoms consistent with novel influenza A infection

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Overview

Human infections with novel influenza A viruses include influenza A virus subtypes that are different from the seasonal H1 and H3 influenza viruses in circulation (e.g., H2, H5, H7, H9) as well as H1 and H3 ‘variant’ subtypes originating from a non-human species or from reassortment between animal and human viruses (N.B., novel influenza

variants are denoted by adding a letter ‘v’ to the end of the subtype, e.g., H1N1v).[2] Avian influenza A viruses are categorized as either highly pathogenic avian influenza (HPAI) or low pathogenic avian influenza (LPAI) based on their pathogenicity in poultry. HPAI and LPAI designations do not correlate with the severity of illness in cases of human infection. Both HPAI and LPAI viruses have caused mild to severe illness in infected humans.[3]

Avian influenza A viruses are not readily spread from person to person. If and when they gain this ability, they can cause pandemics.[4]

2.2 Etiologic Agent

Avian influenza A viruses are subtyped according to two viral surface proteins—hemagglutinin (HA) and neuraminidase (NA). There are 18 known HA subtypes and 11 known NA subtypes, and many different combinations of HA and NA subtypes are possible. Influenza A(H5N1) has an HA5 protein and an NA1 protein.

2.3 Description of illness

Novel influenza A symptoms are the same as for non-novel influenza A infection, and may include:

- Fever/feeling feverish or chills
- Cough
- Sore throat
- Runny or stuffy nose
- Conjunctivitis
- Muscle or body aches
- Headaches
- Fatigue
- Vomiting
- Diarrhea

More severe complications of influenza A infection include otitis media, pneumonia, myocarditis, encephalitis and multi-organ failure.[5]

A significant but unknown proportion of influenza A infections, including novel influenza A infections, may be asymptomatic.[6]

2.4 Reservoirs

Influenza A viruses commonly circulate in seven animal species or groups—humans, wild water birds, domestic poultry, swine, horses, dogs, and bats. Influenza A viruses have infected many other species but have not spread readily among them. Most influenza A subtypes can infect birds. Five subtypes of avian influenza A viruses are known to have caused human infections (H5, H6, H7, H9, H10). Avian influenza A viruses with pandemic potential include HPAI A(H5N1) and A(H7N9) viruses. Only two influenza A viruses currently circulate in humans—A(H3N2) and A(H1N1)pdm09.[3]

2.5 Modes of Transmission

Three modes of transmission have been established for human influenza A viruses—droplet, aerosol, and, to a lesser extent, contact.[7] Novel influenza A may be transmitted from animals to humans through these routes as well as through additional routes yet to be determined.

2.6 Incubation Period

The incubation period for human influenza viruses is typically 1–4 days.[8] The incubation period for novel influenza A viruses is unknown. Current data suggest that the incubation period for human infection with HPAI A(H5N1) and A(H7N9) viruses is 3–5 days but may be as long as 10 days.[9, 10]

2.7 Period of Communicability

The duration of shedding for human influenza viruses is typically from one day prior to symptom onset through 5–7 days after symptom onset.[8] Since the 2009 H1N1 pandemic, novel influenza A viruses have resulted in only limited, non-sustained, human-to-human transmission.[11, 12] The duration of shedding of novel influenza A viruses in humans is unknown; limited data suggest that viral shedding may persist for 7 days or longer.[13]

2.8 Treatment

Confirmed, presumptive and suspect cases who meet epidemiologic exposure criteria and develop symptoms compatible with novel influenza A should receive prompt antiviral treatment as soon as possible (and *before* test results are available). Clinical benefit is greatest when treatment is initiated within 48 hours of symptom onset. Oral oseltamivir twice daily for five days is recommended for most patients. A 10-day treatment course should be considered for severely ill patients.[14]

OHA has oral oseltamivir available at no cost to facilitate treatment for novel influenza infection. To obtain oseltamivir from OHA, call the on-call epidemiologist at 971-673-1111.

2.9 Chemoprophylaxis

Chemoprophylaxis for persons without symptoms who meet epidemiologic criteria for exposure to avian influenza A(H5), A(H7), or A(H9) virus infected birds or other animals may be considered on a case-by-case basis. Chemoprophylaxis considerations should include intensity of exposure and the exposed person's risk of severe disease. Chemoprophylaxis is not recommended for persons who used personal protective equipment throughout their exposure to infected animals.[15]

Chemoprophylaxis for persons without symptoms with exposure to novel influenza A virus is recommended for high-risk groups and should be considered for moderate-risk groups:

- High-risk groups:
    - Household or close family member contacts with unprotected,

prolonged close contact to a confirmed or probable case in an enclosed space, or
    - Healthcare personnel with prolonged unprotected close contact with a confirmed or probable case in a healthcare setting
- Moderate-risk groups:
    - Household or close family member contacts with unprotected, prolonged close contact to a confirmed or probable case outside of an enclosed space, or
    - Laboratory personnel with unprotected direct exposure to a novel influenza A virus

When chemoprophylaxis is indicated, oral oseltamivir treatment dosing at twice daily is recommended. Chemoprophylaxis should be provided for 5 days if the exposure is not ongoing and should be provided for 10 days if the exposure is ongoing (e.g., a household setting).[16]

OHA has oral oseltamivir available at no cost to facilitate prophylaxis following novel influenza exposure. To obtain oseltamivir from OHA, call the on-call epidemiologist at 971-673-1111.

2.10 Vaccine

Seasonal influenza vaccines do not provide protection against human infection with novel influenza A viruses.[15] The development of zoonotic influenza candidate vaccine viruses is coordinated by the World Health Organization.[17] FDA has approved one vaccine for immunization of persons ≥6 months of age against influenza A(H5N1).[18]

3. NOVEL INFLUENZA A CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Case Definitions

The case definitions below are derived from the National Notifiable Diseases Surveillance System (NNDSS) Novel Influenza A Virus Infections 2024 case definition.[19] Novel influenza A refers to an influenza A virus subtype that is different from currently circulating human influenza H1 and H3 viruses. Novel subtypes include, but may not be limited to, H2, H5, H7, and H9 subtypes.

Clinical Criteria

In the absence of a more likely alternative diagnosis, an acute illness characterized by either:

One or more of the following: cough, sore throat, fever (measured or subjective), shortness of breath, conjunctivitis

OR

Two of more of the following: headache, myalgia, arthralgia, fatigue, rhinorrhea, nasal congestion, diarrhea, vomiting

Laboratory Criteria

Confirmatory laboratory evidence include three categories. Category 1 confirmatory laboratory evidence includes novel virus detection through RT-PCR for a novel influenza subtype or genomic sequencing. Category 2 confirmatory laboratory evidence includes viable virus isolation from a clinical specimen. Category 3 confirmatory laboratory evidence includes evidence of infection (i.e., a 4-fold or greater rise in a quantitative titer or seroconversion) in paired and convalescent serum IgG in the absence of an alternative explanation such as vaccination.

Presumptive laboratory evidence includes two categories. Category 1 presumptive laboratory evidence includes presumptive positive results on tests designed to detect novel influenza, such as H5 and H7. Category 2 presumptive laboratory evidence includes virus testing indicative of a variant influenza as determined in consultation with subject matter experts at CDC.

Epidemiologic Criteria

Epidemiologic criteria include any of the following: close contact with a confirmed case of novel influenza A, a common exposure (e.g., an agricultural fair) with a confirmed case of novel influenza A, direct or indirect contact with animals with confirmed novel influenza A, or exposure to novel influenza A in a laboratory setting.

Case Classifications

Confirmed Case
Meets clinical criteria AND category 1 confirmatory laboratory evidence
OR
Meets category 2 or 3 confirmatory laboratory evidence

Probable Case
Meets category 1 confirmatory laboratory evidence
OR
Meets clinical criteria AND category 1 presumptive laboratory evidence
OR
Meets clinical criteria AND epidemiologic criteria AND category 2 presumptive laboratory evidence

Suspect Case
Meets clinical criteria AND epidemiologic criteria AND no laboratory evidence is available that would rule out novel influenza A

Any case of human infection with an influenza A virus that is different from currently circulating human influenza H1 and H3 viruses is classified as a suspect case until laboratory confirmation is complete.

3.2 Laboratory Testing at Oregon State Public Health Laboratory

Oregon clinical laboratories are required to forward to OSPHL viral isolates of and clinical specimens with influenza A virus that cannot be subtyped with commercially distributed assays, or that are otherwise suspected to represent novel influenza A.

Persons otherwise suspected to have novel influenza A should have respiratory specimens collected, as soon as possible following symptom onset, according to the CDC Influenza Specimen Collection protocol. The following specimens are preferred:

- **Nasal and oropharyngeal swabs combined into one viral transport media vial. If two swabs cannot be collected, a single nasal or oropharyngeal swab will be accepted.**
- Nasopharyngeal (NP) swab in viral transport media may also be collected, however, nasal and oropharyngeal swabs appear to be more sensitive than NP swabs in detecting avian influenza A(H5).
- For patients with severe lower respiratory tract illness, a lower respiratory tract specimen (e.g., an endotracheal aspirate or bronchoalveolar lavage fluid) should be collected.
- For hospitalized patients, multiple respiratory specimens from different sites should be obtained on at least two consecutive days to improve the sensitivity of detecting novel influenza A.[20]
- For patients with conjunctivitis, a conjunctival specimen should be collected in addition to respiratory specimens.[21]

Instructions for collecting, storing and transporting specimens are available on the OSPHL Lab Test Menu for influenza A subtyping.

Any specimens consistent with novel influenza A (i.e., different from currently circulating human influenza H1 and H3 viruses) will be shipped to CDC for confirmatory testing.

4. ROUTINE CASE INVESTIGATION

4.1 One Health Approach

In the case of animal outbreaks of a novel influenza A virus, public health will work closely with the Oregon Department of Agriculture (ODA) using a One Health approach to identify and educate persons exposed to infected animals. In such cases, ODA notifies OHA of the animal outbreak and may invite local and state public health officials to the farm to investigate the case or outbreak. Alternatively, ODA may provide public health with a roster of exposed persons and their contact information.

4.2 Identify the Source of Infection

The case investigation should aim to identify the source of novel influenza A infection. In the case of persons exposed to animal outbreaks of a novel influenza A virus, the source may be obvious. In sporadic cases, the source may not be obvious, and identifying risk factors such as large event attendance, travel and animal exposure on the CDC Human Infection with Novel Influenza A Virus Case Report Form will be

essential. These questions have been embedded into the Orpheus Novel Influenza module.

4.3 Identify Close Contacts

The case investigation should aim to identify all persons with significant, unprotected exposure to a novel influenza A-infected person, animal or laboratory specimen.

Close contacts of a person with novel influenza A infection are defined as persons within approximately six feet or within the room or care area of a confirmed or probable novel influenza A case-patient 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).[22]

Close contacts of an animal with novel influenza A infection will be determined by OHA in collaboration with ODA.

5. CONTROLLING FURTHER SPREAD

5.1 Education and Activation of Persons Under Monitoring Approach

All people with unprotected exposure to a confirmed or probable case (i.e., close contacts), animal, or laboratory specimen infected with a novel influenza A virus should be actively monitored for new symptoms of influenza-like illness for 10 days following their last exposure. Education regarding the risk of novel influenza A infection and the rationale behind symptom monitoring should be provided in an appropriate language. All persons under monitoring should be instructed to call public health immediately should new symptoms develop during their monitoring period so that testing and treatment may be expedited.[22]

CDC asks that persons exposed to dairy cattle infected with novel influenza A(H5N1) infection be actively monitored throughout their monitoring period—which may be as long as 40 days if they are continuing to care for the cattle throughout their convalescence. Because daily active monitoring of people working on farms over a long period of time may be difficult to achieve, asking a proxy (such as a farm manager) to monitor and report symptoms to public health on behalf of the group is acceptable.

People being monitored for symptoms should be entered into Orpheus as a person under monitoring (PUM).

5.2 Isolation of Cases

All confirmed, presumptive, and suspect novel influenza A cases should be isolated at home until their symptoms resolve.[22]

5.3 Protective Actions and Personal Protective Equipment

Protective actions around birds and other animals that may be infected with avian influenza viruses include:

- Avoiding direct contact with wild birds;

- Avoiding unprotected (not using respiratory or eye protection) exposure to sick or dead animals including poultry, dairy cattle and other animals;
- Avoiding unprotected exposure to animal feces, litter, or materials contaminated by sick or dead animals including poultry, dairy cattle and other animals;
- Do not prepare or eat uncooked or undercooked food or related uncooked food products, such as unpasteurized (raw) milk, or raw cheeses.[23]

Personal protective equipment (PPE) should be worn when in direct contact with or within about six feet of sick or dead animals including wild birds, poultry, dairy cattle, and other animals, animal feces, litter, or materials potentially contaminated with avian influenza viruses. Recommended PPE to protect against novel influenza A viruses includes:

- Disposable or non-disposable fluid-resistant coveralls, and depending on task(s), add disposable or non-disposable waterproof aprons
- Any NIOSH-approved particulate respirator (e.g., N95 or greater filtering facepiece respirator, elastomeric half-mask respirator with a minimum of N95 filters)
- Properly-fitted unvented or indirectly vented safety goggles or a face shield if there is risk of liquid splashing onto the respirator
- Rubber boots, or rubber boot covers with sealed seams that can be sanitized, or disposable boot covers for tasks taking a short amount of time
- Disposable or non-disposable head cover or hair cover
- Disposable or non-disposable gloves[24]

When ODA suspects an animal outbreak, they provide 3-day PPE packs to all workers on affected farms upon initial contact. If the outbreak is confirmed as novel influenza A, ODA provides 30-day PPE packs to all workers.

6. REFERENCES

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7. UPDATE LOG

June 2024. Created (Andie Hendrick, Melissa Sutton, Paul Cieslak).

July 2024. Presumptive case definition updated (Melissa Sutton).

October 2024. Updated to align with new 2024 case definition and revised chemoprophylaxis recommendations (Melissa Sutton).

December 2024. Updated preferred swab types and added link for conjunctival swab collection (Melissa Sutton).