

## INFLUENZA A NOVEL VIRUS INFECTION

### REPORTING INFORMATION

- **Class A:** Report immediately via telephone the case or suspected case and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report immediately via telephone to the local public health department in which the reporting health care provider or facility is located. Local health departments should report immediately via telephone the case or suspected case and/or a positive laboratory result to the Ohio Department of Health (ODH).
- The local health department should enter the case into the Ohio Disease Reporting System (ODRS) within 24 hours after the telephone report.
- The following forms may be needed when reporting a case of Novel Influenza A:
  - [Human Infection with Novel Influenza A Virus Case Report Form](http://www.odh.ohio.gov/pdf/IDCM/frmnovflu.pdf) (<http://www.odh.ohio.gov/pdf/IDCM/frmnovflu.pdf>): is available for use to assist in local health department with case reporting and preliminary disease investigation activities. Information collected from the form should be entered into ODRS. A .pdf copy of this form **should be uploaded to the administration section of ODRS via the document upload feature**<sup>1</sup>
  - [ODH Lab Microbiology Specimen Submission Form](http://www.odh.ohio.gov/pdf/forms/hea2530.pdf) (<http://www.odh.ohio.gov/pdf/forms/hea2530.pdf>): should be completed and a print copy included with the specimen sent to the Ohio Department of Health Laboratory
  - [CDC Specimen Submission Form 50.34](http://www.odh.ohio.gov/pdf/IDCM/frm5034.pdf) (<http://www.odh.ohio.gov/pdf/IDCM/frm5034.pdf>): should be completed in **TYPED TEXT ONLY** and uploaded to the administration section of ODRS via the document upload feature<sup>1</sup>

### AGENT

The causative agent of novel influenza A infection is the influenza virus. Influenza A strains are subclassified by two antigens, hemagglutinin (H) and neuraminidase (N). Novel influenza virus infections are human infections with influenza A viruses that are different (i.e. novel) from currently circulating human influenza H1 and H3 viruses. These viruses include those that are subtyped as non-human in origin (i.e. avian, swine, or other mammalian influenza viruses) and those that are unsubtypeable with standard methods and reagents (e.g. new viruses from genetic reassortment between animal and human viruses). One of the reasons that novel influenza viruses are a concern is because of their potential to lead to an influenza pandemic.

Novel influenza virus is a Class A reportable disease, necessitating an immediate investigation regarding the possible source of the novel influenza virus exposure within 24 hours of initial report.

### CASE DEFINITION (CDC, 2010)

#### Clinical Presentation

An illness compatible with an influenza virus infection (fever >100 degrees Fahrenheit with cough or sore throat).

#### Laboratory Criteria for Diagnosis

- A human case of infection with an influenza A virus subtype that is different from currently circulating human influenza H1 and H3 viruses. Novel subtypes can be detected with methods

available for detection of currently circulating human influenza viruses at the ODH Laboratory (e.g. real-time reverse transcriptase polymerase chain reaction [RT-PCR]). Confirmation that an influenza A virus represents a novel virus will be performed by the Centers for Disease Control and Prevention's (CDC's) influenza laboratory. Once a novel virus has been identified by CDC, confirmation may be made by the ODH Laboratory and other public health laboratories following CDC-approved protocols for that specific virus, or by laboratories using an FDA-authorized test specific for detection of that novel influenza virus.

### **Comment**

Novel subtypes include, but are not limited to, H2, H5, H7, and H9 subtypes. Influenza H1 and H3 subtypes originating from a non-human species or from genetic reassortment between animal and human viruses are also novel subtypes. Non-human influenza viruses include avian subtypes (e.g. H5, H7, or H9 viruses), swine and other mammalian subtypes.

### **Case Classification**

Suspect: A case meeting the clinical criteria, pending laboratory confirmation. 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 suspected case until the confirmation process is complete.

Probable: A case meeting the clinical criteria and epidemiologically linked to a confirmed case, but for which no confirmatory laboratory testing for novel influenza virus infection has been performed or test results are inconclusive for a novel influenza A virus infection.

Confirmed: A case of human infection with a novel influenza A virus confirmed by CDC's influenza laboratory or using methods agreed upon by CDC and CSTE as noted in Laboratory Criteria, above.

Not a Case: This status will not generally be used when reporting a case, but may be used to reclassify a report if investigation revealed that it was not a case.

### **Comment**

Criteria for epidemiologic linkage:

- The case has had contact with one or more persons who either have/had the disease, AND
  - transmission of the agent by the usual modes of transmission is plausible
- OR
- A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory-confirmed. Laboratory testing for the purposes of case classification should use methods mutually agreed upon by CDC and the Council of State and Territorial Epidemiologists (CSTE). Currently, only viral isolation, RT-PCR, gene sequencing, or a 4-fold rise in strain-specific serum antibody titers are considered confirmatory.

Once a novel virus is identified by CDC, it will be nationally notifiable until the Council of State and Territorial Epidemiologists (CSTE) in consultation with CDC determines that it is no longer necessary to report each case.

## **SIGNS AND SYMPTOMS**

Although the exact symptoms of infection and severity of illness are unknown until the novel influenza virus begins circulating in people, clinical symptoms will likely resemble typical influenza-like illness (ILI) symptoms. Seasonal influenza infections may be asymptomatic or may produce a wide spectrum of manifestations from mild to severe. "Classic" ILI is characterized by the abrupt

onset of fever, myalgia (muscle aches), sore throat, nonproductive cough, and headache. The fever is usually 101° – 102° F, and accompanied by extreme exhaustion. Additional symptoms may include rhinorrhea (runny nose), headache, substernal chest burning and ocular symptoms (e.g. eye pain, sensitivity to light). Gastrointestinal symptoms (e.g. nausea, vomiting, and diarrhea) may sometimes occur. Most uncomplicated infections subside in 3-7 days. Complications associated with seasonal influenza include febrile convulsions, viral pneumonia, bacterial pneumonia (e.g. pneumococcal, staphylococcal), otitis media, sinusitis, acute myositis, Reye's syndrome, and (very rarely) parotitis. Illness caused by infections with Novel Influenza A may vary from mild to severe.

## **DIAGNOSIS**

- Influenza virus isolation in tissue cell culture from respiratory specimens
- Reverse-transcriptase polymerase chain reaction (RT-PCR) testing of respiratory specimens
- Immunofluorescent antibody staining [direct (DFA) or indirect (IFA)] of respiratory specimens
- Rapid influenza diagnostic (RIDT) testing of respiratory specimens

## **EPIDEMIOLOGY**

### **Source**

Humans are the reservoir of human influenza viruses. Different antigenic subtypes occur in other species; mammalian reservoirs (e.g. swine) and avian reservoirs (e.g. ducks) may be the sources of new human subtypes via genetic reassortment.

### **Occurrence**

Influenza occurs in pandemics, epidemics, localized outbreaks and as sporadic cases. Epidemics and pandemics can follow the introduction of influenza strains that are different (e.g. novel) from the previously circulating strains. New strains occur when there is a slight variation of an existing strain (i.e. antigenic drift) or the appearance of completely different strain (i.e. antigenic shift). Attack rates are higher for school aged children than for preschoolers or adults.

### **Mode of Transmission and Reservoir**

Novel influenza viruses are transmitted from person to person (or from birds or other mammals) through droplet spread, direct contact with nasopharyngeal secretions, or via objects recently contaminated with secretions. Although birds and non-human mammals may be the source for the novel influenza virus, humans are the primary reservoir for human influenza infections. Some novel influenza strains, such as H3N2v and H1N1v, have primarily been transmitted from swine to humans after exposure to swine. Reports of Highly Pathogenic Avian Influenza A (HPAI) in North America have been found in some domestic and wild birds.

### **Incubation Period**

Incubation periods for novel influenza are unknown until the virus begins to circulate, however incubation periods will likely be similar to seasonal influenza; usually 2 days, but can vary from 1 to 4 days.

### **Period of Communicability**

Human to human spread of novel influenza may not occur or may be limited. Most adults with seasonal influenza may be able to infect others beginning 1 day before symptoms develop and up to 5 days after the onset of illness. Children may be infectious for up to 7 days after onset of symptoms. Communicability of novel influenza could be similar to seasonal influenza.

## **PUBLIC HEALTH MANAGEMENT**

### **Public Health Significance**

The detection or confirmation by a state public health laboratory of either an influenza A virus that cannot be subtyped with standard methods (e.g. real-time RT-PCR assays for human influenza A H3 or H1 viruses) or a non-human influenza virus (e.g. H5) from a human specimen could be the initial identification of a virus with pandemic potential. Prompt notification of CDC by a state epidemiologist in conjunction with the public health laboratory will permit rapid confirmation of results and reporting to the World Health Organization (WHO). Additionally, it will aid prompt viral characterization and the development of virus-specific diagnostic tests.

### **Case Reporting**

Report immediately via telephone the case or suspected case and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report immediately via telephone to the local public health department in which the reporting health care provider or facility is located. Local health departments should report immediately via telephone the case or suspected case and/or a positive laboratory result to the Ohio Department of Health (ODH). The local health department should enter the case into the Ohio Disease Reporting System (ODRS) within 24 hours after the telephone report.

### **Surveillance**

Public health personnel should use the [CDC Human Infection with Novel Influenza A Virus Case Report Form](http://www.cdc.gov/odhcc/ncid/dzdx/influenza/2015/nov/151121_noviflu_report_form.pdf) for disease investigation and contact tracing activities. This form can be found at: <http://www.odh.ohio.gov/pdf/IDCM/frmnovflu.pdf>. Additional forms may be developed by ODH/CDC for investigations related to specific novel influenza viruses.

### **Treatment**

Influenza antivirals, such as the neuraminidase inhibitors Oseltamivir (Tamiflu®) and Zanamivir (Relenza®), are recommended for cases of novel influenza A virus infection. Antiviral treatment should be given as soon as possible after development of symptoms, within 48 hours of onset of symptoms is optimal. **Clinicians should NOT wait for laboratory confirmation of influenza before administering antiviral therapy.**

### **Infection Control Recommendations**

If the case is hospitalized, appropriate isolation precautions should be undertaken. CDC recommends contact, droplet, and airborne precautions for all cases of Novel Influenza A infection (airborne isolation in a negative pressure room if possible). If the case is not hospitalized, the individual should be asked to voluntarily isolate him/herself at home to avoid exposing others to possible infection. Contacts should self-monitor for onset of influenza-like illness.

### **Contacts**

Public health personnel should attempt to identify all known close contacts of suspected novel influenza A cases. Close contacts are defined as persons who were within 6 feet of an ill suspected, probable or confirmed case while the case was symptomatic.

Data gathered from human cases of the H5N1 virus suggest that the incubation period for human infection with a novel influenza A virus is generally  $\leq 7$  days. Therefore, all identified close contacts should be monitored daily for 7 days after the last known exposure to a person ill with novel influenza A. The following should be assessed each day during this period:

- a) Measured temperature; and
- b) Presence of any illness symptoms.

Any close contacts that have a measured temperature of  $\geq 38.0^{\circ}\text{C}$  ( $100.4^{\circ}\text{F}$ ) or any illness symptoms should be referred for prompt medical evaluation and possible testing for the novel influenza A virus.

#### Discontinuing Follow-up of Close Contacts

Monitoring of close contacts of a suspected novel influenza A case may be discontinued when laboratory testing by RT-PCR of appropriately collected respiratory specimens by a state health department laboratory or CDC has excluded infection with virus. Monitoring may also be discontinued in the absence of any illness symptoms among contacts during the 7-day surveillance period described above.

#### Antiviral Use

Influenza antivirals, such as the neuraminidase inhibitors Oseltamivir (Tamiflu®) and Zanamivir (Relenza®) can and should be used to prophylactically treat contacts of confirmed or suspected cases novel influenza A.

### **Prevention and Control**

The best means of preventing the spread of and exposure to a novel influenza A virus is a vaccine that is well-matched to the virus causing illness. However, since the virus is novel a vaccine does not exist and it is not likely that a vaccine will be available until well after the virus emerges. In the absence of a vaccine (and in conjunction with one when it becomes available), community strategies referred to as non-pharmaceutical interventions (NPI) may delay or mitigate the spread of the novel virus.

NPI guidelines (i.e. measures intended to reduce contact between people) issued by the World Health Organization (WHO) include, but are not limited to, the following:

- Closing schools
- Canceling public gatherings
- Public wearing of face masks
- Avoidance of crowds
- Voluntary isolation of cases; and
- Voluntary quarantine of household contacts.

### **Special Information**

An outbreak of infections with a novel influenza A virus demonstrating human-to-human transmission could signal the beginning of the next pandemic. Robust epidemiologic and laboratory surveillance systems are required for a coordinated public health response to novel influenza A virus infections. Early detection of an influenza A virus with pandemic potential will permit identification of viral characteristics (e.g. genetic sequence, antiviral susceptibility, and virulence) that will affect clinical management and public health response measures. It should also facilitate development of a virus-specific vaccine and testing strategies.

## LABORATORY SPECIMENS

Initial investigation of novel virus infection is conducted and treatment is recommended before confirmation is often available; however, laboratory confirmation should be obtained for all reported cases, unless otherwise indicated by ODH during investigations of larger ILI/influenza outbreaks.

### **What needs to be done right away about lab specimens?**

Depending on the particular novel influenza virus causing the infection, identification of the virus will be done at either the Ohio Department of Health (ODH) Laboratory or the Centers for Disease Control and Prevention (CDC). Definitive identification of suspect H5N1 and H7N9 cases can be done at the ODH Lab. In other instances, initial screening may be conducted at the ODH lab before specimens are sent to CDC for confirmation if the ODH lab does not have the capability to confirm cases.

Nasopharyngeal swabs placed in viral transport media (VTM) are the preferred specimen type for the detection of novel influenza viruses. Optimal specimens for detection of influenza are collected within the first 3 days of the onset of illness. Other clinical samples accepted for influenza polymerase chain reaction (PCR) testing include nasal swabs or oropharyngeal swabs in VTM, Bronchoalveolar lavage (BAL), tracheal aspirate, and sputum.

When sending clinical specimens, include an [ODH Lab Microbiology Specimen Submission Form](#) and note “Novel Influenza Surveillance” on all materials and specimens sent. An electronic copy of the [CDC Specimen Submission Form 50.34](#) should also be completed and uploaded to the Administration section of the ODRS case created for the patient under investigation<sup>1</sup>.

Follow protocols for the standard interstate shipment of etiologic agents available at <http://www.cdc.gov/od/ohs/biosfty/shipregs.htm>. All shipments must comply with current DOT/IATA shipping regulations for Category B Biological Substances.

### **Transport to ODH Lab**

**Overnight shipment is preferred for receipt within 24 hours<sup>2</sup>.** Samples should be shipped on cold packs as stated in shipping regulations. If testing is unlikely to be performed within 72 hours, the specimens should be frozen at  $\leq -70^{\circ}\text{C}$  and shipped on dry ice. For delivery of packages using DHL, UPS, US Cargo and other carriers, ship specimens to:

**Ohio Department of Health Laboratory**

**Attn: Virology**

**8995 E. Main Street, Building 22**

**Reynoldsburg, Ohio 43068**

## References

The Centers for Disease Control and Prevention web site for the 2010 Case Definition for Novel influenza A virus infections:

<http://www.cdc.gov/NNDSS/script/casedef.aspx?CondYrID=787&DatePub=1/1/2010%2012:00:00%20AM>

Non-pharmaceutical Interventions for Pandemic Influenza, National and Community Measures:

<http://wwwnc.cdc.gov/eid/article/12/1/pdfs/05-1371.pdf>

### <sup>1</sup> To upload the CDC Submission Form 50.34 (or any other document) to an ODRS case:

- Complete the form and save the file on your computer ("Save As") with the word "Novel" followed by the ODRS Case ID: **Novel#####**
- Within the ODRS Case summary click "Edit" within the Administration section.
- On the right side at the top of the Administration section, click "Add Document"
- In the pop up that appears, use the same name of the file for the "Title of the file. Browse for the
- file in the location where you saved it in step 1 above.
- Click Save
- Be sure to **CLICK "FINISH"** in the Administration section or the file will not save.

<sup>2</sup> Shipping on Fridays may not be possible as lab staff at ODH Laboratory or CDC may not be available to receive the specimen. Shipping of specimens should be assessed on a case by case basis until an event specific protocol can be put into practice.

If you have and questions, please contact the **Ohio Department of Health Bureau of Infectious Diseases at (614) 995-5599.**