Influenza - Novel or Unsubtypable Strain

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To detect emerging threats such as avian and other novel influenza strains.
2. To determine the clinical severity, epidemiology, and communicability of novel influenza viruses.

B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction**
2. Health care facilities: **immediately notifiable to local health jurisdiction**
3. Laboratories: **immediately notifiable to local health jurisdiction**; specimen submission required – isolate or clinical specimen (2 business days)
4. Veterinarians: suspected human cases **immediately notifiable to local health jurisdiction;** animal cases notifiable to Washington State Department of Agriculture (see: http://app.leg.wa.gov/WAC/default.aspx?cite=16-70)
5. Local health jurisdictions: **immediately notifiable to Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (OCDE)**

C. Local Health Jurisdiction Investigation Responsibilities

1. Contact CDE **immediately** regarding suspected novel influenza infections. Determine exposures for the case.
2. Facilitate the transport of specimens to the Washington State Public Health Laboratories for testing.
3. Ensure appropriate infection control practices are implemented while testing is pending.
4. For confirmed cases, perform a contact investigation to assess transmission from the case.
5. Complete the influenza case report form and enter the data into the Public Health Issues Management System (PHIMS) as Influenza.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

There are two main types of influenza, influenza A and influenza B. Influenza A viruses are divided into subtypes based on the hemagglutinin (H) and neuraminidase (N) proteins on their surfaces. Influenza A viruses infecting humans have been primarily subtypes H1, H2, and H3 while influenza A subtypes H1 through H17 can infect birds and other animals such as pigs. There are in addition ten different neuraminidase surface proteins.

Seasonal influenza causes annual winter outbreaks affecting 5-20% of the population.

The specific strains of influenza change frequently, necessitating parallel changes in the seasonal influenza vaccine. Since 1977, three types of influenza viruses had been in circulation in humans: influenza A(H3N2), influenza A(H1N1), and influenza B.

Novel influenza virus infections are human infections due to an influenza A virus that is different from currently circulating human influenza viruses, such as an avian or swine influenza virus. In April 2009, a novel influenza A(H1N1) virus was identified in several states and Mexico and caused the first influenza pandemic of the 21st century. This virus is no longer considered "novel" and is circulating as a seasonal strain, replacing the previous influenza A(H1N1) virus. If a novel influenza strain begins to infect humans and is easily transmitted person to person, there is potential for an influenza pandemic. Avian influenza viruses are one possible source of novel influenza strains.

While wild waterfowl shedding the virus are often unaffected by influenza A, domestic poultry infected by the wild birds may be severely affected. In birds, influenza infects both the respiratory and gastrointestinal tracts. As a result, both respiratory and fecal secretions of infected birds carry the virus, which can survive in the environment for weeks to months. Human cases of avian influenza infection, called novel influenza infections, have been associated with a variety of avian influenza strains.

In 1997, human infections due to avian influenza A(H5N1) virus were identified in Asia. During 2003 through June 2013, 630 laboratory-confirmed cases mainly in Asia and Africa have been reported and have resulted in 375 deaths (case fatality ratio = 60%). In 2013, human illness due to a novel avian influenza A(H7N9) virus was reported in China. As of May 2013, 132 confirmed cases, including 37 deaths, have been reported (case fatality ratio = 28%). Additional cases were reported during that fall. Avian influenza A(H5N1) and A(H7N9) virus infections are primarily transmitted from birds to humans although limited person-to-person transmission has also likely occurred. A small number of other human infections have been reported worldwide including A(H7N2), A(H7N3), A(H7N7), and A(H9N2) novel influenza infections. Worldwide surveillance information on avian influenza is available at: http://www.who.int/influenza/human_animal_interface/avian_influenza/en/.

Human infections with swine influenza viruses have been occasionally detected in the United States (see: http://www.cdc.gov/flu/swineflu/). During 2012, over 300 infections due to a swine variant influenza A(H3N2v) virus were detected in the United States. Most infections detected have been associated with exposure to swine at agricultural fairs, but limited person-to-person transmission of this virus has been described.

Other than the 2009 H1N1 strain, no novel influenza infections have been detected in Washington. However, in late 2014 and early 2015 A(H5N8) and A(H5N2) were detected in birds in Whatcom County and A(H5N2) was detected in backyard poultry in Benton and Clallam Counties.

B. Description of Illness

Patients with uncomplicated seasonal influenza may have symptoms that include fever, chills, cough, headache, sore throat and other upper respiratory tract symptoms (rhinorrhea), myalgias, arthralgias, fatigue, vomiting, and diarrhea. Symptoms can be minimal.

Persons infected with influenza A(H3N2v) viruses have had symptoms similar to those of seasonal influenza. Compared to seasonal influenza, a high proportion of persons with influenza A(H5N1) and (H7N9) virus infections progress to severe disease including severe pneumonia, acute respiratory distress syndrome (ARDS), septic shock and multi-organ failure leading to death. Other cases of novel influenza infection have tended to result in relatively mild illnesses or apparent asymptomatic infection.

C. Reservoirs

Reservoirs for influenza A viruses include humans, swine, poultry and other birds and mammals. Humans are the primary reservoir for influenza B.

D. Modes of Transmission

Seasonal influenza viruses spread person-to-person primarily through large-particle respiratory droplet transmission (e.g., when an infected person coughs or sneezes near a susceptible person). Transmission via large-particle droplets requires close proximity between source and recipient persons because droplets do not remain suspended in the air and generally travel only a short distance (<6 feet). Other possible routes of influenza transmission are mucosal inoculation from hands touching contaminated surfaces and airborne transmission. The relative contribution of each type of transmission has not been defined but for airborne transmission is thought to be small.

Avian and swine influenza viruses are generally less transmissible from person-to-person than seasonal influenza viruses. These viruses are primarily transmitted from animals to humans directly or through environmental contamination. However, limited person-to-person transmission has been described with these viruses.

E. Incubation Period

The incubation period for seasonal influenza is typically 1–4 days, but can range from 1–7 days. The incubation period for novel influenza viruses is estimated as 2-10 days.

F. Period of Communicability

Most healthy adult with seasonal influenza are infectious to others beginning from one day before to up to 7 days following illness onset although communicability decreases rapidly 24 hours after fever resolves (without fever reducing medication). Persons who continue to be ill longer than 7 days after illness onset should be considered potentially contagious until symptoms have resolved. Children, especially younger children, can shed virus for 10 or more days. Immunocompromised persons can shed virus for weeks or months. The period of communicability for novel influenza viruses is not well described.

G. Treatment

CDC recommends appropriate antiviral medications for treatment of human infections with avian and swine influenza A viruses based on known or likely resistance patterns. Guidance is available at: http://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm

3. CASE DEFINITIONS

A. Case Definition for Novel Influenza Infections (2013)

1. **Clinical Description**: An illness compatible with influenza virus infection (fever >100° F with cough and/or sore throat).
2. **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 include, but are not limited to, H2, H5, H7, and H9 subtypes. Influenza A (H1) and (H3) subtypes originating from a non-human species or from genetic reassortment between animal and human viruses are also novel subtypes. Novel subtypes will be detected at state public health laboratories with methods available for detection of currently circulating human influenza viruses (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 influenza laboratory at Centers for Disease Control and Prevention (CDC). Once a novel virus has been identified by CDC, confirmation may be made by 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.
3. **Criteria for epidemiologic linkage:**

    - The patient has had contact with one or more persons who either have or had laboratory-confirmed influenza AND
    - Transmission of the agent by the usual modes of transmission is plausible.

    A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in a 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.

4. **Case Classification**

    Suspected: 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 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.

    Note: Once a novel virus is identified by CDC, it will be nationally notifiable until CSTE in consultation with CDC determines that it is no longer necessary to report each case.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Healthcare providers who clinically suspect a novel influenza virus infection and laboratories that identify an unsubtypable influenza virus specimen using a PCR assay should immediately contact their local health jurisdiction and submit a specimen to the Washington State Public Health Laboratories. Rapid influenza tests should not be used to rule in or rule out avian flu.

B. Tests Available at Washington State Public Health Laboratories (PHL)

PHL uses the RT-PCR assays developed by Centers for Disease Control and Prevention (CDC) to distinguish seasonal influenza viruses from novel influenza viruses. Confirmatory testing for novel influenza viruses and serologic testing for both symptomatic and asymptomatic infections are performed at CDC.

C. Specimen Collection

Airborne precautions are preferred and include placement of patient in a negative air pressure room and appropriate PPE with a respirator (fitted N-95 or Powered Air Purifying Respirator), eye protection, gown, and gloves. If airborne precautions are not possible, institute droplet precautions by placing patient in a private room and instructing staff to wear a surgical mask, eye protection, gown, and gloves.

For more information on infection control: http://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm

Information regarding testing for novel influenza viruses is available at: http://www.cdc.gov/flu/avianflu/h7n9/specimen-collection.htm

The following should be collected as soon as possible after illness onset: (i) a nasopharyngeal swab, or (ii) a nasal aspirate or wash, or (iii) two swabs combined into one viral transport media vial (e.g., nasal or nasopharyngeal swab combined with an oropharyngeal swab). If these specimens cannot be collected, a single nasal, or oropharyngeal swab is acceptable. For patients with lower respiratory tract illness, a lower respiratory tract specimen (e.g., an endotracheal aspirate or bronchoalveolar lavage fluid) is preferred because these specimens have a higher yield for detecting avian influenza H5N1 and H7N9 viruses. Specimens should be placed into sterile viral transport media and immediately placed on refrigerant gel-packs or at 4°C (refrigerator) for transport to the laboratory.

If possible, in order to increase the potential for H7N9 or H5N1 virus detection, multiple respiratory specimens from different sites should be obtained from the same patient on at least two consecutive days.

Swab specimens should be collected using swabs with a synthetic tip (e.g., polyester or Dacron®) and an aluminum or plastic shaft. Swabs with cotton tips and wooden shafts are not recommended. Specimens collected with swabs made of calcium alginate are not acceptable. The swab specimen collection vials should contain 1-3ml of viral transport

medium (e.g., containing protein stabilizer, antibiotics to discourage bacterial and fungal growth, and buffer solution).

Note that PHL require all clinical specimens have two patient identifiers, a name and a second identifier (e.g., date of birth) on both the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

Specimens need to be shipped with a completed PHL Virology Submission form which is available at: http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf.

5. ROUTINE CASE INVESTIGATION

A. Evaluate the Diagnosis

1. Use the full case report form to itemize clinical symptoms, illness severity, and potential exposures to novel viruses, such as travel or animal contact.
2. Facilitate the transport of specimens to PHL for novel influenza testing.

B. Manage the Case

1. Hospitalized persons with confirmed or suspected seasonal influenza should be placed on droplet precautions for 7 days after illness onset or until 24 hours after the resolution of fever and respiratory symptoms, whichever is longer. In some cases, facilities may choose to apply droplet precautions for longer periods based on clinical judgment, such as in the case of young children or severely immunocompromised patients who may shed influenza virus for longer periods of time. Complete infection control recommendations for seasonal influenza are available at:
   http://www.cdc.gov/flu/professionals/infectioncontrol/healthcaresettings.htm

   CDC advises that the infections control principles and actions relevant for seasonal influenza are appropriate for the control of influenza A (H3N2v) as well.

   http://www.cdc.gov/flu/swineflu/prevention-strategies.htm

   More stringent infection control practices are recommended for patients suspected of having other novel influenza viruses such as influenza A(H5N1) or A(H7N9). When these infections are suspected, healthcare facilities should immediately implement airborne, contact and standard precautions. Patients should be placed in an airborne isolation room and healthcare personnel caring for these patients should wear gloves, gowns, eye protection and an N95 or higher respirator for all patient care activities. Prolonged influenza viral shedding in the lower respiratory tract has been documented for critically ill patients with A(H5N1) and A(H7N9) infections.

   For infection control guidance for novel influenza A viruses see:
   http://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm
2. Antiviral treatment should be administered according to current CDC guidance (see section 2G above).
3. Persons with suspected or confirmed novel influenza virus infections who do not require hospitalization should be counseled to stay home and away from other persons in the household and follow respiratory hygiene recommendations (Section 6).

C. Identify Potential Sources of Infection

Inquire about recent travel or exposure to ill persons who have recently traveled, and about exposure to animals such as wild birds, poultry and swine.

D. Identify and Manage Contacts

Contact investigations should be performed for all confirmed cases of novel influenza. Consult with Office of Communicable Disease Epidemiology for managing contacts of known or suspect novel influenza cases.

Guidance for conducting contact investigations for influenza A(H5N1) cases is available at: http://www.cdc.gov/flu/avianflu/novel-av-chemoprophylaxis-guidance.htm

Interim guidance for novel influenza A viruses with the potential to cause severe disease in humans (examples include H5N2, H5N8, and North American H5N1) is available at: http://www.cdc.gov/flu/avianflu/severe-potential.htm

For exposure to H5N2, H5N8, H5N1 and other novel influenza A viruses identified in North America, interview all persons with potential exposure during the past 10 days to confirmed or suspected avian influenza.

Exposure to avian influenza is defined as:

- Persons having direct contact with infected birds, contact with surfaces contaminated with the body fluids of infected birds (including fecally contaminated surfaces) or being in an enclosed location (for example, hen house) with infected birds.

  OR

- Persons who have had contact with a suspect or confirmed human case of novel influenza.

As the incubation of avian influenza is estimated to be 2-10 days, contact within the previous 10 days warrants recommendations for symptom monitoring, as below, as well as consideration of Oseltamivir prophylaxis.

1. If any exposed persons are identified in the initial interview as symptomatic with influenza-like illnesses (fever of 100F or higher with cough and/or sore throat), arrange for collection of a specimen for testing at PHL (see Section 4 for precautions and specimens). Do not send specimens commercially or rely on rapid influenza tests.
2. If the last exposure to avian influenza (contact with infected birds or surfaces contaminated by infected birds, being in an enclosed environment with infected birds, or contact with a human case) occurred within the previous 10 days, consider prophylaxis (treatment dose). See http://www.cdc.gov/flu/avianflu/guidance-exposed-persons.htm
   a. Adults: Oseltamivir 75mg twice daily for 5 days
   b. Pediatric dosing (use treatment dose): http://www.cdc.gov/flu/pdf/professionals/antivirals/antiviral-dosage-duration.pdf

3. Begin ILI symptom monitoring for all contacts (fever of 100F or greater along with cough and/or sore throat):
    a. Active surveillance is strongly advised, such that the LHJ makes contact with the exposed person daily to confirm illness status. Final contact should be made at day 10 to confirm illness status. In the event of elevated temperature or other symptom (cough, sore throat), exposed person should immediately contact LHJ via phone or, if LHJ is unavailable after hours, exposed person should immediately call DOH CD Epi 24/7 on-call number 206-418-5500. In the event of development of ILI in an exposed person under monitoring, LHJ should immediately contact DOH CD Epi.
    b. LHJ should develop a plan for where the patient should go for testing/evaluation in the event of symptoms, and how the patient should be transported to the facility (do not use public or commercial transport such as buses or taxis).
4. Provide instructions for the contact if fever or other symptoms develop:
    a. Call the local health jurisdiction to report the symptoms, or DOH CD Epi on-call if LHJ is unavailable. (Local health jurisdiction should immediately notify DOH CD Epi so that testing at PHL can be arranged.)
    b. Call the healthcare facility identified by the local health jurisdiction and ask to be evaluated for possible avian (bird) influenza. Provide the facility with the HCP letter.
    c. Travel to the healthcare facility without using public (e.g., bus) or commercial (e.g., taxi) vehicles.
    d. Besides travel to the healthcare facility, stay home.
5. Without giving names or identifiers, notify the receiving facility that persons being monitored for avian influenza exposure may seek care at that facility.
    a. Confirm that the facility has private room (closed door, private bathroom) where a person could be evaluated, like is done for measles.
    b. Confirm that the facility has personnel trained in use of standard, contact, and airborne precautions who could evaluate a patient.
    c. Provide hospital with the infection control guidelines: http://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm

E. Evaluate the Environment

Environmental investigations may be necessary for the exposure source of persons with novel influenza virus infection. An affected area may need to be disinfected and left without flocks for months. Consult with Communicable Disease Epidemiology and the Zoonotic Disease Program regarding the need for an environmental evaluation. Personal protective equipment is necessary for removing birds and cleaning a farm.

6. ROUTINE PREVENTION

A. Vaccine Recommendations:

Routine annual vaccination is recommended for all persons 6 months and older. Annual vaccination is particularly important for persons at increased risk of complications and for persons in contact with those at high risk for complications (See: http://www.cdc.gov/flu/protect/vaccine/index.htm). Seasonal influenza vaccines are not likely to provide significant protection against novel influenza viruses, but will prevent dual infection with the risk of viral reassortment.

B. Routine Prevention Recommendations

General respiratory hygiene measures are recommended at all times, and particularly during periods when respiratory viruses are circulating:

- Cover your nose and mouth with a tissue when you cough or sneeze. Throw the tissue in the trash after you use it and then clean your hands;
- Wash your hands with soap and water frequently, especially after you cough or sneeze. Alcohol-based hand cleaners are also effective;
- Try to avoid close contact with people ill with respiratory symptoms;
- If you get sick with respiratory symptoms, stay home the recommended period and limit contact with others to keep from infecting them;
- Avoid touching your eyes, nose or mouth;
- Don a mask when entering a healthcare facility if you are coughing or sneezing.

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UPDATES

June 2012: The document was reviewed for accuracy. No significant changes were made.

December 2013: The existing guideline for influenza was divided into a guideline for novel influenza and a guideline for influenza-associated death.

June 2015: Updated to include recommendations for evaluating and monitoring human contacts of avian influenza infected birds.