

**IN THIS ISSUE: NOVEL INFLUENZA A VIRUSES**

**NOVEL INFLUENZA A VIRUSES: HUMAN INFECTIONS FROM ZONOTIC INFLUENZAS**

**Introduction**

There are four types of influenza viruses (A, B, C, D), with A and B viruses causing annual seasonal epidemics.<sup>1</sup> Influenza A viruses, however, are the most important for public health as they are the only type to have caused pandemics. The natural reservoir for influenza A viruses is wild waterfowl, they can infect and circulate among many different animals, and animal to human transmission of these viruses can occur.<sup>2</sup> Human infection with an influenza A virus of animal-origin ("novel influenza A virus infections"), are most often of avian or swine origin. These viruses are genetically and antigenically different from seasonal influenza A viruses (H1N1 and H3N2), so seasonal influenza vaccination does not provide protection.<sup>3</sup> If novel influenza A viruses infect people, cause disease, and lead to sustained transmission, a pandemic may occur as most of the world's population lacks immunity.<sup>3</sup> Additionally, infected mammals may be infected with influenza viruses from different species (e.g., ducks and humans) at the same time and could lead to mixing of the genes of these viruses to create a new virus.

Novel influenza A infections became nationally notifiable in 2007.<sup>2</sup> It is especially important to be aware of these viruses with the recent spread of highly pathogenic avian influenza A(H5N1) amongst birds (detected in 49 states), mammals and even some humans since 2022 and swine influenzas ("variant influenza A viruses") becoming more commonly detected associated with agricultural fairs since 2012 (>500 detections).<sup>4,5</sup>

**Epidemiology**

Many avian influenza A viruses, subtypes divided into low and highly pathogenic avian influenzas (LPAI and HPAI, respectively), have caused sporadic human infections and a wide spectrum of disease (uncomplicated such as conjunctivitis, to severe such as pneumonia, and even death).<sup>2</sup> Infection is primarily through direct and close exposure to infected poultry (sick, dead, or well-appearing). Such exposures can be associated with backyard poultry, live markets, farms, or contact with wild birds. There have been rare and limited human-to-human

transmission, which occurred only after prolonged, unprotected close exposure (e.g., household). However, no mammal-to-human transmission of avian influenza A viruses have been reported. Since 1997, 896 human H5N1 cases have been reported worldwide (13 since 2022) with over a 50% mortality rate. Cases in the Americas were identified starting in 2022 and as of June 2023, there have been 17 detections of highly pathogenic avian influenza in wild birds in Washoe County, but no human cases.<sup>6</sup>

Swine/variant influenza A viruses also have caused sporadic human infections, although mostly reported in children and usually mild.<sup>2</sup> Since 2010, 492 variant influenza A infections have been reported in the United States, more recently associated with swine exposure at agricultural fairs.<sup>7</sup> Infection occurs after exposure to infected pigs (e.g., when the pig coughs or sneezes, droplets with virus are spread through the air or land on surfaces). There is evidence that some limited human-to-human transmission has occurred, but no evidence of transmission through eating properly handled or prepared pork or pork products.<sup>3</sup> Between 2010 and 2023, there were no human cases of variant influenza A in Washoe County or Nevada, but there have been reported cases in surrounding states (CA, OR, UT) as recently as the 2021-2022 influenza season.<sup>7</sup>

**Signs & Symptoms**

Symptoms of avian influenza A infections often begin three days (range two to seven days) after exposure with a clinical progression from typical influenza-like-illness (fever, cough, muscle aches, malaise, headache, sore throat, myalgia, abdominal pain, vomiting, diarrhea) to lower respiratory tract disease (difficulty breathing, shortness of breath, chest pain, tachypnea).<sup>2</sup> Those with severe disease have a median time from symptom onset to hospitalization of six days, upon which they may show signs of hypoxia, pneumonia, leukopenia, lymphopenia, mild to moderate thrombocytopenia, and patchy, interstitial, lobar, and/or diffuse infiltrates and opacities, consolidation, and pleural effusion on radiographic tests. The most common complications are respiratory failure and acute respiratory distress

syndrome (ARDS), as well as acute kidney injury, cardiac failure, and sepsis. Unlike typical influenza that circulates annually, co-infections are uncommon with avian influenza A infections.

Symptoms of swine/variant influenza A infections are often similar to normal seasonal influenza symptoms and are typically mild.<sup>2</sup> However, severe illness or death can occur, particularly for those at higher risk of serious complications (children under 5 years old, people with chronic conditions like asthma, diabetes, heart disease, weakened immune systems, pregnant people, and people 65 years and older).<sup>3</sup>

## Diagnosis & Testing

Testing should be done as soon as possible after illness onset, ideally within seven days.<sup>8</sup> Commercially available influenza tests cannot distinguish avian or variant influenza A viruses from normal seasonal influenza A viruses.<sup>4</sup> If a patient tests positive for influenza A and novel influenza A virus infection is suspected due to animal exposure history, subtyping is necessary.<sup>2</sup>

If the patient has mild illness, it is recommended to collect a NP swab, and combined nasal and throat swabs for RT-PCR testing at the Nevada State Public Health Laboratory (NSPHL).<sup>8</sup> If NSPHL is unable to subtype it as either H1 or H3 influenza A but find it positive for influenza A, the specimen will be sent to CDC to test for avian influenza A.<sup>2</sup> If NSPHL is able to detect H1 or H3 and there is recent swine exposure, CDC will perform confirmatory testing. For those with lower respiratory tract disease, it is recommended to also collect a sputum sample and if intubated, collect endotracheal aspirate specimens (or BAL fluid). If it is suspected avian influenza A virus infection, collect multiple respiratory tract specimens from multiple sites on at least two consecutive days for hospitalized patients.

## Treatment

If novel influenza A infection is suspected, antiviral treatment should be started as soon as possible.<sup>8,9</sup> Oseltamivir is recommended twice daily for five days (or longer if illness more severe) for progressive/severe disease and hospitalized patients. Oseltamivir, other neuraminidase inhibitors (zanamivir, peramivir), or baloxavir are recommended for outpatients who are at risk for influenza complications or infected with a variant influenza A virus. Avoid moderate to high dose corticosteroids due to increased risk for ventilator associated pneumonia and death, as well as prolonged viral shedding.<sup>2</sup>

Post-exposure antiviral chemoprophylaxis may be considered in specific situations after considering type of exposure, duration of exposure, known infection status of the animal exposed to, and length of time since exposure (must be less than two days).<sup>10</sup>

For more treatment and prophylaxis information, visit <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>.

## Infection Prevention and Control<sup>9</sup>

Visit <https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm> for recommendations.

## Reporting

If novel influenza A virus is suspected, a report should be made to the Washoe County Health District either by phone (775-328-2447) or fax (775-328-3764) per [NAC 441A0.40](#).<sup>11</sup> Reporting forms can be found at: <http://tinyurl.com/WashoeDiseaseReporting>

## References

1. Centers for Disease Control and Prevention. Influenza (Flu). Types of Influenza Viruses. Accessed June 2023 <https://www.cdc.gov/flu/about/viruses/types.htm>
2. Centers for Disease Control and Prevention. Clinician Outreach and Communication Activity (COCA). What Providers Need to Know about Zoonotic Influenza. June 20, 2023. [https://emergency.cdc.gov/coca/calls/2023/callinfo\\_062023.asp](https://emergency.cdc.gov/coca/calls/2023/callinfo_062023.asp)
3. Centers for Disease Control and Prevention. Influenza (Flu). Variant Influenza Viruses: Background and CDC Risk Assessment and Reporting. Accessed June 2023 <https://www.cdc.gov/flu/swineflu/variant.htm>
4. Centers for Disease Control and Prevention. Influenza (Flu). Brief Summary for Clinicians: Evaluating and Managing Patients Exposed to Birds Infected with Avian Influenza A Viruses of Public Health Concern. Accessed June 2023 <https://www.cdc.gov/flu/avianflu/clinicians-evaluating-patients.htm>
5. Centers for Disease Control and Prevention. Influenza (Flu). Key Facts about Human Infections with Variant Viruses. Accessed June 2023 <https://www.cdc.gov/flu/swineflu/keyfacts-variant.htm>
6. Centers for Disease Control and Prevention. Influenza (Flu). H5N1 Bird Flu: Current Situation Summary. Accessed June 2023 <https://www.cdc.gov/flu/avianflu/avian-flu-summary.htm>
7. Centers for Disease Control and Prevention. FluView Interactive. Novel Influenza A Virus Infections. Accessed June 2023 [https://gis.cdc.gov/grasp/fluview/Novel\\_Influenza.html](https://gis.cdc.gov/grasp/fluview/Novel_Influenza.html)
8. Centers for Disease Control and Prevention. Influenza (Flu). Interim Guidance on Testing and Specimen Collection for Patients with Suspected Infection with Novel Influenza A Viruses with the Potential to Cause Severe Disease in Humans. Accessed June 2023 <https://www.cdc.gov/flu/avianflu/severe-potential.htm>
9. Centers for Disease Control and Prevention. Influenza (Flu). Interim Guidance for Infection Control Within Healthcare Settings When Caring for Confirmed Cases, Probable Cases, and Cases Under Investigation for Infection with Novel Influenza A Viruses Associated with Severe Disease. Accessed June 2023 <https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm>
10. Centers for Disease Control and Prevention. Influenza (Flu). Interim Guidance on Influenza Antiviral Chemoprophylaxis of Persons Exposed to Birds with Avian Influenza A Viruses Associated with Severe Human Disease or with the Potential to Cause Severe Human Disease. Accessed June 2023 <https://www.cdc.gov/flu/avianflu/guidance-exposed-persons.htm>
11. NAC: CHAPTER 441A - INFECTIOUS DISEASES; TOXIC AGENTS. www.leg.state.nv.us. Accessed June 2023. <https://www.leg.state.nv.us/nac/nac-441a.html>