



Nebraska Department of Health and Human Services
HEALTH ALERT NETWORK
Update



TO: Healthcare Providers, Infection Control, Hospitals, Labs, and Public Health
FROM: Robin M. Williams Matthew Donahue, MD Gary Anthonie, MD
 Influenza Surveillance Coordinator State Epidemiologist Director/CMO Public Health
 PHONE: 402-471-2937 PHONE: 402-471-2937 PHONE: 402-471-8566

RE: Important Seasonal Influenza Updates and Recommendations; Increased Influenza Activity Identified in Midwest Universities

DATE: December 10, 2021

- Nebraska's Influenza and other Respiratory Diseases Surveillance System reports increases in influenza activity that marks the beginning of the 2021-2022 influenza season, see weekly report here: [Nebraska Influenza & Other Respiratory Disease Surveillance Report](#). Additional respiratory data is also available on the [Nebraska Hospital Capacity & Respiratory Illness Dashboard](#).
- The increase in influenza activity as the holiday season begins underscores the importance of influenza vaccination. Influenza and COVID-19 vaccinations CAN be coadministered at the same visit, as [recommended by CDC and its Advisory Committee on Immunizations Practices \(ACIP\)](#). If a patient is due for both vaccines, providers are encouraged to offer both vaccines at the same visit.
- Concomitant influenza and COVID-19 testing is encouraged as well and is available through NPHL to healthcare providers seeing inpatients and outpatients.
- The predominant influenza A subtype detected in Nebraska this year, H3N2, tends to be more virulent and is associated with a higher incidence of concomitant secondary bacterial pneumonias. Consider secondary bacterial pneumonias in your differential diagnosis. Influenza predisposes individuals to developing bacterial community-acquired pneumonia. During each of the influenza pandemics of the 20th century, secondary bacterial pneumonia was a frequent cause of illness and death. *Staphylococcus aureus* and *Streptococcus pneumonia* have been identified as the most common etiologies.

Influenza vaccination: encourage vaccination and permit coadministration

During the 2020-21 season, influenza activity was historically low, likely due to strict COVID-19 prevention measures (e.g., masks, distancing). On college campuses, influenza viruses are known to spread rapidly in close quarters (e.g., common living spaces, classrooms, shared restrooms) and through social activities. This elevated risk is compounded by low flu vaccination coverage. CDC estimates suggest that influenza vaccine uptake this year is lower than last season, including among children, younger adults, and pregnant women.

Influenza testing: concomitant influenza and COVID-19 testing is encouraged

Symptoms of COVID-19 and influenza are similar and symptomatic patients should be tested for both SARS-CoV-2 and influenza viruses. Review CDC's Information for Clinicians on Influenza Virus Testing [here](#). Please contact NE DHHS at 402-471-3927 or dhhs.epi@nebraska.gov, or your local health department (LHD) [here](#) if you have questions or unusual situations.

For healthcare providers seeing inpatients or outpatients with concerns for COVID-19, testing is still highly encouraged as we continue monitoring and tracking associations between variants of concern, reinfections, vaccine breakthroughs and outcomes. As influenza cases increase, co-testing for both influenza and COVID-19 might prove increasingly valuable. Testing for SARS-CoV-2 will remain available to local health departments and healthcare providers through the Nebraska Public Health Laboratory (NPHL). ALL specimens sent to NPHL for SARS-CoV-2 testing are simultaneously tested for influenza A virus, influenza B virus and SARS-CoV-2 and test results for all three viruses will be sent back to the provider. These specimens will not be serotyped.

DHHS is encouraging providers/laboratories who utilize a molecular influenza test to send any specimens to NPHL with a cycle threshold (CT) of 25 or lower for confirmatory influenza surveillance testing. Additionally, if you believe you might have a false positive or false negative influenza test result, NPHL will confirm up to five specimens. These specimens are tested on the CDC Influenza-PCR assay and determine what viruses are currently circulating in Nebraska. This tests for influenza A virus, influenza B virus, influenza A virus subtype H3 [seasonal], influenza A virus subtype 2009 [H1N1], influenza B Yamagata lineage or influenza B Victoria lineage (if positive B). In turn, these specimens are sent to CDC for antigenic characterization of the virus. This information helps determine what viruses should be included in the upcoming season's influenza vaccine.

Instructions to order influenza testing at NPHL

Use NUIrt (NPHL's Internet-based, electronic lab information system) to complete an order for [FLUPCR](#). To access NUIrt, click here (<https://nulirt.nebraskamed.com/login>) using your existing NUIrt account. If you are a new user, follow the link to register and create a new account. Please complete all the requested data fields included with the Ask On Entry (AOE) questions. A properly completed requisition is required for order processing. For orders created electronically, submitters should print a completed batch list to accompany the specimen by clicking within the NUIrt system. For issues related to NUIrt access, contact the NUIrt support group via email nulirtsupport@nebraskamed.com or contact client service representatives at 402-559-2440; or toll-free: 1-866-290-1406.

Specimen Collection Requirements (NPHL only): The optimal specimen is a nasopharyngeal swab placed in a single tube of transport medium. See Collecting, Handling and transport of Influenza Laboratory Specimens, <http://www.nphl.org/>.

Influenza reporting: report pediatric deaths, novel viruses, and outbreaks

Pediatric influenza-associated deaths and variant/novel viruses ARE [reportable](#). Outbreaks of influenza or influenza-like illness ARE reportable in congregate settings such as long-term care facilities, correctional facilities, or group homes. Reporting should occur when there are two or more cases of influenza-like illness among residents within 72 hours with at least one of the ill residents having laboratory-confirmed influenza. Outbreaks of influenza and other diseases in schools/daycares are also reportable to public health (either NE DHHS or your LHD). Individual cases of influenza are NOT reportable unless the case is tested and resulted by a laboratory who currently participates in automated electronic laboratory reporting (ELR).

This is an official
CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
November 24, 2021, 11:00 AM ET
CDCHAN-00458

Increasing Seasonal Influenza A (H3N2) Activity, Especially Among Young Adults and in College and University Settings, During SARS-CoV-2 Co-Circulation

Summary

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory about increased influenza A(H3N2) activity that could mark the beginning of the 2021-2022 influenza season. The purpose of this HAN Health Advisory is to

1. Remind public health practitioners and clinicians to recommend and offer the current seasonal influenza vaccine to all eligible persons aged six months and older (Flu vaccine and COVID-19 vaccine can be given at the same visit).
2. Remind clinicians to consider testing for both influenza virus and SARS-CoV-2 in patients with influenza-like illness (ILI).
3. Advise clinicians that antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who is: a) hospitalized; b) at higher risk for influenza complications; or c) developing progressive illness. In patients with suspected influenza, decisions about starting antiviral treatment should not wait for laboratory confirmation of influenza, however COVID-19 should be excluded if a rapid assay is available.
4. Remind public health practitioners and clinicians to consider mitigation measures including antiviral post-exposure prophylaxis during influenza outbreaks in institutions (e.g., long-term care facilities, university dormitories) in the setting of co-circulation of SARS-CoV-2.
5. Remind the public to use non-pharmaceutical interventions (NPI) or everyday preventive actions, in addition to getting a flu vaccine. Everyday preventive actions include staying home when sick, covering coughs and sneezes, and washing hands often.

Background

Recent increases in influenza activity in many places in the United States could mark the beginning of the 2021-2022 influenza season in the United States. While influenza activity is still low overall nationally, an increase of influenza A(H3N2) viruses has been detected in recent weeks, with most of these infections occurring in young adults. CDC also is aware of influenza outbreaks in colleges and universities in several states. Influenza vaccination coverage is still low and there is still time this season to benefit from getting an annual influenza vaccine.

Available seasonal influenza vaccines in the United States provide protection against four different influenza viruses: A(H1N1)pdm09, A(H3N2), B/Victoria lineage, and B/Yamagata lineage viruses. In the past, influenza A(H3N2) virus-predominant seasons were associated with more hospitalizations and deaths in persons aged 65 years and older than other age groups than other influenza viruses. Influenza A(H3N2) viruses evolve more rapidly to escape human immunity. The influenza A(H3N2) component of this season's vaccines was recently updated in response to the evolution of a new group of viruses called 2a (i.e., 3C.2a1b.2a) that did not circulate widely last year and were not included in last season's H3N2 vaccine component.¹ Most H3N2 viruses that have been analyzed in the United States so far are genetically closely related to the current vaccine's H3N2 component. However, this emerging group has continued to evolve, and there are now two subgroups (2a.1 and 2a.2) that are genetically closely related to each other, but do have some antigenic differences from each other (i.e., post-infection ferret

antibodies from one virus might not efficiently bind the other virus).² CDC virus surveillance data shows that most of the A(H3N2) viruses recently identified in the United States (October–November 2021) are in the 2a.2 group that is related to but distinguishable from the vaccine component (i.e., 2a.1). It is not known what impact the differences in the circulating viruses and the vaccine viruses may have on vaccine effectiveness. However, influenza vaccine effectiveness in general has been lower against A(H3N2) viruses than against the other three influenza viruses that could circulate [influenza A(H1N1)pdm09 or influenza B viruses].³ Influenza activity during the 2020–2021 season was low throughout the United States and the timing and intensity of the upcoming 2021–2022 influenza season is uncertain. Because influenza activity was low last season, we are anticipating a lower level of community protection that we rely on year after year to reduce the risk of a severe influenza season. Thus, CDC is anticipating an increase of influenza illness this winter, and both A(H3N2) and B-Victoria viruses are already co-circulating. Moreover, as SARS-CoV-2 continues to circulate in the United States, illnesses associated with both viruses might stress healthcare systems. A growing body of scientific studies suggest that even when vaccination does not prevent infection it can reduce the severity of influenza illness, helping to avert serious outcomes including hospitalization and death.

CDC recommends that healthcare providers continue to recommend and offer influenza vaccination to persons aged six months and older because influenza activity is ongoing. Vaccination protects against four different viruses and is likely to reduce hospitalization and death associated with currently circulating influenza viruses and other influenza viruses that might circulate later in the season. Influenza antiviral medications are an important adjunct that should be used in addition to influenza vaccination. While vaccination is the primary means for preventing influenza, antiviral medications are a second line of defense used to treat influenza after infection has occurred. Early treatment with influenza antiviral medications is the most effective way to treat influenza and reduce complications.⁴⁻⁸

Influenza antivirals also can be used for post-exposure prophylaxis (PEP) to prevent infection.^{4,5,9} This can reduce the risk of influenza among persons who are exposed to someone who has influenza. Influenza antivirals have historically been used for PEP among residents in institutional settings, such as long-term care facilities, to help control influenza outbreaks. In the context of SARS-CoV-2 co-circulation, influenza antiviral treatment and PEP could also be considered in other communal settings (e.g., shelters, university dormitories, prisons) to reduce strain on healthcare services in these institutions during influenza outbreaks. In general, CDC recommends initiating influenza antiviral PEP within 48 hours of contact with someone who has influenza.

Recommendations for Clinicians and Public Health Practitioners

1. Recommend and offer influenza vaccination for all eligible persons aged six months and older

Anyone who has not received an influenza vaccine this season should get vaccinated now. For 2021-2022, CDC recommends using any licensed, age-appropriate influenza vaccine as an option for vaccination this season.¹⁰ Vaccination coverage is lower this season as of the week ending November 6, 2021 in certain groups at higher risk of severe influenza illness, such as pregnant persons and children, compared with the same period in 2020.¹¹ Vaccination is the best way to reduce the spread of influenza and reduce influenza illness and complications that can result in hospitalization and death. Both influenza and COVID-19 vaccines can be administered at the same visit, without regard to timing. If a patient is due for both vaccines, providers are encouraged to offer both vaccines at the same visit.

2. Treat patients with suspected or confirmed influenza who meet clinical criteria with influenza antivirals

CDC recommends influenza antiviral medications to treat influenza as an important adjunct to vaccination. Treatment with influenza antivirals has been shown to be safe. Influenza antivirals benefit clinical and public health by reducing illness and severe outcomes of influenza based on evidence from observational studies, randomized controlled trials, and meta-analyses of randomized controlled trials.^{4-8,12}

- CDC recommends influenza antiviral treatment **as soon as possible** for patients with suspected or confirmed influenza who are:
 - Hospitalized

- Outpatients at increased risk for complications⁹
- Outpatients with progressive disease ⁹
- Influenza antiviral treatment may be offered to patients with uncomplicated influenza based on clinician judgment to shorten their illness duration or lessen symptoms. The use of antiviral treatment in patients with uncomplicated influenza might help lessen the stress on healthcare systems when both influenza and SARS-CoV-2 are co-circulating.
- Antivirals are most effective when started **within two days after the beginning of illness**. It is also possible that antiviral treatment started after 48 hours may offer some benefit.^{4,8,12}
- Potential also exists for co-infection of influenza and SARS-CoV-2 viruses. In such situations, influenza antivirals can be given for influenza illness.
- Because of the importance of early treatment, **decisions about starting antiviral treatment should not wait for laboratory confirmation of influenza**. However, COVID-19 should be excluded with a rapid diagnostic assay if one is available.

There are two oral influenza antiviral medications approved by the U.S. Food and Drug Administration (FDA) **commonly available by prescription** to treat influenza virus infection that can also be used for PEP following influenza exposure.⁹ These include *oseltamivir* (trade name Tamiflu®), and *baloxavir marboxil* (trade name Xofluza®) (Table 1). **Inhaled zanamivir and intravenous peramivir antiviral medications are used less frequently.**⁹ Additional information on these influenza antiviral medications is available [here](#).

Table 1: Summary of most common antiviral medications for treatment and post-exposure prophylaxis of influenza⁹

Drug	Oseltamivir (Tamiflu®)	Baloxavir (Xofluza®)
Approved by FDA	1999	2018
Mechanism	Neuraminidase inhibitor	Cap-dependent endonuclease inhibitor
Route of administration	Oral	Oral
Treatment dosing	Daily dosing for 5 days <ul style="list-style-type: none"> ● Adults: 75 mg twice daily ● Children: varies by age/weight⁹ 	Single dose only <ul style="list-style-type: none"> ● <80 kg: 40 mg ● ≥80 kg: 80 mg
Post-exposure prophylaxis dosing	Daily dosing for 7 days <ul style="list-style-type: none"> ● Adults: 75 mg once daily ● Children: varies by age/weight⁹ 	Single dose only <ul style="list-style-type: none"> ● <80 kg: 40 mg ● ≥80 kg: 80 mg
Age	Treatment: any age for treatment PEP: ≥3 months	Treatment or PEP: ≥12 years
Contraindications	Known hypersensitivity	Known hypersensitivity

3. Use of influenza antivirals for post-exposure prophylaxis (PEP)

Both oseltamivir and baloxavir are FDA-approved for influenza PEP. The efficacy of PEP in reducing virus acquisition to uninfected household contacts is high for oseltamivir (68%-89%)¹³ and baloxavir (86%).⁵ In general, before the COVID-19 pandemic, CDC did not recommend widespread or routine use of influenza antiviral medications for PEP in the community.⁹ However, PEP has been recommended previously in closed settings such as long-term care facilities or crowded group settings such as refugee resettlement facilities. In these situations, CDC has recommended using clinical judgment for antiviral PEP for certain exposed non-ill close contacts of persons with suspected or confirmed influenza. Given the unique considerations of influenza outbreaks in various settings in the context of co-circulation with SARS-CoV-2, influenza antiviral PEP might be considered for persons

- Who have had recent close contact with a person with influenza (e.g., roommates)
- In confined quarters (e.g., dormitories, shelters, prisons) with increasing incidence of influenza

- Who are at increased risk for severe illness from influenza¹⁴
- Who have had recent close contact with a person with influenza and will be traveling for the holidays to reduce transmission during travel as well as to reduce transmission to family members or friends who may be at higher risk for influenza complications¹⁴

Considerations for choice of PEP antivirals (Table 1):

- A key difference between the drugs relates to the longer half-life of baloxavir (days) vs. the shorter half-life of oseltamivir (hours). Thus, for PEP, **baloxavir can be administered as a single dose** while **oseltamivir requires daily dosing for seven days**.
- **Dosing:** Treatment and prophylaxis (prevention) dosing is the same for baloxavir, but for oseltamivir, treatment dosing is twice daily, and prophylaxis is once daily.
- **Timing of PEP:** CDC recommends initiating PEP within 48 hours of contact with an influenza case, if PEP is provided. In general, PEP for oseltamivir should not be started >48 hours after exposure due to concerns about resistance with lower PEP dose in persons with active influenza.
- **Duration of PEP:** Antiviral medications are effective as PEP only if a person takes them the entire time they are around another person who has influenza.
- Rates of oseltamivir and baloxavir resistance among circulating influenza A viruses remain low. However, additional monitoring is necessary, especially with baloxavir, which has had limited use compared to oseltamivir.

4. Influenza testing

Information to assist clinicians about influenza testing decisions, including in the context of SARS-CoV-2 co-circulation, is available [here](#). The most accurate influenza tests (high sensitivity and specificity) are molecular assays. Molecular assays are recommended for hospitalized patients with suspected influenza. Information on influenza molecular assays is available [here](#).

5. Non-pharmaceutical interventions

Because no single intervention can provide complete protection against influenza virus transmission, emphasis should be placed on multiple strategies, including pharmaceutical (e.g., influenza vaccines and antiviral medications) and non-pharmaceutical interventions. Measures that are used for COVID-19 might also provide protection against influenza. Non-pharmaceutical interventions may include

- Community measures (e.g., physical distancing, masking)
- Environmental measures (e.g., routine surface cleaning)
- Advising and encouraging symptomatic persons to stay home and use frequent hand hygiene, and proper cough etiquette

Recommendations for the Public

1. **Get a flu vaccine as soon as possible.** There's still time to protect yourself from flu this season. You can get a flu vaccine and a COVID-19 vaccine at the same time. Vaccines are the best tool for preventing influenza and can reduce the risk of severe illness and death associated with influenza.
2. **Take everyday preventive actions that can help reduce the spread of germs, like flu.**
 - These [everyday preventive actions](#) include staying home when sick, covering coughs and sneezes, and washing your hands often. While CDC does not recommend wearing a face mask to protect you from getting flu, [wearing a face mask](#) is recommended to protect you and others against COVID-19 at this time.
3. If you develop flu symptoms (which can be similar to symptoms of other respiratory viruses), reach out to your healthcare provider who may test you to determine if your sickness is due to flu or another virus that has similar symptoms, such as COVID-19.
4. **Take antiviral drugs if prescribed by your healthcare provider.**
 - It's important to remember that there also are [drugs that can be used to treat flu illness](#).
 - Antiviral drugs are not meant to replace flu vaccine. A flu vaccine is the best way to help prevent seasonal flu and its potentially serious complications. Antiviral drugs are a second line of defense that can be used to treat flu if you do get sick.

- Flu antiviral drugs work best when started within two days of a person getting sick.
- CDC recommends that people who are very sick or who are at higher risk of developing serious flu complications get antiviral treatment as early as possible without waiting for test results.
- Many patients might not be aware that drugs to treat influenza illness are available. A fact sheet for patients is available [here](#).

For More Information

[CDC Tracking Flu in Young Adults](#)

[Healthy Habits to Help Protect Against Flu](#)

Additional Resources for Clinicians:

- [Summary of Influenza Antiviral Treatment Recommendations for Clinicians](#)
- [Clinical Description and Lab Diagnosis of Influenza](#)
- [Interim Guidance for Influenza Outbreak Management in Long-Term and Post-Acute Care Facilities](#)
- [Influenza Virus Testing in Investigational Outbreaks in Institutional or Other Closed Settings](#)

References

1. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2021-2022 northern hemisphere influenza season. (https://cdn.who.int/media/docs/default-source/influenza/202102_recommendation.pdf Last accessed on: 16 November 2021).
2. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2022 southern hemisphere influenza season. (https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-southern-hemisphere-recommendation-2022/202109_recommendation.pdf?sfvrsn=698a54b9_12&download=true Last accessed on: 16 November 2021).
3. Okoli GN, Racovitan F, Abdulwahid T, Righolt CH, Mahmud SM. Variable seasonal influenza vaccine effectiveness across geographical regions, age groups and levels of vaccine antigenic similarity with circulating virus strains: A systematic review and meta-analysis of the evidence from test-negative design studies after the 2009/10 influenza pandemic. *Vaccine* 2021;39(8):1225-1240. <https://doi.org/10.1016/j.vaccine.2021.01.032>.
4. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clin Infect Dis* 2019;68(6):895-902. <https://doi.org/10.1093/cid/ciy874>.
5. Ikematsu H, Hayden FG, Kawaguchi K, et al. Baloxavir Marboxil for Prophylaxis against Influenza in Household Contacts. *N Engl J Med* 2020;383(4):309-320. <https://doi.org/10.1056/NEJMoa1915341>.
6. Hayden FG, Sugaya N, Hirotsu N, et al. Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents. *N Engl J Med* 2018;379(10):913-923. <https://doi.org/10.1056/NEJMoa1716197>.
7. Muthuri SG, Venkatesan S, Myles PR, et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. *Lancet Respir Med* 2014;2(5):395-404. [https://doi.org/10.1016/S2213-2600\(14\)70041-4](https://doi.org/10.1016/S2213-2600(14)70041-4).
8. Venkatesan S, Myles PR, Bolton KJ, et al. Neuraminidase Inhibitors and Hospital Length of Stay: A Meta-analysis of Individual Participant Data to Determine Treatment Effectiveness Among Patients Hospitalized With Nonfatal 2009 Pandemic Influenza A(H1N1) Virus Infection. *J Infect Dis* 2020;221(3):356-366. <https://doi.org/10.1093/infdis/jiz152>.
9. CDC: Influenza Antiviral Medications: Summary for Clinicians. (<https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm> Last accessed on: 16 November 2021).

10. Grohskopf LA, Alyanak E, Ferdinands JM, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2021-22 Influenza Season. *MMWR Recomm Rep* 2021;70(5):1-28. <https://doi.org/10.15585/mmwr.rr7005a1>.
11. CDC: Weekly National Flu Vaccination Dashboard. (<https://www.cdc.gov/flu/fluview/dashboard/vaccination-dashboard.html>) Last accessed on: 16 November 2021).
12. Campbell AP, Tokars JI, Reynolds S, et al. Influenza Antiviral Treatment and Length of Stay. *Pediatrics* 2021;148(4). <https://doi.org/10.1542/peds.2021-050417>.
13. Fiore AE, Fry A, Shay D, et al. Antiviral agents for the treatment and chemoprophylaxis of influenza --- recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2011;60(1):1-24. (<https://www.ncbi.nlm.nih.gov/pubmed/21248682>).
14. CDC. People at Higher Risk of Flu Complications. (<https://www.cdc.gov/flu/highrisk/index.htm>) Last accessed on: 16 November 2021).

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

Categories of Health Alert Network messages:

Health Alert Requires immediate action or attention; highest level of importance
Health Advisory May not require immediate action; provides important information for a specific incident or situation
Health Update Unlikely to require immediate action; provides updated information regarding an incident or situation
HAN Info Service Does not require immediate action; provides general public health information

##This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations##