Influenza and COVID-19

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<td>• People with acute COVID-19 should receive an inactivated influenza vaccine (BIII).</td>
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<td>• Clinicians should consider deferring influenza vaccination for symptomatic patients with COVID-19 until these patients are no longer moderately or severely ill and have completed their COVID-19 isolation period.</td>
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<td>• Clinicians should advise people with asymptomatic SARS-CoV-2 infection or mild COVID-19 symptoms to seek influenza vaccination when they no longer require isolation. They can be vaccinated sooner if they are in a healthcare setting for other reasons.</td>
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<td>• An influenza vaccine and a COVID-19 vaccine may be administered concurrently at different injection sites. See the recommendations from the Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices for more information.</td>
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**Diagnosis of Influenza and COVID-19 When Influenza Viruses and SARS-CoV-2 Are Cocirculating**

• Only testing can distinguish between SARS-CoV-2 and influenza virus infections and identify SARS-CoV-2 and influenza virus coinfection.

• The COVID-19 Treatment Guidelines Panel (the Panel) recommends influenza testing in addition to SARS-CoV-2 testing in outpatients with acute respiratory illness if the results will change the clinical management strategy for the patient (e.g., administering antiviral treatment for influenza) (BIII).

• The Panel recommends testing for both viruses in all hospitalized patients with acute respiratory illness (AIII).

• Clinicians should consider testing patients for other pathogens based on the specific clinical circumstances. Additional testing for bacterial pathogens is important for patients with influenza and clinical signs that suggest bacterial superinfections, especially for patients who are immunocompromised or intubated.

• See the CDC webpage Information for Clinicians on Influenza Virus Testing and the Infectious Diseases Society of America (IDSA) clinical practice guidelines for more information.

**Antiviral Treatment of Influenza When Influenza Viruses and SARS-CoV-2 Are Cocirculating**

• Antiviral treatment for influenza is the same for all patients regardless of SARS-CoV-2 coinfection (AIII).

• For information on using antiviral drugs to treat influenza in hospitalized and nonhospitalized patients, see the CDC and IDSA recommendations.

• There are no clinically significant drug-drug interactions between the antiviral agents or immunomodulators that are used to prevent or treat COVID-19 and the antiviral agents that are used to treat influenza.

• The Panel recommends that hospitalized patients who are suspected of having either influenza or COVID-19 be started on empiric treatment for influenza with oseltamivir as soon as possible and without waiting for influenza test results (AIIb).

• Antiviral treatment for influenza can be stopped when influenza has been ruled out by the results of a nucleic acid detection assay. The assay should be performed on upper respiratory tract specimens for nonintubated patients and on both upper and lower respiratory tract specimens for intubated patients.

**Rating of Recommendations:** A = Strong; B = Moderate; C = Weak

**Rating of Evidence:** I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

**Introduction**

Influenza activity during the 2021 to 2022 influenza season in the United States occurred in 2 waves and extended from November 2021 through mid-June 2022.¹ The overall severity of the 2021 to 2022 season was lower than the severity of seasonal influenza epidemics that occurred before the emergence...
of SARS-CoV-2. However, in some countries in the southern hemisphere (e.g., Australia), the levels of influenza activity observed during the 2021 to 2022 season were similar to pre-COVID-19 pandemic levels.\textsuperscript{2,3}

Clinicians should monitor local influenza and SARS-CoV-2 activities during influenza season to inform the evaluation and management of patients with acute respiratory illness. This can be done by tracking local and state public health surveillance data, assessing the results of testing performed at health care facilities, and reviewing the Centers for Disease Control and Prevention (CDC) \textit{Weekly U.S. Influenza Surveillance Report}.

\textbf{Influenza Vaccination}

\textbf{For Patients With Acute COVID-19 or Those Recovering From COVID-19}

The Advisory Committee on Immunization Practices (ACIP) recommends offering an influenza vaccine by the end of October to all people aged \textgeq6 months in the United States.\textsuperscript{4} People with acute COVID-19 should receive an inactivated influenza vaccine (BIII).

There are currently no data on the safety, immunogenicity, or efficacy of influenza vaccines in patients with mild COVID-19 or those who are recovering from COVID-19. The safety and efficacy of vaccinating people who have mild illnesses from other etiologies have been documented.\textsuperscript{5} Clinicians should consider deferring influenza vaccination for symptomatic patients with COVID-19 until these patients are no longer moderately or severely ill and have completed their COVID-19 isolation period. People with asymptomatic SARS-CoV-2 infection or mild COVID-19 symptoms should seek influenza vaccination when they no longer require isolation. They can be vaccinated sooner if they are in a health care setting for other reasons.

It is not known whether administering dexamethasone or other immunomodulatory therapies to patients with severe COVID-19 will affect the immune response to an influenza vaccine. Nevertheless, as long as influenza viruses are circulating, people with COVID-19 should receive an influenza vaccine once they have substantially improved or recovered from COVID-19. See the influenza vaccine recommendations from the CDC, the ACIP, and the American Academy of Pediatrics.

\textbf{Coadministration of COVID-19 Vaccines and Influenza Vaccines}

Although there are currently limited data on coadministering COVID-19 vaccines and influenza vaccines, these vaccines may be administered concurrently at different injection sites.\textsuperscript{6-8} Providers and patients should be aware of the potential for increased reactogenicity when both vaccines are administered concurrently. See the recommendations from the CDC and the ACIP for more information.

\textbf{Clinical Presentation of Influenza Versus COVID-19}

The signs and symptoms of uncomplicated, clinically mild influenza overlap with those of mild COVID-19. Ageusia and anosmia can occur with both diseases, but these symptoms are more common with COVID-19 than with influenza. Fever is not always present in patients with either disease, particularly in young infants, adults of advanced age, and patients who are immunosuppressed. Complications of influenza and COVID-19 can be similar, but the onset of influenza complications and severe disease typically occurs within a week of illness onset, whereas the onset of severe COVID-19 usually occurs in the second week of illness.

Because of the overlap in signs and symptoms, when SARS-CoV-2 and influenza viruses are cocirculating, diagnostic testing for both viruses is needed to distinguish between SARS-CoV-2 and influenza virus and to identify coinfection in people with an acute respiratory illness. Coinfection with influenza virus and SARS-CoV-2 has been described in case reports and case series,\textsuperscript{9-13} but it is
uncommon.\textsuperscript{14} Observational studies have reported greater disease severity in patients with influenza virus and SARS-CoV-2 coinfection than in patients with SARS-CoV-2 infection alone.\textsuperscript{15,16}

**Testing for SARS-CoV-2 and Influenza**

When influenza viruses and SARS-CoV-2 are cocirculating in the community, SARS-CoV-2 testing should be performed in outpatients with suspected COVID-19, and influenza testing can be considered if the results will change the clinical management strategy for the patient (e.g., administering antiviral treatment for influenza) (BIII). SARS-CoV-2 testing and influenza testing should be performed in all patients who are hospitalized with an acute respiratory illness (see Testing for SARS-CoV-2 Infection (AIII)). Several multiplex molecular assays and multiplex antigen assays that detect SARS-CoV-2 and influenza A and B viruses have received Food and Drug Administration Emergency Use Authorizations or De Novo classifications and can provide results in 15 minutes to 8 hours using a single respiratory specimen.\textsuperscript{17,18} For more information, see the CDC webpage Information for Clinicians on Influenza Virus Testing and the recommendations from the Infectious Diseases Society of America (IDSA) on the use of influenza tests and the interpretation of test results.\textsuperscript{19}

**Treating Influenza With Antiviral Agents**

Antiviral treatment for influenza is the same for all patients regardless of SARS-CoV-2 coinfection (AIII). There are no clinically significant drug-drug interactions between the antiviral agents or immunomodulators that are used to prevent or treat COVID-19 and the antiviral agents that are used to treat influenza. The IDSA recommends administering antiviral treatment for influenza to all hospitalized patients with influenza.\textsuperscript{19}

The Panel recommends that hospitalized patients who are suspected of having either influenza or COVID-19 be started on empiric treatment for influenza with oseltamivir as soon as possible and without waiting for influenza test results (AIIib). Oseltamivir has no activity against SARS-CoV-2.\textsuperscript{20} The standard dose of oseltamivir is well absorbed even in critically ill patients. For patients who cannot tolerate oral or enterically administered oseltamivir (e.g., because of gastric stasis, malabsorption, or gastrointestinal bleeding), intravenous peramivir is an option.\textsuperscript{19} There are no data on the activity of peramivir against SARS-CoV-2.

See the CDC webpage Influenza Antiviral Medications: Summary for Clinicians for clinical algorithms for using antiviral agents in patients with suspected or laboratory-confirmed influenza, including pregnant people and other people who are at high risk for influenza complications. The IDSA clinical practice guidelines also provide recommendations on using antiviral agents to treat influenza, and the American Academy of Pediatrics provides recommendations on the antiviral treatment of influenza in children.

When the result of an influenza nucleic acid detection assay from an upper respiratory tract specimen is negative in a patient who is receiving antiviral treatment for influenza:

- **In a patient who is not intubated:** Antiviral treatment for influenza can be stopped.
- **In a patient who is intubated:** Antiviral treatment for influenza should be continued, and if a lower respiratory tract specimen (e.g., endotracheal aspirate) can be safely obtained, it should be tested using an influenza nucleic acid detection assay. If the lower respiratory tract specimen is also negative, antiviral treatment for influenza can be stopped.

**COVID-19 Treatment Considerations for Hospitalized Patients With Suspected or Confirmed Influenza Virus Coinfection**

Corticosteroids, which are used to treat patients with severe COVID-19, may prolong influenza viral replication and viral RNA detection and may be associated with poor outcomes for influenza.\textsuperscript{19,21}
Currently, no data are available on the use of corticosteroids in patients with SARS-CoV-2 and influenza virus coinfection. However, because dexamethasone has demonstrated substantial benefits for patients with COVID-19 who require supplemental oxygen, the benefits of using corticosteroids in patients with severe SARS-CoV-2 and influenza virus coinfection likely outweigh any potential harms.

Remdesivir does not have activity against influenza viruses. There are no known drug-drug interactions between remdesivir and oseltamivir. Therefore, remdesivir may be safely coadministered with oseltamivir in patients with COVID-19 and suspected or laboratory-confirmed influenza.

Although severe influenza may be associated with a dysregulated innate immune response, there are no data on the use of immunomodulatory therapies, such as interleukin-6 inhibitors (e.g., tocilizumab, sarilumab) or Janus kinase inhibitors (e.g., baricitinib, tofacitinib), for the treatment of severe influenza. There are also no data on the effect these therapies may have on influenza viral replication. Because these immunomodulators have demonstrated a clinical benefit in certain patients with COVID-19, clinicians should consider engaging in a shared decision-making process on the use of these drugs with patients who have been diagnosed with COVID-19 and who have suspected or laboratory-confirmed influenza.

Observational studies have reported that co-occurrence of community-acquired secondary bacterial pneumonia appears to be infrequent in people with COVID-19; it is more common in people who have influenza. Typical bacterial causes of community-acquired pneumonia with severe influenza are *Staphylococcus aureus* (both methicillin-resistant *S. aureus* [MRSA] and methicillin-susceptible *S. aureus* [MSSA]), *Streptococcus pneumoniae*, and group A *Streptococcus*.

Patients with COVID-19 who develop new respiratory symptoms with or without fever or respiratory distress and who do not have a clear diagnosis should be evaluated for the possibility of nosocomial influenza.

**References**


