

Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza^a

Timothy M. Uyeki,¹ Henry H. Bernstein,² John S. Bradley,³⁴ Janet A. Englund,⁵ Thomas M. File,⁶ Alicia M. Fry,¹ Stefan Gravenstein,⁷ Frederick G. Hayden,⁸ Scott A. Harper,⁹ Jon Mark Hirshon,¹⁰ Michael G. Ison,¹¹ B. Lynn Johnston,¹² Shandra L. Knight,¹³ Allison McGeer,¹⁴ Laura E. Riley,¹⁵ Cameron R. Wolfe,¹⁶ Paul E. Alexander,^{17,18} and Andrew T. Pavia¹⁹

¹Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; ²Division of General Pediatrics, Cohen Children's Medical Center, New Hyde Park, New York; ³Division of Infectious Diseases, Rady Children's Hospital, and ⁴University of California, San Diego; ⁵Department of Pediatrics, University of Washington, Seattle Children's Hospital; ⁶Division of Infectious Diseases, Rady Children's Hospital, and ⁴University, Rootstown; ⁷Providence Veterans Affairs Medical Center and Center for Gerontology and Healthcare Research, Brown University, Providence, Rhode Island; ⁸Division of Infectious Diseases and International Health, University of Virginia Health System, Charlottesville; ⁹Office of Public Health Preparedness and Response, Centers for Disease Control and Prevention, Atlanta, Georgia; ¹⁰Department of Emergency Medicine, Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore; ¹¹Divisions of Infectious Diseases and Organ Transplantation, Northwestern University Feinberg School of Medicine, Chicago, Illinois; ¹²Department of Medicine, Dahousie University, Nova Scotia Health Authority, Halifax, Canada; ¹³Library and Knowledge Services, National Jewish Health, Denver, Colorado; ¹⁴Division of Infectious Diseases, Duke University Medical Center, Durham, North Carolina; ¹⁷McMaster University, Hamilton, Ontario, Canada; ¹⁸Infectious Diseases Society of America, Arlington, Virginia; and ¹⁹Division of Pediatric Infectious Diseases, Duke University of Utah, Salt Lake City

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EXECUTIVE SUMMARY

Seasonal influenza A and B virus epidemics are associated with significant morbidity and mortality each year in the United States and worldwide. One study estimated that during 2010–2016, the seasonal incidence of symptomatic influenza among all ages in the United States was approximately 8% and varied from 3% to 11% [1]. Most people recover from uncomplicated influenza, but influenza can cause complications that result in severe illness and death, particularly among very young children, older adults, pregnant and postpartum women within 2 weeks of delivery, people

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Correspondence: T. M. Uyeki, Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA (tuyeki@cdc.gov).

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with neurologic disorders, and people with certain chronic medical conditions including chronic pulmonary, cardiac, and metabolic disease, and those who are immunocompromised [2–8]. During 2010–2018, seasonal influenza epidemics were associated with an estimated 4.3–23 million medical visits, 140 000–960 000 hospitalizations, and 12 000–79 000 respiratory and circulatory deaths each year in the United States [9]. A recent modeling study estimated that 291 243–645 832 seasonal influenza–associated respiratory deaths occur annually worldwide [10].

Use of available diagnostic modalities and proper interpretation of results can accurately identify patients presenting with influenza. Timely diagnosis may decrease unnecessary laboratory testing for other etiologies and use of antibiotics, improve the effectiveness of infection prevention and control measures, and increase appropriate use of antiviral medications [11, 12]. Early treatment with antivirals reduces the duration of symptoms and risk of some complications (bronchitis, otitis media, and pneumonia) and hospitalization, and may decrease mortality among high-risk populations [13–16]. Annual vaccination is the best method for preventing or mitigating the impact of influenza, but in certain situations, chemoprophylaxis with antiviral medications can be used for preexposure or postexposure prevention and can help control outbreaks in certain populations.

These clinical practice guidelines are an update of the guidelines published by the Infectious Diseases Society of America (IDSA) in 2009 [17]. The guidelines consider the care of children, pregnant and postpartum women, and nonpregnant adults and include special considerations for patients who are severely

^aThese clinical practice guidelines are an update of the guidelines published by the Infectious Diseases Society of America (IDSA) in 2009, prior to the 2009 H1N1 influenza pandemic. This document addresses new information regarding diagnostic testing, treatment and chemoprophylaxis with antiviral medications, and issues related to institutional outbreak management for seasonal influenza. It is intended for use by primary care clinicians, obstetricians, emergency medicine providers, hospitalists, laboratorians, and infectious disease specialists, as well as other clinicians managing patients with suspected or laboratory-confirmed influenza. The guidelines consider the care of children and adults, including special populations such as pregnant and postpartum women and immunocompromised patients. It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of a patient's individual circumstances.

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immunocompromised such as hematopoietic stem cell and solid organ transplant recipients. The target audience includes primary care clinicians, obstetricians, emergency medicine providers, hospitalists, and infectious disease specialists. The guidelines may be also useful for occupational health physicians and clinicians working in long-term care facilities. It adds new information on diagnostic testing, use of antivirals, and considerations of when to use antibiotics and when to test for antiviral resistance, and presents evidence on harm associated with routine use of corticosteroids.

The panel followed a process used in the development of previous IDSA guidelines that included a systematic weighting of the strength of recommendations and quality of evidence based upon the US Public Health Service Grading System for ranking recommendations in clinical guidelines as utilized in the previous 2009 guidelines (Table 1) [17]. Summarized below are the recommendations. A detailed description of background, methods, evidence summary, and rationale that support each recommendation, and research needs are included in the full document.

Because prevention and control of influenza is a dynamic field, clinicians should consult the website of the Centers for Disease Control and Prevention (CDC) for the latest information about influenza vaccines, influenza tests, and approved antiviral medications.

DIAGNOSIS

Which Patients Should Be Tested for Influenza?

Recommendations

Outpatients (including emergency department patients).

1. During influenza activity (defined as the circulation of seasonal influenza A and B viruses among persons in the local community):

Table 1. Infectious Diseases Society of America–US Public Health Service Grading System for Ranking Recommendations in Clinical Guidelines

Category and Grade	Definition		
Strength of recommendation			
A	Good evidence to support a recommendation for or against use		
В	Moderate evidence to support a recommendation for or against use		
С	Poor evidence to support a recommendation		
Quality of evidence			
1	Evidence from 1 or more properly randomized controlled trials		
II	Evidence from 1 or more well-designed clinical trials, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments		
111	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees		

Adapted from the Canadian Task Force on the Periodic Health Examination [6].

- Clinicians should test for influenza in high-risk patients, including immunocompromised persons who present with influenza-like illness, pneumonia, or nonspecific respiratory illness (eg, cough without fever) if the testing result will influence clinical management (*A-III*).
- Clinicians should test for influenza in patients who present with acute onset of respiratory symptoms with or without fever, and either exacerbation of chronic medical conditions (eg, asthma, chronic obstructive pulmonary disease [COPD], heart failure) or known complications of influenza (eg, pneumonia) if the testing result will influence clinical management (*A-III*) (see Table 3).
- Clinicians can consider influenza testing for patients not at high risk for influenza complications who present with influenza-like illness, pneumonia, or nonspecific respiratory illness (eg, cough without fever) and who are likely to be discharged home if the results might influence antiviral treatment decisions or reduce use of unnecessary antibiotics, further diagnostic testing, and time in the emergency department, or if the results might influence antiviral treatment or chemoprophylaxis decisions for high-risk household contacts (see recommendations 40–42) (C-III).
- 2. During *low* influenza activity without any link to an influenza outbreak:
 - Clinicians can consider influenza testing in patients with acute onset of respiratory symptoms with or without fever, especially for immunocompromised and high-risk patients (*B-III*).

Hospitalized Patients.

- 3. During influenza activity:
 - Clinicians should test influenza on admission in all patients requiring hospitalization with acute respiratory illness, including pneumonia, with or without fever (*A-II*).
 - Clinicians should test for influenza on admission in all patients with acute worsening of chronic cardiopulmonary disease (eg, COPD, asthma, coronary artery disease, or heart failure), as influenza can be associated with exacerbation of underlying conditions (*A-III*).
 - Clinicians should test for influenza on admission in all patients who are immunocompromised or at high risk of complications and present with acute onset of respiratory symptoms with or without fever, as the manifestations of influenza in such patients are frequently less characteristic than in immunocompetent individuals (*A-III*).
 - Clinicians should test for influenza in all patients who, while hospitalized, develop acute onset of respiratory symptoms, with or without fever, or respiratory distress, without a clear alternative diagnosis (*A-III*).
- 4. During periods of low influenza activity:
 - Clinicians should test for influenza on admission in all patients requiring hospitalization with acute respiratory illness, with or without fever, who have an epidemiological

Table 3.	Clinical	Manifestations	and	Complications	Associated	With
Influenza						

Population	Clinical Manifestation/Complication
Infants and preschool children	Fever without respiratory complications, "sepsis-like syndrome" Otitis media Parotitis Bronchiolitis Croup Reactive airway disease Pneumonia Myocarditis, pericarditis Rhabdomyolysis Febrile seizures Encephalopathy and encephalitis Invasive bacterial coinfection Reye syndrome (with aspirin exposure) Sudden death Exacerbation of chronic disease
School-aged children	Otitis media Parotitis Bronchitis Sinusitis Reactive airway disease Pneumonia Myocarditis, pericarditis Myositis (bilateral gastrocnemius, soleus) Rhabdomyolysis Encephalopathy and encephalitis Invasive bacterial coinfection Reye syndrome (with aspirin use) Toxic shock syndrome Sudden death Exacerbation of chronic disease
Adults	Parotitis Bronchitis Sinusitis Reactive airway disease Pneumonia Myocarditis, pericarditis Myositis Rhabdomyolysis Invasive bacterial coinfection Invasive fungal coinfection (rare) Toxic shock syndrome due to <i>Staphylococcus aureus</i> or <i>Streptococcus pyogenes</i> Precipitation of acute cardiovascular events (eg, cardiac failure, myocardial infarction, heart failure, cerebrovascular accident) Acute kidney injury and acute renal failure (with rhabdomyolysis or multiorgan failure) Encephalopathy and encephalitis Exacerbation of chronic disease
Elderly patients	Pneumonia Invasive bacterial coinfection Myositis Exacerbation of chronic disease
Special groups: pregnant and postpartum women	Dehydration Pneumonia Cardiopulmonary disease Premature labor Fetal loss
Special groups: immu- nocompromised, immunosuppressed All ages	Complications similar to immunocompetent patients, but severe pneumonia and acute respiratory distress syndrome may be more common. Respiratory failure Acute respiratory distress syndrome Multiorgan failure Sepsis Liver inflammation

Adapted from Jani AA, Uyeki TM. Chapter 46. Influenza. In: Emergency management of infectious diseases. 2nd ed. Chin RL, ed. Cambridge, UK: Cambridge University Press, 2018. link to a person diagnosed with influenza, an influenza outbreak or outbreak of acute febrile respiratory illness of uncertain cause, or who recently traveled from an area with known influenza activity (*A-II*).

• Clinicians can consider testing for influenza in patients with acute, febrile respiratory tract illness, especially children and adults who are immunocompromised or at high risk of complications, or if the results might influence antiviral treatment or chemoprophylaxis decisions for high-risk household contacts (see recommendations 41–43) (*B-III*).

What Specimen(s) Should Be Collected When Testing Patients for Influenza?

Recommendations

- 5. Clinicians should collect upper respiratory tract specimens from outpatients for influenza testing as soon after illness onset as possible, preferably within 4 days of symptom onset (*A-II*).
 - Nasopharyngeal specimens should be collected over other upper respiratory tract specimens to increase detection of influenza viruses (*A-II*).
 - If nasopharyngeal specimens are not available, nasal and throat swab specimens should be collected and combined together for influenza testing over single specimens from either site (particularly over throat swabs) to increase detection of influenza viruses (*A*-*II*).
 - Mid-turbinate nasal swab specimens should be collected over throat swab specimens to increase detection of influenza viruses (*A-II*).
 - Flocked swab specimens should be collected over nonflocked swab specimens to improve detection of influenza viruses (*A-II*).
- 6. Clinicians should collect nasopharyngeal (optimally, as for outpatients), mid-turbinate nasal, or combined nasal–throat specimens from hospitalized patients without severe lower respiratory tract disease for influenza testing as soon as possible (*A-II*).
- 7. Clinicians should collect endotracheal aspirate or bronchoalveolar lavage fluid specimens from hospitalized patients with respiratory failure receiving mechanical ventilation, including patients with negative influenza testing results on upper respiratory tract specimens, for influenza testing as soon as possible (*A-II*).
- 8. Clinicians should not collect or routinely test specimens for influenza from nonrespiratory sites such as blood, plasma, serum, cerebrospinal fluid, urine, and stool (*A-III*).
- 9. Clinicians should not collect serum specimens, including single or paired sera, for serological diagnosis of seasonal influenza virus infection for clinical management purposes (*A-III*).

What Test(s) Should Be Used to Diagnose Influenza? *Recommendations*

10. Clinicians should use rapid molecular assays (ie, nucleic acid amplification tests) over rapid influenza diagnostic

tests (RIDTs) in outpatients to improve detection of influenza virus infection (*A-II*) (see Table 6).

- 11. Clinicians should use reverse-transcription polymerase chain reaction (RT-PCR) or other molecular assays over other influenza tests in hospitalized patients to improve detection of influenza virus infection (*A-II*) (see Table 6).
- 12. Clinicians should use multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses, in hospitalized immunocompromised patients (*A-III*).
- 13. Clinicians can consider using multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses, in hospitalized patients who are not immunocompromised if it might influence care (eg, aid in cohorting decisions, reduce testing, or decrease antibiotic use) (*B-III*).
- 14. Clinicians should not use immunofluorescence assays for influenza virus antigen detection in hospitalized patients except when more sensitive molecular assays are not available (*A-II*), and follow-up testing with RT-PCR or other molecular assays should be performed to confirm negative immunofluorescence test results (*A-III*).
- 15. Clinicians should not use RIDTs in hospitalized patients except when more sensitive molecular assays are not available (*A-II*), and follow-up testing with RT-PCR or other molecular assays should be performed to confirm negative RIDT results (*A-II*).
- 16. Clinicians should not use viral culture for initial or primary diagnosis of influenza because results will not be available in a timely manner to inform clinical management (*A-III*), but viral culture can be considered to confirm negative test

results from RIDTs and immunofluorescence assays, such as during an institutional outbreak, and to provide isolates for further characterization (*C-II*).

17. Clinicians should not use serologic testing for diagnosis of influenza because results from a single serum specimen cannot be reliably interpreted, and collection of paired (acute/convalescent) sera 2–3 weeks apart are needed for serological testing (*A-III*).

TREATMENT

Which Patients With Suspected or Confirmed Influenza Should Be Treated With Antivirals?

Recommendations

- 18. Clinicians should start antiviral treatment as soon as possible for adults and children with documented or suspected influenza, irrespective of influenza vaccination history, who meet the following criteria:
 - Persons of any age who are hospitalized with influenza, regardless of illness duration prior to hospitalization (*A-II*).
 - Outpatients of any age with severe or progressive illness, regardless of illness duration (*A-III*).
 - Outpatients who are at high risk of complications from influenza, including those with chronic medical conditions and immunocompromised patients (*A-II*).
 - Children younger than 2 years and adults ≥65 years (A-III).
 - Pregnant women and those within 2 weeks postpartum (A-III).
- 19. Clinicians can consider antiviral treatment for adults and children who are not at high risk of influenza complications,

Testing Category	Method	Influenza Viruses Detected	Distinguishes Influenza A Virus Subtypes	Time to Results	Performance
Rapid molecular assay	Nucleic acid amplification	Influenza A or B viral RNA	No	15–30 minutes	High sensitivity; high specificity
Rapid influenza diagnostic test	Antigen detection	Influenza A or B virus antigens	No	10–15 minutes	Low to moderate sensitivity (higher with analyzer device); high specificity;
Direct and indirect immunofluorescence assays	Antigen detection	Influenza A or B virus antigens	No	1–4 hours	Moderate sensitivity; high specificity
Molecular assays (including RT-PCR)	Nucleic acid amplification	Influenza A or B viral RNA	Yes, if subtype primers are used	1–8 hours	High sensitivity; high specificity
Multiplex molecular assays	Nucleic acid amplification	Influenza A or B viral RNA, other viral or bacterial targets (RNA or DNA)	Yes, if subtype primers are used	1–2 hours	High sensitivity; high specificity
Rapid cell culture (shell vial and cell mixtures)	Virus isolation	Influenza A or B virus	Yes	1–3 days	High sensitivity; high specificity
Viral culture (tissue cell culture)	Virus isolation	Influenza A or B virus	Yes	3–10 days	High sensitivity; high specificity

Table 6. Influenza Diagnostic Tests for Respiratory Specimens

Negative results may not rule out influenza. Respiratory tract specimens should be collected as close to illness onset as possible for testing. Clinicians should consult the manufacturer's package insert for the specific test for the approved respiratory specimen(s). Most US Food and Drug Administration (FDA)–cleared influenza diagnostic tests are approved for upper respiratory tract specimens but not for sputum or lower respiratory tract specimens. Specificities are generally high (>90%) for all tests compared to RT-PCR. FDA-cleared rapid influenza diagnostic tests are Clinical Laboratory Improvement Amendments (CLIA)–waived; most FDA-cleared rapid influenza molecular assays are CLIA-waived, depending on the specimen. Abbreviation: RT-PCR, reverse-transcription polymerase chain reaction.

with documented or suspected influenza, irrespective of influenza vaccination history, who are either:

- Outpatients with illness onset ≤2 days before presentation (*C*-*I*).
- Symptomatic outpatients who are household contacts of persons who are at high risk of developing complications from influenza, particularly those who are severely immunocompromised (*C-III*).
- Symptomatic healthcare providers who care for patients who are at high risk of developing complications from influenza, particularly those who are severely immuno-compromised (*C-III*).

For Patients Who Are Recommended to Receive Antiviral Treatment for Suspected or Confirmed Influenza, Which Antiviral Should Be Prescribed, at What Dosing, and for What Duration?

Recommendations

- 20. Clinicians should start antiviral treatment as soon as possible with a single neuraminidase inhibitor (NAI) (either oral oseltamivir, inhaled zanamivir, or intravenous peramivir) and not use a combination of NAIs (*A-1*).
- 21. Clinicians should not routinely use higher doses of US Food and Drug Administration–approved NAI drugs for the treatment of seasonal influenza (*A-II*).
- 22. Clinicians should treat uncomplicated influenza in otherwise healthy ambulatory patients for 5 days with oral oseltamivir or inhaled zanamivir, or a single dose of intravenous peramivir (*A*-1).
- 23. Clinicians can consider longer duration of antiviral treatment for patients with a documented or suspected immunocompromising condition or patients requiring hospitalization for severe lower respiratory tract disease (especially pneumonia or acute respiratory distress syndrome [ARDS]), as influenza viral replication is often protracted (*C-III*).

In a Patient With Suspected or Confirmed Influenza, When Should Bacterial Coinfection of the Upper or Lower Respiratory Tract Be Considered, Investigated, and Treated?

Recommendations

- 24. Clinicians should investigate and empirically treat bacterial coinfection in patients with suspected or laboratory-confirmed influenza who present initially with severe disease (extensive pneumonia, respiratory failure, hypotension, and fever), in addition to antiviral treatment for influenza (*A*-*II*).
- 25. Clinicians should investigate and empirically treat bacterial coinfection in patients who deteriorate after initial improvement, particularly in those treated with antivirals *(A-III)*.
- 26. Clinicians can consider investigating bacterial coinfection in patients who fail to improve after 3–5 days of antiviral treatment (*C-III*).

If a Patient With Influenza Does Not Demonstrate Clinical Improvement With Antiviral Treatment or Demonstrates Clinical Deterioration During or After Treatment, What Additional Testing and Therapy Should Be Considered?

Recommendation

27. Clinicians should investigate other causes besides influenza virus infection in influenza patients who fail to improve or deteriorate despite antiviral treatment (*A-III*).

When Should Testing Be Done for Infection With an Antiviral-resistant Influenza Virus?

Recommendations

28. Influenza NAI resistance testing can be considered for:

- Patients who develop laboratory-confirmed influenza while on or immediately after NAI chemoprophylaxis (*C-III*).
- Patients with an immunocompromising condition and evidence of persistent influenza viral replication (eg, after 7–10 days, demonstrated by persistently positive RT-PCR or viral culture results) and remain ill during or after NAI treatment (*B-III*).
- Patients with laboratory-confirmed influenza who inadvertently received subtherapeutic NAI dosing (*C-III*).
- Patients with severe influenza who do not improve with NAI treatment and have evidence of persistent influenza viral replication (eg, after 7–10 days) (*C-II*).
- 29. Clinicians should remain informed on current CDC and World Health Organization surveillance data on the frequency and geographic distribution of NAI-resistant influenza viruses during influenza season, and with the latest CDC antiviral treatment recommendations (*A-III*).

Should Adjunctive Therapy Be Administered to Patients With Suspected or Confirmed Influenza?

Recommendations

- 30. Clinicians should not administer corticosteroid adjunctive therapy for the treatment of adults or children with suspected or confirmed seasonal influenza, influenza-associated pneumonia, respiratory failure, or ARDS, unless clinically indicated for other reasons (*A-III*).
- 31. Clinicians should not routinely administer immunomodulation using immunoglobulin preparations such as intravenous immunoglobulin for treatment of adults or children with suspected or confirmed seasonal influenza (*A-III*).

ANTIVIRAL CHEMOPROPHYLAXIS IN COMMUNITY SETTINGS

Who Should Be Considered for Antiviral Chemoprophylaxis to Prevent Influenza in the Absence of Exposure or an Institutional Outbreak (Preexposure Chemoprophylaxis)?

Recommendations

Antiviral drugs should not be used for routine or widespread chemoprophylaxis outside of institutional outbreaks; antiviral chemoprophylaxis can be considered in certain situations:

- 32. Clinicians can consider antiviral chemoprophylaxis for the duration of the influenza season for adults and children aged ≥3 months who are at very high risk of developing complications from influenza and for whom influenza vaccination is contraindicated, unavailable, or expected to have low effectiveness (eg, persons who are severely immuno-compromised) (*C*-*II*).
- 33. Clinicians can consider antiviral chemoprophylaxis for the duration of the influenza season for adults and children aged ≥3 months who have the highest risk of influenza-associated complications, such as recipients of hematopoietic stem cell transplant in the first 6–12 months posttransplant and lung transplant recipients (*B-II*).
- 34. Clinicians can consider short-term antiviral chemoprophylaxis in conjunction with prompt administration of inactivated influenza vaccine for unvaccinated adults and children aged ≥3 months who are at high risk of developing complications from influenza in whom influenza vaccination is expected to be effective (but not yet administered) when influenza activity has been detected in the community (*C-II*).
- 35. Clinicians can consider short-term antiviral chemoprophylaxis for unvaccinated adults, including healthcare personnel, and for children aged ≥3 months who are in close contact with persons at high risk of developing influenza complications during periods of influenza activity when influenza vaccination is contraindicated or unavailable and these high-risk persons are unable to take antiviral chemoprophylaxis (*C-III*).
- 36. Clinicians can consider educating patients and parents of patients to arrange for early empiric initiation of antiviral treatment as an alternative to antiviral chemoprophylaxis *(C-III)*.

Which Antiviral Drugs Should Be Used for Preexposure Chemoprophylaxis for Influenza?

Recommendation

37. Clinicians should use an NAI (oral oseltamivir or inhaled zanamivir) if preexposure chemoprophylaxis for influenza is administered rather than an adamantane antiviral *(A-II)*.

What Is the Duration of Preexposure Antiviral Chemoprophylaxis to Prevent Influenza?

Recommendations

38. Clinicians should administer preexposure antiviral chemoprophylaxis for adults and children aged ≥3 months who are at very high risk of developing complications from influenza (eg, severely immunocompromised persons such as hematopoietic stem cell transplant recipients) for whom influenza vaccination is contraindicated, unavailable, or expected to have low effectiveness, as soon as influenza activity is detected in the community and continued for the duration of community influenza activity (*A-II*).

39. Clinicians should test for influenza and switch to antiviral treatment dosing in persons receiving preexposure antiviral chemoprophylaxis who become symptomatic, preferably with an antiviral drug with a different resistance profile if not contraindicated (*A-II*).

Which Asymptomatic Persons Exposed to Influenza Should Be Considered for Postexposure Antiviral Chemoprophylaxis in a Noninstitutional Setting?

Recommendations

- 40. Clinicians can consider postexposure antiviral chemoprophylaxis for asymptomatic adults and children aged ≥3 months who are at very high risk of developing complications from influenza (eg, severely immunocompromised persons) and for whom influenza vaccination is contraindicated, unavailable, or expected to have low effectiveness, after household exposure to influenza (*C-II*).
- 41. Clinicians can consider postexposure antiviral chemoprophylaxis (in conjunction with influenza vaccination) for adults and children aged \geq 3 months who are unvaccinated and are household contacts of a person at very high risk of complications from influenza (eg, severely immunocompromised persons), after exposure to influenza (*C-II*).
- 42. Clinicians can consider educating patients and arranging for early empiric initiation of antiviral treatment as an alternative to postexposure antiviral chemoprophylaxis (*C-III*).

When Should Postexposure Antiviral Chemoprophylaxis Be Started? *Recommendations*

- 43. If chemoprophylaxis is given, clinicians should administer postexposure antiviral chemoprophylaxis as soon as possible after exposure, ideally no later than 48 hours after exposure (*A-III*).
- 44. Clinicians should not administer once-daily postexposure antiviral chemoprophylaxis if >48 hours has elapsed since exposure. Full-dose empiric antiviral treatment should be initiated as soon as symptoms occur, if treatment is indicated (*A-III*).

How Long Should Postexposure Antiviral Chemoprophylaxis Be Given? Recommendations

- 45. Clinicians should administer postexposure antiviral chemoprophylaxis in a nonoutbreak setting for 7 days after the most recent exposure to a close contact with influenza (*A-III*).
- 46. Clinicians should test for influenza and switch to antiviral treatment dosing in persons receiving postexposure antiviral chemoprophylaxis who become symptomatic, preferably with an antiviral drug with a different resistance profile if not contraindicated (*A-III*).

Which Antiviral Drugs Should Be Used for Postexposure Chemoprophylaxis? Recommendation

47. Clinicians should administer an NAI (inhaled zanamivir or oral oseltamivir) if postexposure chemoprophylaxis for influenza is given, rather than an adamantane antiviral (*A-II*).

INSTITUTIONAL OUTBREAK CONTROL

When Is There Sufficient Evidence of an Influenza Outbreak in a Longterm Care Facility or Hospital to Trigger Implementation of Control Measures Among Exposed Residents or Patients and Healthcare Personnel to Prevent Additional Cases of Influenza?

Recommendations

- 48. Active surveillance for additional cases should be implemented as soon as possible when one healthcare-associated laboratory-confirmed influenza case is identified in a hospital or one case of laboratory-confirmed influenza is identified in a long-term care facility (*A-III*).
- 49. Outbreak control measures should be implemented as soon as possible, including antiviral chemoprophylaxis of residents/patients, and active surveillance for new cases, when 2 cases of healthcare-associated laboratory-confirmed influenza are identified within 72 hours of each other in residents or patients of the same ward or unit (*A-III*).
- 50. Implementation of outbreak control measures can be considered as soon as possible if one or more residents or patients has suspected healthcare-associated influenza and results of influenza molecular testing are not available on the day of specimen collection (*B-III*).

Which Residents/Patients Should Be Considered to Have Influenza and Be Treated With Antivirals During an Influenza Outbreak in a Long-term Care Facility or Hospital?

Recommendations

- 51. When an influenza outbreak has been identified in a longterm care facility or hospital, influenza testing should be done for any resident/patient with one or more acute respiratory symptoms, with or without fever, or any of the following without respiratory symptoms: temperature elevation or reduction, or behavioral change (*A-III*).
- 52. Empiric antiviral treatment should be administered as soon as possible to any resident or patient with suspected influenza during an influenza outbreak without waiting for the results of influenza diagnostic testing (*A-III*).

To Control an Influenza Outbreak in a Long-term Care Facility or Hospital, Should Antiviral Chemoprophylaxis Be Administered to Exposed Residents/Patients?

Recommendation

53. Antiviral chemoprophylaxis should be administered as soon as possible to all exposed residents or patients who do not have suspected or laboratory-confirmed influenza regardless of influenza vaccination history, in addition to implementation of all other recommended influenza outbreak control measures, when an influenza outbreak has been identified in a long-term care facility or hospital (*A-III*).

During an Influenza Outbreak at a Long-term Care Facility, Should Antiviral Chemoprophylaxis Be Administered to Residents Only on Affected Units or to All Residents in the Facility?

Recommendation

54. Antiviral chemoprophylaxis should be administered to residents on outbreak-affected units, in addition to implementing active daily surveillance for new influenza cases throughout the facility (*A-II*).

Which Healthcare Personnel Should Receive Antiviral Chemoprophylaxis During an Institutional Outbreak?

Recommendations

- 55. Clinicians can consider antiviral chemoprophylaxis for unvaccinated staff, including those for whom chemoprophylaxis may be indicated based upon underlying conditions of the staff or their household members (see recommendations 41–43) for the duration of the outbreak (*C-III*).
- 56. Clinicians can consider antiviral chemoprophylaxis for staff who receive inactivated influenza vaccine during an institutional influenza outbreak for 14 days postvaccination (*C-III*).
- 57. Clinicians can consider antiviral chemoprophylaxis for staff regardless of influenza vaccination status to reduce the risk of short staffing in facilities and wards where clinical staff is limited and to reduce staff reluctance to care for patients with suspected influenza (*C-III*).

How Long Should Antiviral Chemoprophylaxis Be Given to Residents During an Influenza Outbreak in a Long-term Care Facility? *Recommendation*

58. Clinicians should administer antiviral chemoprophylaxis for 14 days and continue for at least 7 days after the onset of symptoms in the last case identified during an institutional influenza outbreak (*A-III*).

Notes

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the Standards and Practice Guidelines Committee (SPGC) Chair, the SPGC

liaison to the development panel and the Board of Directors (BOD) liaison

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ment of disclosed relationships for possible COI will be based on the relative

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References

- 1. Tokars JI, Olsen SJ, Reed C. Seasonal incidence of symptomatic influenza in the United States. Clin Infect Dis 2018; 66:1511-18.
- 2. Poehling KA, Edwards KM, Weinberg GA, et al; New Vaccine Surveillance Network. The underrecognized burden of influenza in young children. N Engl J Med 2006; 355:31-40.
- 3. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. JAMA 2010; 303:1517-25.
- 4. Zhou H, Thompson WW, Viboud CG, et al. Hospitalizations associated with influenza and respiratory syncytial virus in the United States, 1993-2008. Clin Infect Dis 2012; 54:1427-36.
- 5. Thompson WW, Moore MR, Weintraub E, et al. Estimating influenza-associated deaths in the United States. Am J Public Health 2009; 99(Suppl 2):S225-30.
- 6. Molinari NA, Ortega-Sanchez IR, Messonnier ML, et al. The annual impact of seasonal influenza in the US: measuring disease burden and costs. Vaccine 2007; 25:5086-96.
- 7. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. JAMA 2004; 292:1333-40.
- 8. Centers for Disease Control and Prevention. Estimates of deaths associated with seasonal influenza-United States, 1976-2007. MMWR Morb Mortal Wkly Rep 2010; 59:1057-62.
- 9. Centers for Disease Control and Prevention. Estimated influenza illnesses, medical visits, hospitalizations, and deaths averted by vaccination in the United States. Available at: https://www.cdc.gov/flu/about/disease/2015-16.htm.
- 10. Iuliano AD, Roguski KM, Chang HH, et al; Global Seasonal Influenza-Associated Mortality Collaborator Network. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet 2018; 391:1285-300.
- 11. Bonner AB, Monroe KW, Talley LI, Klasner AE, Kimberlin DW. Impact of the rapid diagnosis of influenza on physician decision-making and patient management in the pediatric emergency department: results of a randomized, prospective, controlled trial. Pediatrics 2003; 112:363-7.
- 12. Falsey AR, Murata Y, Walsh EE. Impact of rapid diagnosis on management of adults hospitalized with influenza. Arch Intern Med 2007; 167:354-60.
- 13. Hsu J, Santesso N, Mustafa R, et al. Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. Ann Intern Med 2012; 156:512-24.
- 14. Jefferson T, Jones MA, Doshi P, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. Cochrane Database Syst Rev 2014; CD008965.
- 15. Muthuri SG, Myles PR, Venkatesan S, Leonardi-Bee J, Nguyen-Van-Tam JS. Impact of neuraminidase inhibitor treatment on outcomes of public health importance during the 2009-2010 influenza A(H1N1) pandemic: a systematic review and meta-analysis in hospitalized patients. J Infect Dis 2013; 207:553-63.
- 16. Muthuri SG, Venkatesan S, Myles PR, et al; PRIDE Consortium Investigators. 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; 2:395-404.
- 17. Harper SA, Bradley JS, Englund JA, et al; Expert Panel of the Infectious Diseases Society of America. Seasonal influenza in adults and children-diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis 2009; 48:1003-32.