Highlights From Clinical Practice Guidelines by the Infectious Diseases Society of America for the Diagnosis and Treatment of Seasonal Influenza

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Abstract: Seasonal influenza remains a significant cause of morbidity and mortality. The Infectious Diseases Society of America has published an update of the clinical practice guidelines for the diagnosis and treatment of seasonal influenza. The guideline provides new recommendations for management of this infection. Clinicians should use rapid molecular assays for diagnosis. Antiviral therapy of patients with severe or progressive illness should be started regardless of illness duration.

Key Words: influenza, guideline, diagnosis, antiviral

In March, 2019 an update of the Infectious Diseases Society of America (IDSA) clinical guideline for management and prevention of seasonal influenza was published in print form (also available at http://www.idsociety.org). These guidelines are an update of the guidelines published by IDSA in 2009, before the 2009 H1N1 influenza pandemic.

The following are selected recommendations from this new guideline regarding diagnosis and treatment of acute influenza. My comments are in italics.

Diagnosis

• Who to test during influenza activity (defined as the circulation of seasonal influenza A and B viruses among persons in the local community)
• In outpatient settings (including emergency rooms):
  ○ Clinicians should test for influenza in high-risk patients who present with influenza-like illness, pneumonia, or nonspecific respiratory illness (e.g., cough without fever) if the testing result will influence clinical management
  ○ 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 (e.g., asthma, chronic obstructive pulmonary disease [COPD], heart failure) or known complications of influenza (e.g., pneumonia) if the testing result will influence clinical management.
  ○ 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 (e.g., cough without fever) and who are likely to be discharged home (e.g., from emergency department) if the results might influence antiviral treatment decisions or reduce use of unnecessary antibiotics
  • For patients admitted to hospital
    ○ Clinicians should test for influenza on admission in all patients requiring hospitalization with acute respiratory illness, including pneumonia, with or without fever.
    ○ Clinicians should test for influenza on admission in all patients with acute worsening of chronic cardiopulmonary disease (e.g., COPD, asthma, coronary artery disease, or heart failure), as influenza can be associated with exacerbation of underlying conditions.

The guideline emphasizes that during times of influenza activity, a clinical diagnosis is adequate for the decision to initiate antiviral therapy without the need for testing. Abrupt onset of cough and fever provide the most predictive signs and symptoms when influenza viruses are circulating in the community. In such cases, the clinical diagnosis is high enough that testing is not necessary to start antiviral therapy. This is particularly important for patients who are at higher risk of complications such as those with underlying conditions (e.g., COPD, asthma, congestive heart failure). Therapy should not be delayed in this group to await testing results. Influenza is also associated with a variety of different signs and symptoms that may vary by age, underlying chronic disease, complications, host immune status, and influenza virus type or influenza A virus subtype. Other commonly reported symptoms include nasal congestion, fatigue/malaise, headache, poor appetite, sore throat, and myalgia/muscle aches; testing can be helpful in such cases. The guideline also emphasizes that influenza is a common cause of exacerbation of chronic conditions such as COPD or congestive heart failures even without manifestation and treatment with or without testing should be highly considered.

The rationale to test all patients admitted to the hospital for respiratory symptoms includes the identification of infected patients so appropriate infection control precautions are initiated to reduce transmission within the healthcare setting. During influenza season, even in the absence of fever, the presence of new onset or worsening or unexplained cough in a hospitalized patient should prompt testing for influenza.

Antimicrobial Stewardship

A positive test can also be helpful to assist with a decision to withhold or discontinue antibacterial agents. It has been a usual practice to add antibacterial agents to antivirals for patients who are influenza positive and require admission especially if they have a pulmonary infiltrate consistent with pneumonia; the reason is to cover possible concomitant bacterial pathogens. However, in our experience, it has been safe to withhold or...
discontinue antibacterial in patients who test influenza positive if the procalcitonin is low suggesting a low likelihood of concomitant bacterial infection. This promotes antimicrobial stewardship by avoiding or reducing unnecessary antibacterials. The guideline references studies that use of procalcitonin to exclude bacterial co-infection among influenza patients. Procalcitonin-guided treatment reduces antibacterial exposures and related adverse effects.

What Test
- Clinicians should use rapid molecular assays (ie, nucleic acid amplification tests) over rapid influenza diagnostic tests to improve detection of influenza virus infection.

The newer molecular tests are much more accurate (ie, higher sensitivity) at detecting influenza as compared with the older rapid antigen tests. Molecular rapid influenza tests are now available, which are Clinical Laboratory Improvement Amendment waived and provide highly accurate results on user-friendly devices.

Treatment
- 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 before hospitalization.
  - Outpatients of any age with severe or progressive illness, regardless of illness duration.
  - 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 or older (A-III).
  - Pregnant women and those within 2-week postpartum (A-III).
- Clinicians can consider antiviral treatment for adults and children who are not at high risk of influenza complications, with documented or suspected influenza, irrespective of influenza vaccination history, who are either:
  - Outpatients with illness onset 2 days or less before presentation (C-I).
  - Outpatients with symptoms who are household contacts of persons who are at high risk of developing complications from influenza, particularly those who are severely immunocompromised (C-III).

An important recommendation emphasized in this version of the guideline is to treat outpatients with severe or progressive illness and all hospitalized patients regardless of duration of illness. Thus, it is appropriate to treat even if symptoms have been present for more than 48 hours. To withhold antiviral therapy because symptoms have been present greater than 48 hours denies potential benefit to patients, especially those at higher risk of complications. The guideline references evidence that treatment even up to 7 days after the start of symptoms has benefited in selected patients. The guideline is less definitive regarding antiviral therapy for “healthy” patients and recommends to consider in such patients. My preference is to treat non–high-risk patients to potentially reduce duration of illness, reduce transmission to others, and reduce complications.

What Treatment
- 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 NAI.
- Clinicians should not routinely use higher doses of US Food and Drug Administration–approved NAI drugs for the treatment of seasonal influenza.
- 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.
- Clinicians can consider longer duration of antiviral treatment for patients with a documented or suspected immunocompromising condition or patients requiring hospitalization.

The guideline recommends one of the NAI for treatment. Findings of studies suggest no advantage of higher than standard doses. The recommended duration is 5 days; however, longer duration can be considered for higher-risk, higher-severity illness patients and especially those critically ill patients who remain polymerase chain reaction positive at day 5. After the guideline was finalized but before in print publication, beloxavir was approved in United States. This has a different mechanism of action of NAI because it is a polymerase acidic endonuclease inhibitor. Clinical trials have demonstrated the clinical outcome as far as reduction of symptoms is similar to oseltamivir and it is generally well tolerated. However, the median duration of infectious virus detection in upper respiratory tract specimens was significantly shorter for beloxavir compared with oseltamivir (24 vs 72 hours, respectively). This potentially might be important for reduction of transmission. One downside of beloxavir is that 10% of recipients had emergence of viral mutants with reduced drug susceptibility. Further experience will clarify the utility of this agent.

The guideline addresses other issues of seasonal influenza including chemoprophylaxis and institutional outbreaks. The reader is referred to the guideline for an update concerning these issues. Finally, as indicated in the guideline, the best way to prevent influenza and its complications is by immunization.

REFERENCES