Editorial

Seasonal Influenza Guidelines update

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Seasonal Influenza A and B virus infection frequently causes epidemics, that are associated with significant morbidity and mortality. Uncomplicated influenza usually presents with acute onset of respiratory and systemic signs and symptoms, such as rhinorrhea, sore throat, nonproductive cough, weakness with myalgia and arthralgia, gastrointestinal symptoms and fatigue with or without fever. Most common complications include pneumonia, respiratory failure and acute respiratory distress syndrome (ARDS), invasive bacterial coinfection, embolic events, myositis and exacerbation of chronic disease[1-3]. At high risk for development of complications are young children, elderly patients, pregnant and postpartum women, immunocompromised patients, people with chronic medical conditions (e.g. COPD, heart failure, diabetes mellitus) and extremely obese patients (BMI >40)[4]. Recently, the Infectious Diseases Society of America (IDSA) published an evidence based update to the 2009 guidelines on diagnosis, treatment, chemoprophylaxis and institutional outbreak management of seasonal influenza[5].

The rationale for diagnostic testing is to aid decisions regarding the use of antibiotics, continuation of antiviral medications, further diagnostic investigation and stricter infection prevention measures. It is stressed that laboratory confirmation of influenza is not mandatory for antiviral medication prescription, which should be administered as close to the illness onset as possible. Interestingly, history of current seasonal influenza vaccination does not influence the decision for appropriate testing or treatment.

Therefore, during high influenza activity, as defined by a high circulation of influenza A and B viruses in the local community, testing is strongly recommended for high risk outpatients who present with influenza like symptoms or its known complications and for people who present with exacerbation of their chronic medical condition, only if the test results affect clinical management. Conditional recommendation is made for testing only high risk outpatients, during low influenza activity.

During high activity, testing for influenza on admission is warranted for all hospitalized patients with acute febrile or afebrile (especially if they are immunocompromised) respiratory illness or decompensation of their chronic cardiopulmonary disease. Hospitalized patients for other conditions, who develop acute respiratory symptoms, not clearly attributed to another diagnosis, should also be tested for influenza.

Upper respiratory tract specimens and particularly nasopharyngeal specimens, which are preferred over nasal or throat swabs, should be obtained as soon as possible, ideally with 4 days from symptoms onset. Non

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TABLE 1. Antiviral Medications for Influenza Treatment and Chemoprophylaxis in Adults[5-7].

Antiviral Agent	Treatment	Chemoprophylaxis
Oseltamivir (oral)	75mg twice daily	75mg once daily
Zanamivir (inhaled)[1]	10mg twice daily	10mg once daily
Peramivir (intravenous)[2]	600mg IV, single dose	Not recommended
Baloxavir Marboxil (oral)	40mg, single dose (body weight 40-80kg) 80mg, single dose (bodyweight ≥80kg)	Not recommended
Adamantanes[3] (Amantadine and Rimantadine)	Not recommended	Not recommended

[1]Not recommended for use in people with chronic respiratory conditions.
[2]Approved for outpatients. Off label use for hospitalized patients with repeated once daily dosing.
[3]Not active against influenza B viruses, high level of resistance among circulating influenza A viruses.

respiratory tract specimens (e.g. blood, urine) are not appropriate for testing. Lower respiratory tract specimens from intubated patients can also be obtained.

When available, rapid molecular assays (nucleic acid amplification tests) are preferred over the less sensitive rapid influenza diagnostic tests (RIDTs), for outpatients, as they provide their result within 30 minutes. For inpatients, reverse – transcription polymerase chain reaction (RT-PCR) improves influenza detection rate. A multiplex RT-PCR for a panel of respiratory viruses is indicated for immunocompromised hospitalized patients and can be considered for other patients, if it results in reduced further testing and decreased antibiotic use.

Antiviral treatment with a neuraminidase inhibitor (oral oseltamivir, inhaled zanamivir, or intravenous peramivir) should be administered as soon as possible. The optimal treatment duration is 5 days for oseltamivir and zanamivir and a single dose of peramivir, although prolonged administration can be considered for severe cases. Baloxavir marboxil, an oral, cap-dependent endonuclease inhibitor, has recently received an FDA approval for the treatment of acute (symptoms lasting less than 48 hours), uncomplicated influenza in patients older than 12 years. Bacterial coinfection should be appropriately investigated an empirically treated. Use of corticosteroids should be avoided, unless indicated for another reason. In addition, oseltamivir use has been proved to be safe during pregnancy.

Preexposure chemoprophylaxis throughout the period of high influenza activity is indicated for immunocompromised patients at very high risk for complications (e.g. lung transplant recipients), for whom influenza vaccinations is expected to be ineffective, and prompt treatment should be started when they become symptomatic.

Finally, during an institutional influenza outbreak, control measures and antiviral chemoprophylaxis are of paramount importance. Acute respiratory symptoms whether or not accompanied by fever, or even milder symptoms such as behavioral change, should indicate immediate empiric antiviral treatment, prior to the diagnostic test results.

REFERENCES

1. Jani AA, Uyeki TM. Chapter 46. Influenza. In: Emergency management of infectious diseases. 2nd ed. Chin RL, ed. Cambridge, UK: Cambridge University Press, 2018.
2. Dimitroulis I, Katsaras M, Toumbis M. H1N1 infection and embolic events A multifaceted disease. Pneumon 2016; 29:230-35.
3. Dimakakos E, Grapsa D, Vathiotis I, et al; H1N1-Induced Venous Thromboembolic Events? Results of a Single-Institution Case Series, Open Forum Infectious Diseases, Volume 3, Issue 4, 1 October 2016, ofw214, https://doi.org/10.1093/ofid/ofw214.
4. Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2017–18 influenza season. MMWR Recomm Rep 2017; 66:1-20.
5. Uyeki T, Bernstein HH, Bradley SJ, 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 (2018). Clinical Infectious Diseases 2018; pp. 1-47. DOI: 10.1093/cid/ciy866 [Epub ahead of print]
6. Fiore EA, Fry A, Shay D, Gubareva L, Bresee SJ, Uyeki MT; Centers for Disease Control and Prevention (CDC). Recommendations and Reports "Antiviral agents for the treatment and chemoprophylaxis of influenza". Influenza Division, National Center for Immunization and Respiratory Diseases 2011; 60:1-24.
7. Hayden GF, Sugaya N, Hirotsu N, et al, for the Baloxavir Marboxil Investigators Group. Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents. N Engl J Med 2018; 379:913-23. DOI: 10.1056/NEJMoa1716197.