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Preventing and Controlling Influenza with Available Interventions

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Abstract

Influenza activity has been surging in the United States, and there are reports of critical illness and death in young and middle-aged adults. The predominant virus so far this season is influenza A(H1N1)pdm09, the cause of the 2009 H1N1 pandemic. Despite many challenges, there is much that the public, patients, the public health community, and clinicians can do now to reduce influenza's impact.

The spread of influenza A(H1N1)pdm09 virus suggests that despite its ongoing circulation since 2009, population immunity is not sufficiently high and many people remain susceptible. To date, surveillance data provide no evidence of significant antigenic drift in the circulating virus strains, so susceptibility could be due to the presence of a substantial number of previously unin fected and unvaccinated persons or to waning immunity from prior infection.

Although previously healthy persons can have severe illness, certain groups are at increased risk for complications that can result in severe illness: children younger than 2 years of age, elderly people, pregnant women, people with certain chronic conditions (e.g., pulmonary, cardiac [excluding hypertension], renal, hepatic, metabolic, hematologic, neurologic, or neuromuscular conditions, immunosuppression, or morbid obesity), nursing home residents, American Indians, and Alaska Natives.[1] The highest hospitalization rates for seasonal influenza typically occur among people 65 years of age or older, followed by children younger than 5 years of age; influenza-attributable mortality is highest among those 65 years of age or older.[1] During the 2009 H1N1 pandemic, mortality was high among hospitalized middle-aged adults[2]; since influenza A(H1N1)pdm09 virus is prevalent this season, young and middle-aged adults, women who are pregnant or up to 2 weeks post partum, and people with underlying conditions, including morbid obesity, may also be at particularly high risk for severe complications.[2]

Annual influenza vaccination is recommended for everyone 6 months of age or older in the United States.[1] Prevention strategies for infants younger than 6 months of age include vaccinating pregnant women and vaccinating all household members and caregivers ("cocooning"). The effectiveness of influenza vaccine varies depending on several factors,

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including the recipient's age and immune response and the match between circulating virus strains and vaccine strains. In recent years, influenza vaccine has been moderately effective, though less so among elderly persons, and some vaccinated persons may still develop influenza.[1] To date, circulating influenza A(H1N1)pdm09 virus strains are well matched by the H1N1 strains in all available vaccines this season, and unvaccinated persons should be vaccinated as soon as possible.

After an incubation period of 1 to 3 days, most persons with symptomatic influenza virus infection have uncomplicated illness, with sudden onset of fever, cough, headache, sore throat, rhinor-rhea, nasal congestion, and muscle aches, which resolve over 3 to 5 days, though cough and fatigue may persist longer. Children with influenza may have diarrhea and abdominal pain with respiratory symptoms; some adults with influenza A(H1N1)pdm09 virus infection may also have diarrhea.[2] Signs and symptoms can vary depending on age and underlying conditions (e.g., elderly people may not always have a fever) and cannot be easily distinguished clinically from those of other respiratory viral infections. Influenza complications include exacerbation of chronic conditions (e.g., asthma, chronic obstructive pulmonary disease, congestive cardiac failure) and pneumonia, but other severe complications can occur (bacterial coinfection, myocarditis, pericarditis, croup, bronchi olitis, tracheitis, myositis, rhabdomyolysis, encephalopathy, and encephalitis). Influenza virus infection of the respiratory tract can trigger cytokine dysregulation, resulting in acute lung injury and fulminant progression to respiratory failure, acute respiratory distress syndrome, septic shock, acute kidney injury, and multiorgan failure.[2]

Diagnostic testing may inform clinical decisions. Nasopharyngeal swab or aspirate specimens collected within 3 to 4 days after illness begins have the highest yield for detection of influenza viruses, but nasal swab specimens may also be acceptable. Antigen-detection tests (rapid influenza diagnostic tests [RIDTs] and immunofluorescence assays) lack sensitivity as compared with other assays. When there is influenza activity in the community, negative results of antigen testing (especially RIDTs) do not rule out influenza in a symptomatic patient.[2,3] Reverse-transcription–polymerase-chain-reaction (RTPCR) assay is recommended for influenza testing in hospitalized patients. For mechanically ventilated patients, testing an endotracheal aspirate or bronchoalveolar-lavage fluid by RT-PCR assay can yield the diagnosis when influenza virus is not detectable in upper respiratory specimens.[2]

Randomized, controlled trials have established the efficacy of the neuraminidase inhibitors (oral oseltamivir, inhaled zanamivir) as compared with placebo for early treatment (beginning within 48 hours after illness onset) of un-complicated influenza, showing that they reduce fever and illness duration by approximately 1 day.[3] Physicians should encourage high-risk persons with influenza signs and symptoms to seek care promptly for assessment and possible early antiviral treatment. Early oseltamivir treatment in young children can reduce the risk of otitis media, and oseltamivir can reduce the risk of moderate influenza complications requiring antibiotics. Observational studies suggest that for the greatest clinical benefit in hospitalized patients, neuraminidase inhibitor treatment should be started early, but there may be some benefit of oral oseltamivir treatment beginning more than 2 days after illness onset.[4] Empirical antiviral treatment with oral or enteric oseltamivir should

be started as soon as possible in hospitalized patients with suspected influenza, without waiting for the results of RT-PCR assays. For outpatients who are at a higher risk for complications from influenza, neuraminidase inhibitor treatment as soon as possible is also recommended (www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm). The standard duration of anti-viral treatment is 5 days, with longer treatment recommended for critically ill patients with respiratory failure and prolonged viral replication in the lower respiratory tract.[2]

Resistance of influenza A(H1N1)pdm09 viruses to oseltamivir has been documented. Surveillance indicates that the prevalence of oseltamivir-resistant influenza viruses is low to date, but monitoring is ongoing and must continue. Clinicians should know that the condition of critically ill patients with influenza may not improve with oseltamivir treatment and can deteriorate, but such deterioration is usually at tributable not to resistance but to the natural history of acute lung injury and progression of pulmonary damage or other complications (e.g., septic shock, acute renal failure, or ventilator-associated pneumonia). Severely immunosup-pressed patients, however, are at high risk for emergence of oseltamivir resistance during or after oseltamivir treatment due to prolonged viral replication.[2] For severely ill patients with influenza who have strongly suspected or documented oseltamivir resistance or malabsorption, gastric stasis, or gastrointestinal bleeding, intravenous zanamivir, an investigational drug, can be considered; it is available through enrollment in a clinical trial (http://clinicaltrials.gov/show/NCT01231620) or a request to the manufacturer (www.clinicalsupporthd.gsk.com).

For patients with community-acquired pneumonia (CAP) during influenza season, diagnoses of both primary influenza viral pneumonitis and secondary bacterial pneumonia should be considered. Bacterial pathogens most commonly associated with influenza include methicillin-susceptible and methicillin-resistant *Staphylococcus aureus, Streptococcus pneumoniae*, and *Streptococcus pyogenes*.[2,3] Empirical antimicrobial therapy should cover these pathogens, and guidelines for CAP should be followed, with appropriate deescalation of antibiotic treatment based on microbiologic testing results. Systemic glucocorticoid treatment should be avoided in patients with severe or progressive illness because of the risk of prolonged viral replication, opportunistic infections, and poor outcomes.[5] Glucocorticoid treatment can be continued for patients receiving long-term glucocorticoid therapy for other conditions and can be administered for certain complications (refractory shock or suspected adrenal insufficiency). Children younger than 18 years of age should not receive aspirin because of the risk of Reye's syndrome.

Influenza viruses are usually spread from symptomatic persons to susceptible contacts through respiratory droplets. Persons are most contagious during the first 3 to 4 days of illness, and contagion declines with fever resolution. Infants, immunocompromised people, and critically ill patients may have prolonged viral replication. Among previously healthy persons with influenza, staying at home away from contacts, covering coughs and sneezes, and washing hands may help to reduce spread. Infection prevention and control measures are essential for preventing nosocomial influenza. Hospitalized patients with influenza should be isolated or, if necessary, cohorted (grouped together in the same room), and standard and droplet precautions should be implemented (www.cdc.gov/flu/professionals/

infectioncontrol/healthcaresettings.htm). For medical procedures during which a patient may generate an aerosol, a fit-tested N95 respirator is indicated for health care personnel. Influenza prevention should be strengthened throughout the hospital, with active surveillance for nosocomial influenza, restriction of sick health care personnel, and screening of visitors for illness.

We need more effective influenza vaccines and better therapies, especially for severely ill patients. However, there is much we can do with available interventions to reduce the spread and burden of influenza this season — and it's not too late to get vaccinated.

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