

## Management of Influenza in the 2014-2015 Season: Recommendations and Limitations

RONALD H. GOLDSCHMIDT, MD

*San Francisco General Hospital, San Francisco, California*

► See related Practice Guideline on page 584.

The start of influenza season marks a familiar call to action for primary care physicians. The viral strains for the 2014-2015 season are expected to be nearly identical to last year's strains, principally influenza A (H1N1) and influenza B, with some influenza A (H3N2). The well-established tools for managing influenza will again be paramount. These include promoting hand and sneeze/cough hygiene; telephone triage of possible influenza cases; encouraging patients with suspected influenza to remain at home and use symptomatic treatment; maintaining office and emergency department isolation procedures for patients who do come for medical evaluation; and avoiding unnecessary antibacterial agents. This editorial summarizes some of the understanding of the extent of benefits expected from immunization, testing, and antiviral treatment of influenza for the 2014-2015 season.

Vaccination to decrease influenza-like illness among all persons older than six months remains the key public health strategy, although the effectiveness of current vaccines in preventing influenza (47% to 61% over the past three years)<sup>1-3</sup> is less than optimal. There is a lack of study evidence that vaccination prevents hospitalizations, pneumonia, and other serious complications.<sup>4</sup>

The lack of evidence, however, does not prove vaccination is not effective, because many of the studies on which these conclusions are based were not designed to show those benefits. In addition, immunization is less effective among persons 65 years and older, a population at greatest risk of serious complications. Nevertheless, the strategy of broad-scale immunization to decrease total cases and disease burden continues to be a sound one.

Multiple vaccine preparations are described in this issue of *American Family Physician*.<sup>5</sup> Trivalent vaccine preparations identical to the 2013-2014 vaccine, with two influenza A strains (H1N1 and H3N2) and one influenza B strain, will be available. In addition, live attenuated quadrivalent vaccines will have an additional strain of influenza B-like virus. Whether the quadrivalent vaccine will be the better choice will not be apparent

until well into the season, when it is known which strains have emerged. A high-dose trivalent vaccine is available for persons 65 years and older; this preparation generates a stronger antibody response and a small incremental increase in the number of persons obtaining a clinical response, compared with the standard-dose trivalent vaccine.<sup>6</sup> It is not known whether the high-dose trivalent vaccine or the quadrivalent vaccine will be more effective for this population.

The role of rapid testing is limited, because decisions generally are made on clinical, rather than laboratory, grounds. Although there are some circumstances when a positive rapid influenza diagnostic test result will change management, the extraordinarily high false-negative rate makes this test an unnecessary expense in most cases. For patients hospitalized and for those in whom establishing an influenza diagnosis would change clinical management, the reverse-transcriptase polymerase chain reaction test, if available, can provide results within three to eight hours.

The 2014-2015 influenza season will overlap with the international outbreak of the Ebola virus. There will be concerns that patients with signs and symptoms common to many viral illnesses might be caused by Ebola rather than influenza. Patient travel and contact exposure history, not laboratory testing, will be of most help in the early evaluation for Ebola virus. Diagnosis by symptom presentation will offer limited diagnostic specificity, although influenza generally features rhinorrhea and upper respiratory symptoms (rare with the Ebola virus), and Ebola generally features gastrointestinal symptoms (not prominent with influenza). Influenza testing will have limited immediate value.<sup>7</sup> Although a positive influenza reverse-transcriptase polymerase chain reaction test generally confirms the presence of influenza and a positive rapid influenza diagnostic test is generally considered sufficient for diagnosing influenza, ruling in influenza does not necessarily rule out Ebola. Possible or suspected Ebola virus will require isolation and evaluation regardless of influenza laboratory testing. A variety of real-time polymerase chain reaction tests for the Ebola virus are available at designated laboratories.<sup>8</sup> As long as secondary spread of the Ebola virus remains rare in the United States, the differential diagnosis of influenza from Ebola should not be of great concern.

The most striking new finding this year is the understanding of the modest benefits of the widely prescribed neuraminidase inhibitors oral oseltamivir (Tamiflu) ►

and inhaled zanamivir (Relenza). This expanded knowledge was gained from Cochrane reviews published in 2014 that used a new and unique methodology. In addition to the characteristic Cochrane methodology of reviewing published randomized controlled trials, these reviews included a new source of data for the first time: the previously unpublished results of clinical study reports that had been submitted for product approval.<sup>9</sup>

One key finding was that oseltamivir decreases time to first alleviation of symptoms in adults by 16.8 hours (from about 7 days to 6.3 days) and by 29 hours in healthy children (but no decrease in children with asthma).<sup>10</sup> It was concluded that there was no clear evidence of reduction in serious complications such as pneumonia in adults or children, or in hospitalization among adults taking oseltamivir.<sup>10</sup> Zanamivir showed a 14.4-hour decrease in symptoms (6.6 days to 6 days) in adults, no effect among children, and no effect on pneumonia, hospitalization, or death in children.<sup>11</sup>

Most study participants in the reviews of oseltamivir and zanamivir, however, were healthy outpatients without special factors that put them at higher risk of complications. Despite this lack of proven effectiveness of neuraminidase inhibitors in preventing serious complications, a meta-analysis of observational data of adult patients hospitalized with influenza A in 2009 through 2011 reported better outcomes with early neuraminidase inhibitor treatment.<sup>12</sup> The Centers for Disease Control and Prevention recommends initiating neuraminidase inhibitor treatment within the first two days for persons at high risk, including children younger than two years, adults 65 years or older, persons with chronic disease or immunosuppression, pregnant women, patients hospitalized with severe or complicated illness, and persons with severe, complicated, or progressive illness. Neuraminidase inhibitors are not routinely recommended for otherwise healthy outpatients.<sup>13</sup>

The blueprint for managing influenza in the 2014–2015 season is in place. The special challenge will be in adapting to whatever surprises this season might bring.

Address correspondence to Ronald H. Goldschmidt, MD, at [rgoldschmidt@nccc.ucsf.edu](mailto:rgoldschmidt@nccc.ucsf.edu). Reprints are not available from the author.

Author disclosure: No relevant financial affiliations.

## REFERENCES

- Ohmit SE, Thompson MG, Petrie JG, et al. Influenza vaccine effectiveness in the 2011–2012 season: protection against each circulating virus and the effect of prior vaccination on estimates. *Clin Infect Dis*. 2014;58(3):319–327.
- Flannery B, Thaker SN, Clippard J, et al.; Centers for Disease Control and Prevention. Interim estimates of 2013–14 seasonal influenza vaccine effectiveness—United States, February 2014. *MMWR Morb Mortal Wkly Rep*. 2014;63(7):137–142.
- Centers for Disease Control and Prevention. Interim adjusted estimates of seasonal influenza vaccine effectiveness—United States, February 2013. *MMWR Morb Mortal Wkly Rep*. 2013;62(7):119–123.
- Ferroni E, Jefferson T. Influenza. *Clin Evid Handbook*. 2012:280–282.
- Hauk L. ACIP releases updated recommendations on influenza vaccination to include the 2014–2015 season. *Am Fam Physician*. 2014;90(8):584, 586–587.
- DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. *N Engl J Med*. 2014;371(7):635–645.
- Chartrand C, Pai M. How accurate are rapid influenza diagnostic tests? <http://www.medscape.com/viewarticle/766528> [login required]. Accessed November 5, 2014.
- U.S. Food and Drug Administration. Medical devices. Emergency use authorizations. [http://www.fda.gov/medicaldevices/safety/emergency\\_situations/ucm161496.htm](http://www.fda.gov/medicaldevices/safety/emergency_situations/ucm161496.htm). Accessed November 5, 2014.
- Jefferson T, Jones MA, Doshi P, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. *BMJ*. 2009;339:b5106. <http://www.bmj.com/content/339/bmj.b5106>. Accessed July 31, 2014.
- Jefferson T, Jones MA, Doshi P, Spencer EA, Onakpoya I, Heneghan CJ. Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. *BMJ*. 2014;348:g2545. <http://www.bmj.com/content/348/bmj.g2545>. Accessed July 31, 2014.
- Heneghan CJ, Onakpoya I, Thompson MJ, Spencer EA, Jones M, Jefferson T. Zanamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. *BMJ*. 2014;348:g2547. <http://www.bmj.com/content/348/bmj.g2547>. Accessed July 31, 2014.
- Muthuri SG, Venkatesan S, Myles PR, et al. 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(5):395–404.
- Centers for Disease Control and Prevention. Seasonal influenza (flu). Antiviral drugs. <http://www.cdc.gov/flu/professionals/antivirals/index.htm>. Accessed September 11, 2014. ■