THE EFFECTIVE PHYSICIAN

2009 H1N1 and Antivirals

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

The 2009 pandemic influenza A(H1N1) virus (also known as swine flu) was the cause of 98% of influenza cases in the United States this summer. Most people infected with this virus have a self-limited illness, but others require treatment to achieve recovery. To help providers appropriately manage this illness with antiviral medications, the World Health Organization and the Centers for Disease Control and Prevention released interim guidance in late August and early September 2009.

Conclusions

Based on current global data, 2009 H1N1 will likely be the most common influenza virus circulating during this flu season, especially among younger patients.

Approximately 60% of children and 80% of adults hospitalized with 2009 H1N1 flu have a comorbid condition known to increase the risk for severe influenza and/or its complications. As in seasonal influenza, the conditions that increase the risk of complications with this virus are age under 5 years or over 65 years, pregnancy, immunosuppression, and chronic heart (excluding hypertension), lung, kidney, liver, neurologic, metabolic, or muscular disease. Chronic aspirin treatment in patients aged 19 years or less is also a risk factor.

People aged 65 or older have a lower risk of infection with the 2009 H1N1 virus than do younger people. Pandemic H1N1 appears to be transmitted like other influenza viruses; respiratory secretions and bodily fluids of infected persons should thus be considered potentially infectious.

Preliminary data suggest that obese and morbidly obese people may be at increased risk of hospitalization and death caused by 2009 H1N1 influenza, but it is uncertain whether this is due to obesity alone or in association with other complications.

The current circulating H1N1 influenza viruses have continued susceptibility to oseltamivir and zanamivir but are resistant to amantidine and rimantidine. It is important to note that oseltamivir resistance in seasonal H1N1 influenza is common, and that antiviral recommendations may change over the course of this flu season.

Implementation

Antiviral treatment decisions should be based on the clinical suspicion of influenza, the degree of illness, and the risk of complications. The sensitivity of rapid tests ranges from 10% to 70%, and withholding therapy while awaiting results can result in delayed treatment or missed opportunities to treat based on false-negative results. Real-time polymerase chain reaction testing, which has significantly better sensitivity and specificity, should be used only in patients with suspected influenza who require hospitalization.

Antiviral treatment with oseltamivir or zanamivir should be initiated as early as possible in the course of illness for all patients with suspected or confirmed influenza who require hospital admission, and in those who are at high risk for complications.

Pregnant women are at high risk of complications from influenza, and one study estimates a fourfold increased risk for hospitalization in these patients with 2009 H1N1 influenza. Oseltamivir and zanamivir are listed as pregnancy category "C" drugs; however, current data recommend oseltamivir for treatment of suspected or confirmed pandemic H1N1 influenza. The choice of oseltamivir or zanamivir for chemoprophylaxis is not clear.

Patients not at increased risk of complications whose illness is not severe do not routinely require antiviral treatment; however, those who have symptoms of lower respiratory tract illness, dyspnea, hypoxemia, tachypnea, or other warning symptoms of severe illness should be treated promptly with antivirals. All persons with suspected influenza should be counseled on the warning signs for severe or lower respiratory illness and informed of the need for treatment should these develop.

The evidence for effectiveness of the influenza antivirals is based on data in uncomplicated seasonal influenza and is strongest for treatment begun within 48 hours of the onset of illness.

The recommended duration of treatment with influenza antivirals is 5 days, although hospitalized patients with severe infections may benefit from more prolonged treatment and/or higher doses.

Antiviral chemoprophylaxis should be reserved for persons at increased risk of flu-related complications who have close contact with someone likely infected with influenza.

Patients receiving antiviral treatment should be advised that they remain potentially infectious to others for up to 4 days after the start of therapy. Frequent hand washing and good respiratory hygiene remain vital adjuncts to treatment.

Continued surveillance is important to inform clinicians and public health authorities regarding influenza prevalence, strains in communities, and changes in antiviral resistance patterns. Current influenza surveillance data in the United States is updated weekly at www.cdc.gov/flu.

References

CDC H1N1 resources can be found at www.cdc.gov/h1n1flu/guidance. The WHO recommendations are at www.who.int/csr/disease/swineflu/notes/h1n1_use_antivirals_20090820/en/print.html.

DR. GOLDEN (left) is professor of medicine and public health and DR. HOPKINS is program director for the internal medicine/pediatrics combined residency program at the University of Arkansas, Little Rock. Write to Dr. Golden and Dr. Hopkins at our editorial offices or imnews@elsevier.com.

H1N1 Viral Shedding Can Last Past 1 Week

BY MITCHEL L. ZOLER

Some patients with 2009 pandemic influenza A(H1N1) shed live virus a few days longer than commonly occurs with seasonal flu, according to a Canadian study with 100 patients.

The public health implications of the finding aren't clear, Dr. Gaston De Serres said during a press briefing at the annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy.

The results show that it's not enough to isolate people infected with pandemic H1N1 flu for just a couple of days after they become sick or until their fever resolves. People "may be tempted to reduce their time at home [when infected by H1N1], but our results show that would not be wise," said Dr. De Serres, a medical epidemiologist at the National Public Health Institute of Quebec.

The study focused on 43 patients with symptomatic flu who were culture positive for the pandemic virus. In this group, eight (19%) remained culture positive 8 days after their symptom onset. In contrast, all patients with seasonal flu are routinely culture negative a week after symptom onset. "We can say that H1N1 appears to be shed longer [than seasonal flu] but not much longer," said Dr. De Serres, who also is professor of epidemiology at Laval University, Quebec. All 43 H1N1 patients in the study were culture negative 10 days after symptom onset.

Another 57 family members of these cases had concurrent flulike symptoms, but all 57 were culture negative the first time they were tested. Adding these 57 to the first 43 produced a total of 100 patients apparently infected with H1N1, of whom 8 were culture positive a week after their illness began, establishing a minimum 8% rate for the persistence of H1N1 shedding beyond 1 week.

Dr. De Serres cautioned that the findings don't mean that all eight patients remained contagious at day 8. Contagion requires more than just shedding live virus; it also requires transmission of an adequate virus dose. ■

Triple Antiviral Shows Synergy Against H1N1

BY MITCHEL L. ZOLER

A triple antiviral-drug regimen may be more effective than any single drug alone against 2009 pandemic influenza A(H1N1) as well as seasonal flu strains, based on results from preclinical, tissue-culture studies.

A clinical trial has launched to assess the safety and efficacy against all influenza type A infections of a specific combination of oseltamivir, amantadine, and ribavirin, Amy Patick, Ph.D., said during a press briefing at the annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy.

The tissue culture results suggest a synergistic antiviral interaction among the three agents that gives them an efficacy 5- to 20-fold higher than any of the three drugs alone or any combination of two of the drugs, said Dr. Patick, vice president for research at Adamas Pharmaceuticals Inc., in Emeryville, Calif. The results were reported at the meeting by Mark Prichard, Ph.D., a professor of pediatrics at the University of Alabama, Birmingham.

The three-drug combination, called Triple Combination Antiviral Drug (TCAD) therapy, is being developed by Adamas using proprietary formulations and dosages, Dr. Patick said.

Adamas had begun developing TCAD for treating influenza infections before the current H1N1 pandemic began, and the company says it believes the triple-drug combination will also be effective against seasonal strains of influenza A. Patients infected with any type of flu A infection will be enrolled in the two clinical studies, Dr. Patick said in an interview.

One study already underway in the Southern Hemisphere will enroll 250 immunocompromised patients, and will compare the efficacy and safety of TCAD against monotherapy with oseltamivir (Tamiflu). A second study that is planned to start soon in the United States, Canada, and Europe will also examine the efficacy and safety of TCAD in both immunocompromised and immunocompetent patients infected with influenza A. ■