

Weekly Influenza Update

December 23, 2008

CDC ALERT: Antiviral resistance of influenza viruses (see attachment).

Preliminary data from a limited number of states indicate that the prevalence of influenza A (H1N1) virus strains resistant to the antiviral medication oseltamivir is high. Therefore, CDC is issuing interim recommendations for antiviral treatment and chemoprophylaxis of influenza during the 2008-09 influenza season. When influenza A (H1N1) virus infection or exposure is suspected, zanamivir or a combination of oseltamivir and rimantadine are more appropriate options than oseltamivir alone. Local influenza surveillance data and laboratory testing can help with physician decision-making regarding the choice of antiviral agents for their patients.

The 2008-09 influenza vaccine is expected to be effective in preventing or reducing the severity of illness with currently circulating influenza viruses, including oseltamivir-resistant influenza A (H1N1) virus strains. Since influenza activity remains low and is expected to increase in the weeks and months to come, CDC recommends that influenza vaccination efforts continue.

Bottom line for Wisconsin. Across the upper Midwest, 72% of influenza viruses to date have been A(H1N1), 8% A(H3N2) and 21% B. Therefore:

- Oseltamivir alone will be effective in 30% of cases
(cost per Rx = \$119.99)
- Zanamivir alone will be effective in 100% of cases
(cost per Rx = \$72.99)
- Amantadine/Rimantadine alone will be effective in 72% of cases
(cost per rimantadine Rx = \$28.19)
(cost per Amantadine Rx = \$12.89)
- Oseltamivir plus Amantadine/Rimantadine will be effective in 100% of cases
(cost per combined Rx = \$132.79 - \$148.18)

Wisconsin:

Influenza activity appears to be rising in Wisconsin. There have been 11 confirmed influenza detections in Wisconsin [5 A(H1), 3 A(H3), 1 A (not yet subtyped), and 2 B coming from Dane, Kenosha, Milwaukee, Racine, Waukesha, and Wood Counties. The prevalence of influenza-like illness [fever of 100°F or higher and either cough or sore throat] in Wisconsin's primary care patients is an estimated to be 2.3%.

13.1% of last week's primary care patients had acute respiratory infections (ARI).

The prevalence of acute diarrheal illness (ADI) in Wisconsin's primary care patients is at 1.6%.

CLINICAL NOTES:

Prophylaxis

Continue to offer influenza vaccine to anyone interested. Full immunity is achieved within 2 weeks of vaccination.

Vaccinate:

- all high risk individuals
- children from 6 months to 18 years
- adults 50 years and above
- pregnant women
- healthcare workers

Diagnosis

- influenza infections are rare at this time
- PPV of rapid influenza tests is poor, NPV is excellent

Treatment [see attached CDC Health Advisory regarding antiviral resistance] Antivirals need to be started with 48 hours of symptom onset to be effective

- a limited number of viruses have been tested for neuraminidase inhibitor resistance this season
 - 48 out of 50 A(H1) viruses were resistant to Oseltamivir (98%)
 - 0/8 A(H3) and 0/20 B viruses have been resistant to oseltamivir.

- All viruses tested have been sensitive to zanamivir
- a limited number of viruses have been tested for adamantane resistance this season
 - 0/50 A(H1N1) viruses were resistant to adamantanes
 - 8/8 A(H3N2) viruses were resistant to adamantanes (100%)
- Adamantane antivirals are ineffective against influenza B viruses

Other

- Rhinovirus and adenovirus continue to circulate in Wisconsin
- RSV prevalence is slowly increasing
- Rotavirus isolations are at low levels

Across the U.S.:

As of December 13th, 638 positive surveillance cultures have been recorded in the United States. 3.5% of respiratory specimens during week 50 (December 7-13) were positive for influenza.

- 79.3% of isolates have been type A
 - 90.3% of all sub-typed A viruses have been H1N1
 - 9.7% of A viruses have been H3N2
- 20.7% of isolates have been type B

- 6.8% of deaths during week 50 (December 7-13) were due to pneumonia or influenza
[below the epidemic threshold of 7.3%] -One pediatric influenza death has been reported to CDC this season

Global News [from the WHO]: Since 2003, there have been 391 laboratory-confirmed cases of Avian influenza (A-H5N1). The cases been confined to Laos, Viet Nam, Thailand, Indonesia, Cambodia, the People's Republic of China, Turkey, Iraq, Azerbaijan, Egypt, Djibouti Nigeria, Myanmar and Pakistan. There have been 247 associated deaths (case fatality rate= 63.2%). There is enhanced avian influenza surveillance in Wisconsin. Contact Tom Haupt at the Wisconsin Division of Public health (608-266-5326) prior to submitting specimens for fee-exempt testing for patients with influenza-like illness returning from Southeast Asia within 10 days.

VIROLOGY CLINICAL CASE PRESENTATION:

The patient was a 7 year old male who presented for evaluation of ARI. He had symptoms of fever, cough and sore throat. This ARI started about 4 days prior to the visit. He was exposed to similar illness last week at school. He also reported some stomach pain on the day prior to evaluation. He had influenza vaccine earlier this season.

On examination, he was in NAD. He appeared mildly ill, but non-toxic and well hydrated. Vital signs were: BP 102/54; Pulse 84; Temp 99.1 °F (37.3 °C) (Oral). The ear canals and TMs were normal in appearance. The posterior pharynx was mildly erythematous with tonsillar hypertrophy, but no exudates. The neck was S/FROM with mild, non-tender adenopathy. The chest was CTA and heart had RRR. The abdomen was benign.

A rapid strep test was (-); A specimen was obtained for viral surveillance

The assessment was that of an influenza-like illness with cough and use of antipyretics was encouraged along with fluids and prn follow-up.

He returned to clinic on the following day due to the onset of conjunctivitis with bilateral redness, itching and mattering.

The viral multiplex PCR test was (+) for Adenovirus

Comment: Adenovirus is a common cause of ARI in Wisconsin with an incubation time of 2-14 days after exposure through respiratory secretions. Common manifestations include URI symptoms, pharyngitis, tonsillitis, otitis media, and pharyngoconjunctival fever.

Other Observations:

Christmas Truce, 1914. The 1914 Christmas Truce of World War I, on the Western and Eastern Fronts, may well represent the last time that the face of humanity would be seen in what was rapidly becoming the ultimate nightmare of the industrial revolution. The concept of total war would soon replace any outdated notion of chivalry.

The informal truce from hostilities began on Christmas Eve, December 24, 1914, when German troops began decorating the area around their trenches in the region of Ypres, Belgium, for Christmas. They placed candles on trees, and then continued the celebration by singing Christmas carols, most notably Stille Nacht (Silent Night). Scottish troops in the trenches across from them responded by singing English carols.

The two sides continued by shouting Christmas greetings to each other.

Soon there were calls for visits across the "No Man's Land" where small gifts were exchanged - whisky, jam, cigars, chocolate, and the like.

The soldiers exchanged gifts, sometimes addresses, and drank together.

The artillery in the region fell silent that night. The truce also allowed a breathing spell where recently-fallen soldiers could be brought back behind their lines by burial parties. Proper burials took place as soldiers from both sides mourned the dead together and paid their respects.

The truce spread to other areas of the lines, and there are many stories of football matches between the opposing forces. In many sectors, the truce lasted through Christmas night, but in some areas, it continued until New Year's Day.

The truce occurred in spite of opposition at higher levels of the military. British commanders vowed that no such truce would be allowed again. In all of the following years of WWI, artillery bombardments were ordered on Christmas Eve to ensure that there were no further lulls in the combat. Troops were also rotated through various sectors of the front to prevent them from becoming overly familiar with the enemy.

Despite those measures, there were a few friendly encounters between enemy soldiers, but on a much smaller scale than in 1914.

I thank my wife for introducing me to a fitting tribute, provided by folk singer John McCutcheon in his "Christmas in the Trenches." I encourage each of you to take a couple minutes out of your busy lives and reflect on a fine video:

www.youtube.com/watch?v=s9coPzDx6tA

Soon daylight stole upon us and France was France once more
With sad farewells we each prepared to settle back to war
But the question haunted every heart that lived that wondrous night
"Whose family have I fixed within my sights?"

May the peace of this holiday season be with you all...

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This is an official

CDC Health Advisory

Distributed via Health Alert Network

December 19, 2008, 11:50 EST (11:50 AM EST)
CDCHAN-00279-08-12-19-ADV-N

CDC Issues Interim Recommendations for the Use of Influenza Antiviral Medications in the Setting of Oseltamivir Resistance among Circulating Influenza A (H1N1) Viruses,

2008-09 Influenza Season

Although influenza activity is low in the United States to date, preliminary data from a limited number of states indicate that the prevalence of influenza A (H1N1) virus strains resistant to the antiviral medication oseltamivir is high. Therefore, CDC is issuing interim recommendations for antiviral treatment and chemoprophylaxis of influenza during the 2008-09 influenza season. When influenza A (H1N1) virus infection or exposure is suspected, zanamivir or a combination of oseltamivir and rimantadine are more appropriate options than oseltamivir alone. Local influenza surveillance data and laboratory testing can help with physician decision-making regarding the choice of antiviral agents for their patients. The 2008-09 influenza vaccine is expected to be effective in preventing or reducing the severity of illness with currently circulating influenza viruses, including oseltamivir-resistant influenza A (H1N1) virus strains. Since influenza activity remains low and is expected to increase in the weeks and months to come, CDC recommends that influenza vaccination efforts continue.

Background

Influenza A viruses, including two subtypes (H1N1) and (H3N2), and influenza B viruses, currently circulate worldwide, but the prevalence of each can vary among communities and within a single community over the course of an influenza season. In the United States, four prescription antiviral medications (oseltamivir, zanamivir, amantadine and rimantadine) are approved for treatment and chemoprophylaxis of influenza. Since January 2006, the neuraminidase inhibitors (oseltamivir, zanamivir) have been the only recommended influenza antiviral drugs because of widespread resistance to the adamantanes (amantadine, rimantadine) among influenza A (H3N2) virus strains. The neuraminidase inhibitors have activity against influenza A and B viruses while the adamantanes have activity only against influenza A viruses. In 2007-08, a significant increase in the prevalence of oseltamivir resistance was reported among influenza A (H1N1) viruses worldwide. During the 2007-08 influenza season, 10.9% of H1N1 viruses tested in the U.S. were resistant to oseltamivir.

Influenza activity has been low thus far this season in the United States. As of December 19, 2008, a limited number of influenza viruses isolated in the U.S. since October 1 have been available for antiviral resistance testing at CDC. Of the 50 H1N1 viruses tested to date from 12 states, 98% were resistant to oseltamivir, and all were susceptible to zanamivir, amantadine and rimantadine. Preliminary data indicate that oseltamivir-resistant influenza A (H1N1) viruses do not cause different or more severe symptoms compared to oseltamivir sensitive influenza A (H1N1)

viruses. Influenza A (H3N2) and B viruses remain susceptible to oseltamivir. The proportion of influenza A (H1N1) viruses among all influenza A and B viruses that will circulate during the 2008-09 season cannot be predicted, and will likely vary over the course of the season and among communities. Oseltamivir-resistant influenza A (H1N1) viruses are antigenically similar to the influenza A (H1N1) virus strain represented in 2008-09 influenza vaccine, and CDC recommends that influenza vaccination efforts continue as the primary method to prevent influenza.

Oseltamivir resistance among circulating influenza A (H1N1) virus strains presents challenges for the selection of antiviral medications for treatment and chemoprophylaxis of influenza, and provides additional reasons for clinicians to test patients for influenza virus infection and to consult surveillance data when evaluating persons with acute respiratory illnesses during influenza season. These interim guidelines provide options for treatment or chemoprophylaxis of influenza in the United States if oseltamivir-resistant H1N1 viruses are circulating widely in a community or if the prevalence of oseltamivir resistant H1N1 viruses is uncertain.

Interim Recommendations

Persons providing medical care for patients with suspected influenza or persons who are candidates for chemoprophylaxis against influenza should consider the following guidance for assessing and treating patients during the 2008-09 influenza season (see attached Antiviral Guidance Table):

- 1) Review local or state influenza virus surveillance data weekly during influenza season, to determine which types (A or B) and subtypes of influenza A virus (H3N2 or H1N1) are currently circulating in the area. For some communities, surveillance data might not be available or timely enough to provide information useful to clinicians.
- 2) Consider use of influenza tests that can distinguish influenza A from influenza B.
 - a. Patients testing positive for influenza B may be given either oseltamivir or zanamivir (no preference) if treatment is indicated.
 - b. At this time, if a patient tests positive for influenza A, use of zanamivir should be considered if treatment is indicated. Oseltamivir should be used alone only if recent local surveillance data indicate that circulating viruses are likely to be influenza A (H3N2) or influenza B viruses. Combination treatment with oseltamivir and rimantadine is an acceptable alternative, and might be necessary for patients that cannot receive zanamivir, (e.g., patient is <7 years old, has chronic underlying airways disease, or cannot use the zanamivir inhalation device), or zanamivir is unavailable. Amantadine can be substituted for rimantadine if rimantadine is unavailable.
 - c. If a patient tests negative for influenza, consider treatment options based on local influenza activity and clinical impression of the likelihood of influenza. Because rapid antigen tests may have low sensitivity, treatment should still be considered during periods of high influenza activity for persons with respiratory symptoms consistent with influenza who test negative and have no alternative diagnosis. Use of zanamivir should be considered if treatment is indicated. Combination treatment with oseltamivir and rimantadine (substitute amantadine if rimantadine unavailable) is an acceptable alternative. Oseltamivir should be used alone only if recent local surveillance data indicates that circulating viruses are likely to be influenza A(H3N2) or influenza B viruses.
 - d. If available, confirmatory testing with a diagnostic test capable of distinguishing influenza caused by influenza A (H1N1) virus from influenza caused by influenza A (H3N2) or influenza B virus can also be used to guide treatment. When treatment is indicated, influenza A (H3N2) and influenza B virus infections should be treated with oseltamivir or zanamivir (no preference).

Influenza A (H1N1) virus infections should be treated with zanamivir or combination treatment with oseltamivir and rimantadine is an acceptable alternative.

3) Persons who are candidates for chemoprophylaxis (e.g., residents in an assisted living facility during an influenza outbreak, or persons who are at higher risk for influenza-related complications and have had recent household or other close contact with a person with laboratory confirmed influenza) should be provided with medications most likely to be effective against the influenza virus that is the cause of the outbreak, if known. Respiratory specimens from ill persons during institutional outbreaks should be obtained and sent for testing to determine the type and subtype of influenza A viruses associated with the outbreak and to guide antiviral therapy decisions. Persons whose need for chemoprophylaxis is due to potential exposure to a person with laboratory-confirmed influenza A (H3N2) or influenza B should receive oseltamivir or zanamivir (no preference). Zanamivir should be used when persons require chemoprophylaxis due to exposure to influenza A (H1N1) virus. Rimantadine can be used if zanamivir use is contraindicated.

Enhanced surveillance for influenza antiviral resistance is ongoing at CDC in collaboration with local and state health departments. Clinicians should remain alert for additional changes in recommendations that might occur as the 2008--09 influenza season progresses. Oseltamivir resistant influenza A (H1N1) viruses are antigenically similar to the influenza A(H1N1) viruses represented in the vaccine, and vaccination should continue to be considered the primary prevention strategy regardless of oseltamivir sensitivity. Information on antiviral resistance will be updated in weekly surveillance reports (available at <http://www.cdc.gov/flu/weekly/fluactivity.htm>).

For more information on antiviral medications and additional considerations related to antiviral use during the 2008-09 influenza season, visit <http://www.cdc.gov/flu/professionals/antivirals/index.htm>.