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HEALTH ADVISORY

INTERIM RECOMMENDATIONS FOR THE USE OF ANTIVIRAL MEDICATIONS DURING THE 2008-2009 INFLUENZA SEASON

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At present influenza activity in the United States and California is low. However, preliminary testing of a small number of 2008 isolates by the Centers for Disease Control and Prevention (CDC) reveals a high prevalence of oseltamivir resistance in select influenza A strains. These findings prompted changes in the influenza treatment and prophylaxis recommendations. Testing by CDC also reveals that the 2008-9 influenza vaccine contains currently circulating strains. Vaccination remains the best method of preventing disease.

Actions requested of all clinicians

1. Consider the guidance outlined below when assessing and treating symptomatic patients and asymptomatic candidates for chemoprophylaxis.
2. Consider use of **rapid influenza tests** that can distinguish influenza A from influenza B.
3. **Test** symptomatic individuals living in large group or institutional settings in San Francisco.
4. **Report** laboratory-confirmed cases of seasonal influenza that *meet specific criteria** and suspected cases of avian influenza A (H5N1) to SFDPH Disease Control (415-554-2830). *Specific criteria are described in our Oct. 30, 2008 Influenza Health Advisory (www.sfdcdp.org/healthalerts).
5. Encourage and **facilitate** influenza and/or pneumococcal **vaccination**.
6. Implement **respiratory hygiene/cough etiquette** and **hand hygiene** among staff, patients and visitors in all health care settings as described in our Oct. 30, 2008 Flu Health Advisory (www.sfdcdp.org/healthalerts).

This advisory and past advisories are posted on the SFDPH website at: www.sfdcdp.org/healthalerts. Additional reporting and reference materials (including laboratory guidelines, management of cases and outbreaks of influenza in residents of large group or institutional settings and management of suspect avian influenza A (H5N1) cases) are posted at: www.sfdcdp.org/diseasereporting and www.sfdcdp.org/influenzareporting.html.

BACKGROUND

As of December 19, 2008, approximately 600 influenza isolates from the United States (US) have been tested by CDC. Roughly 80% were influenza A, and of those, 39% were influenza A (H1N1), 4% were influenza A (H3N2) and 57% were untyped. Resistance testing was performed on a subset of isolates. The results are shown in Table 1 below and demonstrate resistance to oseltamivir (one of the primary drugs previously recommended for treatment and prophylaxis) in influenza A (H1N1) isolates. However, the influenza A (H1N1) isolates were susceptible to adamantanes (rimantadine and amantadine). Influenza A (H3N2) and influenza B isolates were susceptible to oseltamivir.

Treatment and prophylaxis decisions during the 2008-9 influenza season should be guided by available information on type and subtype of the patient's influenza isolate and/or the circulating type or subtype (or strain) in the community. However, at present, there is little information available on the type and subtype of isolates circulating in San Francisco and California. Until more data are available about viruses that are circulating in our community, San Francisco clinicians should consider following the CDC's antiviral medication recommendations for scenarios where the predominant virus(es) in the community are unknown, outlined in Table 2 below.

Categories of urgency levels

Health Alert: conveys the highest level of importance; warrants immediate action or attention

Health Advisory: provides important information for a specific incident or situation; may not require immediate action

Health Update: provides updated information regarding an incident or situation; unlikely to require immediate action

Table 1. Antiviral Resistance in 2008-2009, US, Influenza Isolates

	Isolates tested	Resistant viruses, number (%)		Isolates tested	Resistant viruses, number (%)
		Oseltamivir	Zanamivir		
Influenza A (H1N1)	50	49 (98%)	0 (0 %)	50	0 (0 %)
Influenza A (H3N2)	8	0 (0%)	0 (0%)	8	8 (100%)
Influenza B	20	0 (0%)	0 (0%)	N/A*	N/A*

*The adamantanes are not effective against influenza B isolates.

ANTIVIRAL TREATMENT AND CHEMOPROPHYLAXIS FOR SEASONAL INFLUENZA

Table 2 below outlines the interim treatment and chemoprophylaxis recommendations which apply to the current situation in San Francisco where the predominant viruses circulating in the community are unknown. If a patient has a positive test for influenza A or a positive test for influenza A+B, zanamivir is the preferred medication. If the patient has a positive test for influenza B, either zanamivir or oseltamivir are preferred medications. If more information becomes available about which influenza viruses are predominant in the San Francisco community, local recommendations will be refined. In some select situations, the subtype of a patient’s influenza isolate might be known; in these cases, for treatment and prophylaxis recommendations, consult SFDPH Disease Control or consult the more comprehensive CDC interim recommendations. For the full text and the complete table of the Dec. 19, 2008, CDC interim recommendations, visit www.cdc.gov/flu/professionals/antivirals.

Table 2. Interim recommendations for the selection of antiviral medications for treatment and prophylaxis of influenza using laboratory test results, United States, 2008-09 season^{§‡}

Predominant virus(es) in community	Results of rapid antigen or other laboratory test	Treatment and Prophylaxis medication(s)	
		Preferred	Alternative
Unknown	Not done or negative, but clinical suspicion for influenza	Zanamivir	Oseltamivir + Rimantadine* °
	Positive for Influenza A	Zanamivir	Oseltamivir + Rimantadine* °
	Positive for Influenza A and B**	Zanamivir	Oseltamivir + Rimantadine* °
	Positive for Influenza B	Oseltamivir or Zanamivir	None

§ Modified from Interim Recommendation Treatment Table in Dec 19, 2008, CDC Health Advisory.

‡ Influenza antiviral medications used for treatment are most beneficial when initiated within the first two days of illness. Clinicians should consult the package insert of each antiviral medication for specific dosing information, approved indications and ages, contraindications/warnings/precautions, and adverse effects.

* The adamantanes are not effective against influenza B isolates.

° Amantadine can be substituted for rimantadine but has increased risk of adverse events. Human data are lacking to support the benefits of combination antiviral treatment of influenza; however, these interim recommendations are intended to assist clinicians treating patients who might be infected with oseltamivir-resistant influenza A (H1N1) virus.

** Positive for Influenza A and B indicates a rapid antigen test that cannot distinguish between influenza A and influenza B viruses

Chemoprophylaxis

Chemoprophylaxis should be considered for residents in an assisted living or long term care facility during an influenza outbreak and for persons who are at higher risk for influenza-related complications and who have had recent household or other close contact with a person with laboratory confirmed influenza. The antiviral medication selection recommendations for chemoprophylaxis are similar to those for treatment. However, it may be possible to tailor therapy if the subtype of the isolate is determined. **Please consult SFDPH Disease Control (415-554-2830) for assistance in managing cases and outbreaks in patients living in large group or institutional settings.** Written guidance specifically addressing management of cases and outbreaks in these settings is available at <http://www.sfcddcp.org/influenzareporting.html>.

LABORATORY: TESTS, SPECIMEN COLLECTION AND SUBMISSION

Some point-of-service rapid antigen tests can distinguish between influenza A and influenza B. If a clinician is considering treatment or chemoprophylaxis for a patient or contacts, **a rapid antigen test that distinguishes between influenza A and B is preferred** as the result would guide which antiviral medication regimen would be most efficacious. Although some clinical labs may be able to type and subtype isolates, results may not be available in time to guide treatment decisions. *For select cases* SFDPH may be able to type and subtype isolates, such as in **residents of large group or institutional settings, severely ill pediatric patients, patients possibly infected with avian influenza A (H5N1)** and others on a case-by-case basis. ALL testing by SFDPH **must** be coordinated through SFDPH Disease Control (415-554-2830). SFDPH can test for influenza A virus, including subtypes H1, H3 and H5N1, and influenza B virus by Polymerase Chain Reaction (PCR) and a panel of other viral respiratory pathogens using culture and antigen detection methods.

Collection of Seasonal Influenza Specimens: In general, nasal washes are preferred; other acceptable specimens include nasopharyngeal swabs and pharyngeal swabs. If submitting swabs, use Dacron with an aluminum or plastic shaft. Cotton or alginate-tipped swabs may compromise performance of lab tests and are not recommended. Specimens are accepted Monday - Friday, 8am to 5pm, and must be accompanied by an SFDPH lab form. Detailed instructions and forms are available on our website: www.sfcddcp.org/influenzareporting.html.

VACCINE FOR SEASONAL INFLUENZA

Preliminary testing indicates that the 2008-9 vaccine contains currently circulating isolates. Influenza vaccine, in both intranasal and injectable form, is still available in San Francisco. Vaccination is the best method to prevent influenza. Please encourage vaccination of your healthcare staff and your patients.

For questions on influenza vaccine in San Francisco, go to: www.sfdph.org/flu or leave a message on the flu information line (415-554-2681).

RESOURCES

General Influenza Information

SFDPH website: <http://www.sfcddcp.org/flu>

CDC website: <http://www.cdc.gov/flu/>

Influenza Surveillance Information

California data: <http://www.cdph.ca.gov/programs/vrddl/Pages/CaliforniaInfluenzaSurveillanceProject.aspx>

National data: <http://www.cdc.gov/flu/weekly/fluactivity.htm>