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HEALTH ALERT–Influenza Activity in Los Angeles County

July 2, 2009

Summary

Influenza activity in Los Angeles County (LAC) is increasing. Clinicians should expect visits from significant numbers of patients with influenza-like illness (ILI)¹ over the upcoming days and weeks. • Currently, most influenza A infections in LAC are due to novel influenza A H1N1 virus. • The symptoms and severity of novel H1N1 infections are similar to seasonal flu. • Although most cases have been mild, additional hospitalizations and deaths are anticipated during the upcoming weeks and months. • Distinguishing between seasonal and novel H1N1 does not alter the appropriate care of patients with influenza-like illness. • Early empiric antiviral treatment is strongly recommended for all hospitalized patients with acute febrile respiratory illness, including hospitalized patients with presumed community acquired pneumonia. • Clinicians should treat patients as they would treat cases of seasonal flu, reserving treatment for those who are seriously ill; clinicians are encouraged to test and prescribe antiviral agents for persons with influenza-like illness who have underlying conditions that increase their risk for severe influenza. • Consider other causes of ILI such as RSV, pertussis, mycoplasma, and bacterial bronchitis and pneumonia, and obtain appropriate diagnostic specimens. • Implement standard and droplet infection control measures for all patients with fever and respiratory symptoms, especially in emergency rooms and other waiting room settings to decrease the spread of infections. • Practice of infection control measures is preferred over use of antiviral chemoprophylaxis of healthcare workers; screen workers for influenza-like illness and remove them from work as quickly as possible to prevent nosocomial transmission. • The LAC Department of Public Health (DPH) requests you to report only hospitalized or fatal influenza cases and possible outbreaks of ILI. • Limited subtyping for novel influenza H1N1 is available; specimens must be pre-approved for testing in the Public Health Laboratory. See below for specific details.

Contents Of Health Alert

- Situational update
- Actions requested of all clinicians, including testing and reporting
- Infection control precautions
- Antiviral treatment and chemoprophylaxis
- Resources

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**

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Changed sections include: situational update, testing and reporting criteria, an explanation of laboratory tests, treatment recommendations, chemoprophylaxis recommendations, infection control recommendations (standard and droplet precautions), and resources available to the public. Check our website for updates, forms, FAQs and useful links:

<http://www.lapublichealth.org/acd/Flu.htm>

Public Health is responsible for providing guidance to healthcare providers and the public in order to reduce disease transmission – prevention, and monitor disease trends – surveillance. The ongoing disease containment goals are to:

- Slow spread, especially within large group residential and institutional settings
- Encourage healthy habits in the general population to reduce transmission.

The ongoing surveillance goals are to:

- Identify severe disease and contribute information to better understand risk factors for complications
- Identify cases in long-term care and large group residential institutions², and
- Identify outbreaks³ of cases.

Situational Update (as of 6/30/09)

Per clinician reports and lab testing requests and results, influenza activity in LAC appears to be increasing. Although the Centers for Disease Control (CDC) reports an overall decrease in influenza activity in the US, multiple jurisdictions are experiencing continued influenza activity and some are experiencing increased activity. We expect to see an increase in cases in LAC including hospitalized cases, deaths and outbreaks during the next few weeks. The dominant strain in LAC during the first two weeks of June was the novel influenza A H1N1 virus. Although our understanding of novel H1N1 is evolving, the symptoms and severity still appear to be similar to seasonal flu. The expected increase in severe cases arises from the increase in total cases.

On June 11, the World Health Organization (WHO) raised the worldwide pandemic alert level to Phase 6, indicating that a global pandemic is underway. Because there is already widespread pandemic H1N1 disease in the US, the WHO declaration does not change what the US, California, and LAC are currently doing. At LAC DPH, surveillance, disease control, and other response and preparedness activities for the fall and winter are continuing.

Actions Requested of All Clinicians (updated 6/30/09)

1. **Suspect** influenza in patients with acute febrile respiratory illness or community acquired pneumonia. Obtain a rapid influenza antigen test or culture, recognizing that rapid tests may be only 60-80% sensitive. For specimen collection instructions see <http://www.lapublichealth.org/acd/Flu.htm> . Consider other causes of ILI such as RSV, pertussis, mycoplasma, adenovirus, and bacterial bronchitis and pneumonia, and obtain appropriate diagnostic specimens.
2. **Treat** patients who have influenza-like illness and are hospitalized and/or at high risk for complications with antiviral medication as soon as possible, ideally within 48 hours after person first develops symptoms. Early empiric antiviral treatment pending diagnosis is strongly recommended for all hospitalized patients with acute febrile respiratory illness, including hospitalized patients with presumed community acquired pneumonia.
3. **Report** to Acute Communicable Disease Control (213-240-7941) any patients with influenza like illness who
 - have died or are severely ill (hospitalized and requiring ICU care), or
 - are part of an outbreak of influenza-like illness.
4. **Submit respiratory specimens only from the following patients** for PCR subtyping by the LAC Public Health Laboratory (specimens not meeting these criteria will NOT be tested):

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Patients with influenza A as determined by a rapid diagnostic test or culture, or ICU patients with acute respiratory distress syndrome regardless of previous influenza test results, who also meet at least one of the following criteria:

- Died or have been hospitalized for >24 hours
- Are part of an outbreak or suspected outbreak, such as in a school or other institutional setting²

5. **Provide chemoprophylaxis** to certain close contacts⁴ of any influenza cases, as described below.
6. **Implement** infection control precautions as described below.
7. **Provide** guidance about home care of persons with influenza. See <http://www.lapublichealth.org/acd/Flu.htm>

Testing for Influenza (6/30/09)

Rapid influenza antigen tests are widely available to clinicians. Some rapid tests can distinguish between influenza A and B virus types, while others cannot. Test accuracy for seasonal flu can be problematic with rapid antigen tests; their sensitivity and specificity ranges from 60-80% compared to viral culture. Sensitivity and specificity in detecting novel influenza A H1N1 virus is unknown although early data suggest performance worse than with seasonal influenza. Thus when evaluating a patient with influenza-like illness, false positive and false negative rapid tests are common. Rapid diagnostic test results can be confirmed with RT-PCR or viral culture. For more information on rapid influenza tests see: <http://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm>.

Some clinical labs use immunofluorescence techniques on respiratory specimens. Although these tests can distinguish between influenza A and B viruses, their sensitivity and specificity in detecting novel influenza A H1N1 virus is also unknown. Distinguishing between seasonal influenza A subtypes H1N1 and H3N2, and the novel influenza A H1N1 virus requires specialized techniques not available at most clinical labs. This specialized testing can be done by the LAC Public Health Laboratory on specimens meeting the criteria outlined above. When testing for novel influenza A H1N1 virus, the Public Health Laboratory first determines by PCR whether the sample is influenza type A. Specimens positive for influenza type A are further tested by a different PCR for the seasonal H1 subtype, the seasonal H3 subtype, and the novel H1 subtype.

Infection Control Precautions for Influenza (Updated 6/30/09)

All healthcare facilities, including private offices, clinics, and hospitals should adopt standard and droplet precautions when caring for all patients with influenza-like illness, defined as temperature >37.8°C or 100°F and new onset of cough or sore throat.[§]

- Persons with influenza-like illness, including employees, should be instructed to stay at home until they have been afebrile without anti-pyretics for at least 24 hours. (Note - this guideline differs from that of the Centers for Disease Control and the California Department of Public Health.)

[§] There are disagreements about the level of protection required to prevent influenza transmission in healthcare settings. Because upper respiratory illnesses are so common, logistics dictate that droplet precautions be applied to protect workers and patients in most situations. In some settings, specifically aerosol generating diagnostic and treatment procedures, use of full airborne protection is indicated. Due to evidence that novel influenza A (H1N1) is comparable to seasonal influenza in its spectrum of illness and transmission pattern and does not appear to be causing unusual mortality compared to seasonal influenza, LAC DPH continues to recommend that infection control measures for novel influenza A (H1N1) be similar to those taken for seasonal influenza, with exceptions noted in this document. LAC DPH guidance in healthcare settings differs from current CDC guidance. However, it is consistent with the most current scientific evidence available and is consistent with that distributed by several other state and local health departments.

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- Place signs at entryway and in all patient areas instructing ALL PERSONS to cover their mouth and nose when they cough or sneeze and to wash hands or use waterless hand cleanser after coughing or sneezing.
- Instruct all persons to cover the mouth/nose with a tissue when coughing or sneezing. Throw tissue in the trash after use. If tissue is not available then use an elbow to block the sneeze rather than hands. Wash hands or use waterless hand sanitizer after contact with respiratory secretions.
- Request all persons with fever or cough to wear a surgical mask while waiting to see the provider.
- Provide masks, tissues and waterless hand cleanser in all patient areas and entryways;
- Isolate patients with influenza-like illness as soon as possible, ideally in a private exam room or at a distance of at least 3 feet from others.
- Staff entering the exam room of a patient with influenza-like illness should wear a surgical mask until an infectious cause of illness is ruled out. They should wash their hands or use waterless hand cleanser before and after interactions with the patient.
- Aerosol-generating procedures should be performed, when feasible, in a negative pressure airborne infection isolation room (AIIR). Disposable fit-tested N95 respirators, eye protection (goggles or face shield), a clean, non-sterile, long-sleeved gown and gloves should be worn by health care personnel performing these procedures. Aerosol-generating procedures include: bronchoscopy, open suctioning of airway secretions, resuscitation involving emergency intubation or cardiac pulmonary resuscitation, and endotracheal intubation.
- Collection of nasopharyngeal specimens for testing, closed suctioning of airway secretions and administration of nebulized medications are not considered aerosol-generating procedures, thus an N95 mask is not required.
- Nebulized treatments for patients with febrile respiratory illness should be provided in a private room with closed door if at all possible or 6 feet apart at a minimum if a private room is not available. If private rooms are limited, reserve the private rooms for patients with febrile respiratory disease. If no private room is available, use a curtain or other barrier between patients who are in the same room when performing nebulized treatments.

Note: **Respiratory Hygiene** and **Cough Etiquette** are now components of Standard Precautions. To limit disease transmission year round, health care providers should implement respiratory hygiene/cough etiquette and hand hygiene procedures in the health care setting and, when possible, in the community.

Antiviral Treatment for Influenza

Because testing is limited, most cases of novel H1N1 will not be formally diagnosed. Distinguishing between seasonal and novel H1N1 does not alter the appropriate care of patients with influenza-like illness. Most novel H1N1 flu cases in the USA have been mild and have not required antiviral treatment. Therefore antiviral treatment is not specifically indicated unless the case is hospitalized OR at high risk for complications of influenza.

Clinicians should treat patients with suspected or confirmed novel H1N1 as they would treat those with seasonal influenza. Early empiric antiviral treatment is strongly recommended for all hospitalized patients with acute febrile respiratory illness, including hospitalized patients with presumed community acquired pneumonia. Antiviral treatment is for 5 days and, if possible, should be initiated within 48 hours of symptom onset.

People at high risk for influenza complications include:

- Children age 4 years and younger, especially children younger than age 2 years
- Adults age 65 and over
- Pregnant women
- Residents of nursing homes and other chronic-care facilities
- Persons younger than 19 years of age and receiving long-term aspirin therapy
- Persons with the following conditions:

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- chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), or metabolic disorders (including diabetes)
- immunosuppression, including that caused by medications or HIV infection
- any condition that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk of aspiration (e.g., cognitive dysfunction, spinal cord injuries, severe seizure disorders, or other neuromuscular disorders)

Clinicians should consider triaging patients over the telephone rather than in the office. Please exercise prudent judgment in prescribing antiviral medicines for patients not meeting the above criteria, such as persons with mild influenza-like illness who are not at high risk for complications of influenza. These patients should be encouraged to stay home until 24 hours after their fever has resolved. Stress respiratory hygiene in the household and inquire about household and other close contacts⁴ who are at high risk for complications of influenza, since they may benefit from chemoprophylaxis.

Antiviral Post-Exposure Chemoprophylaxis for Influenza (6/30/09)

In general, hospitals, other medical facilities, and physicians should manage exposures to cases of ILI, laboratory confirmed cases of influenza, and probable and confirmed novel H1N1 influenza the same as they usually do with seasonal influenza.⁵ Hospitals should review their current policies and recommendations regarding prophylaxis of health care workers for exposures to influenza. The indication for considering post-exposure chemoprophylaxis is based upon close contact⁴ with a person who has laboratory evidence of influenza virus during the infectious period of the case.

Healthcare institutions should rely on appropriate infection control policies and procedures – specifically standard and droplet precautions – to minimize transmission of influenza (and other respiratory pathogens) to patients and employees (see pages 3-4). Do not rely on influenza chemoprophylaxis for preventing influenza in the healthcare setting.

Asymptomatic household and other close contacts⁴ of ill persons with confirmed or suspected influenza who are at high risk for complications of influenza (see page 4) should be offered prophylaxis. During an outbreak in a closed facility such as a nursing home or long-term residential facility, all residents and staff should be offered prophylaxis.

Duration of antiviral chemoprophylaxis post-exposure is 10 days after the last known exposure to a case of influenza. Post-exposure prophylaxis is not necessary if the exposure occurred more than 7 days earlier. Duration of antiviral chemoprophylaxis in outbreak settings is for a minimum of two weeks. If new cases continue to appear, duration may be extended.

Selection of Antiviral Drugs for Seasonal or Novel Influenza (6/30/09)

Selection of antiviral drugs for treatment or chemoprophylaxis of influenza depends upon:

- which strains of influenza are circulating in the community
- strain-specific resistance to antiviral drugs, and
- the ability of laboratory testing to identify the specific strain infecting a patient.

Circulating Strains. The dominant influenza subtype circulating in LAC since late May 2009 is novel influenza A H1N1.

Strain-Specific Resistance. Novel influenza A H1N1 is sensitive to oseltamivir and zanamivir but resistant to the adamantanes. Seasonal H3N2 and influenza B are also sensitive to oseltamivir

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and zanamivir and resistant to the adamantanes. However seasonal H1N1 is resistant to oseltamivir but sensitive to zanamivir and sensitive to the adamantanes; if this strain begins to circulate again, Public Health will revise the following guideline to take into account the possibility of neuraminidase-resistant influenza infections. See Table 1.

Table 1: Antiviral Resistance 2008-2009, US Influenza Isolates

	Zanamivir	Oseltamivir	Adamantanes
Influenza A H1N1 (Novel swine)	S	S	R
Influenza A H1N1 (Seasonal)	S	R	S
Influenza A H3N2 (Seasonal)	S	S	R
Influenza B (Seasonal)	S	S	Not active

S= sensitive, R= resistant

Laboratory Test Results. Distinguishing between seasonal influenza A subtypes H1N1 and H3N2, and novel influenza A H1N1 virus requires specialized techniques not available at most clinical laboratories. Thus clinicians typically must select an antiviral drug based on rapid diagnostic tests or clinical presentation alone.

Recommendations. Table 2 provides recommendations based on results of rapid diagnostic testing and currently circulating influenza strains. All strains are susceptible to zanamivir, therefore, for empirical treatment, it is a practical single-drug option. Also, given that the strains currently circulating in LAC (novel influenza A H1N1, influenza A H3N2 and influenza B) are susceptible to oseltamivir, it is also an appropriate empirical treatment. For critically ill patients, clinicians may consider treating with both a neuraminidase inhibitor (oseltamivir or zanamivir) and an adamantane (amantadine or rimantadine) in case the patient has seasonal H1N1. Circulating influenza strains may change over time; DPH will monitor this and update the medical community as necessary.

Table 2: Recommended antiviral drug(s) based on results of rapid diagnostic tests*

Rapid Diagnostic Test Result	Single Drug Option
Not done or negative, but clinical suspicion for flu	Oseltamivir or Zanamivir
Positive: Influenza A	Oseltamivir or Zanamivir
Positive: Cannot distinguish Influenza A vs. B	Oseltamivir or Zanamivir
Positive: Influenza B	Oseltamivir or Zanamivir

* Modified from CDC Interim Recommendations for the Selection of Antiviral Treatment Using Laboratory Test Results and Viral Surveillance Data, United States (www.cdc.gov/flu/professionals/antivirals/antiviraltable.htm).

Recommended doses of antiviral drugs for novel influenza A H1N1 infection in adults and children age 1 year and older are the same as those recommended for seasonal influenza – see Table 3. Oseltamivir recently received FDA approval for use in children less than 1 year of age under an Emergency Use Authorization.

Adverse Events from Influenza Antiviral Medications (4/29/09)

For information about influenza antiviral medications, including contraindications and adverse effects, go to

- www.cdc.gov/flu/professionals/antivirals/side-effects.htm
- www.cdc.gov/mmwr/preview/mmwrhtml/rr5707a1.htm

Please report adverse events from influenza antivirals to the FDA: www.fda.gov/medwatch

Local Resources

- LAC DPH Influenza Web page: <http://www.lapublichealth.org/acd/Flu.htm>

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- For more urgent issues clinicians may call the LAC DPH Acute Communicable Disease Control 213-240-7941.
- The public can call 211-Infoline for basic information about influenza and to obtain the locations of low-cost medical services.

Table 3: Recommended doses of antiviral drugs for adults and children¹

Agent	Treatment Dose X 5 days	Prophylaxis Dose X 10 days after last known exposure ²
Zanamivir (Adults; Children age > 5 years) ³	10 mg (two 5mg inhalations) BID	10 mg (two 5mg inhalations) QD
Oseltamivir (Adults; Children > 40 kg)	75 mg BID	75 mg QD
Oseltamivir (Children age >12 months) < 15 kg	30 mg BID	30 mg QD
16-23 kg	45 mg BID	45 mg QD
24-40 kg	60 mg BID	60 mg QD
Oseltamivir (Children <12 months) Age 6-11 months	25 mg BID	25 mg QD
Age 3-5 months	20 mg BID	20 mg QD
Age <3 months	12 mg BID	Not recommended ⁴

1. Modified from Table in CDC Interim Guidance on Antiviral Recommendations for Patients with Novel Influenza A (H1N1) Virus Infection and their Close Contacts (www.cdc.gov/h1n1flu/recommendations.htm).

2. Duration of antiviral chemoprophylaxis for outbreaks is for a minimum of two weeks. If new cases continue to appear, duration may be extended.

3. Zanamivir is approved for treatment in children >7 years old and for chemoprophylaxis in children >5 years old

4. Due to limited data in this age group, oseltamivir is not recommended for prophylaxis for children <3 months old unless the situation is judged critical. If deemed critical, the recommended dosage is 12 mg QD x 10 days after last exposure.

Definitions (updated 6/30/09)

¹ **Influenza-like illness** is defined as fever (>37.8°C or 100°F) with either cough or sore throat.

² **Institutions** include facilities with household-like living arrangements (e.g., long-term care facility, dormitory, jail, shelter and group residential home) and facilities where people gather for significant amounts of time (e.g., daycare, school, university, and other types of campuses, etc.)

³ **Outbreak**, for purposes of this document only, is defined as a greater-than-expected proportion of people from the same institution or setting with influenza-like illness who have illness onsets within a short period.

⁴ **Close contact** to an ill person is defined as having cared for or lived with an ill person, or having been in a setting where there was a high likelihood of contact with respiratory droplets of an ill person. Examples of close contact include kissing or embracing, sharing eating or drinking utensils, performing physical examination or medical procedure, or any other contact between persons likely to result in exposure to respiratory droplets. Close contact typically does not include activities such as walking by an infected person or sitting across from a symptomatic patient in a waiting room or office.

⁵ **IDSA Guidelines** - Seasonal Influenza in Adults and Children—Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America. Clinical Infectious Diseases 2009;48:1003–1032. Accessed 7/1/09 at <http://www.journals.uchicago.edu/doi/full/10.1086/598513> .