

CONTAGIOUS COMMENTS

Department of Epidemiology

Influenza 2007-2008:

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What is influenza?

Influenza is a contagious respiratory disease caused by the influenza virus. Influenza is spread from person to person by direct contact, large droplet infection, or items recently contaminated by nasopharyngeal secretions. The incubation period is short (usually 1 to 4 days) with an average of 2 days.

The illness in adults, adolescents, and older children is characterized by an abrupt onset of fever, chills, myalgias, intense headache, and severe malaise accompanied by cough, sore throat, and nasal congestion.

Illness can differ greatly in children. Neonates often present with a sepsis-like picture including lethargy, decreased eating, and mottling. Infants and toddlers tend to present with gastrointestinal symptoms (nausea, vomiting, and diarrhea), fever, anorexia, and various respiratory syndromes. More severe illness can result if either primary influenza pneumonia or secondary bacterial pneumonia occurs.

The two clinically-significant types of influenza virus are designated Type A and Type B. There are also multiple subtypes and strains of influenza A and B based on the nature of the surface hemagglutinin (H) or neuraminidase (N) protein. Infection with one subtype offers little or no protection against virus of other subtypes. Repeated influenza epidemics persist because the type A and type B viruses undergo constant and rapid change due to antigenic drift. Major antigenic shifts occur with influenza type A and are the reasons for pandemics in susceptible populations. Critical to the propagation of an influenza pandemic is a new circulating influenza A strain, a susceptible population and most importantly human to human spread.

The trivalent influenza vaccine is updated annually to include viruses that have been in worldwide circulation. The antigenic characteristics of current strains provide the basis for selecting which strain to include in each year's vaccine. When there is a good match between the strains in the vaccine and circulating viruses, influenza vaccine has been shown to prevent illness in approximately 70–90% of healthy persons less than 65 years of age.

In the United States, two measures are available that can reduce the impact of influenza: immunoprophylaxis with vaccine (inactivated or attenuated, live virus) and chemoprophylaxis or treatment with influenza specific antiviral drugs (i.e. oseltamivir and zanamivir).

New Advisory Committee on Immunization Practices (ACIP) Recommendations for the 2007-2008 Season:

1. Reemphasis of administering 2 doses of vaccine to all children aged 6 months - 8 years if they have not been vaccinated previously at any time with either live, attenuated influenza vaccine (LAIV) or trivalent inactivated influenza vaccine (TIV) (doses separated by >4 weeks), on the basis of accumulating data indicating that 2 doses are required for protection in these children.
2. New recommendation that children aged 6 months-8 years who received only 1 dose in their first year of vaccination receive 2 doses the following year.
For example: If a 5 year old received only one influenza vaccine the 2006-07 season they should receive two doses of influenza vaccine this year separated by 4 weeks.
3. All persons, including school-aged children, who want to reduce the risk of becoming ill with influenza or of transmitting influenza to others should be vaccinated.
4. Emphasis that immunization providers should offer influenza vaccine and schedule immunization clinics throughout the influenza season.
5. Recommendation that health-care administrators consider the level of vaccination coverage among healthcare personnel (HCP) to be one measure of a patient safety quality program and implement policies to encourage HCP vaccination.

For the full 2007-2008 ACIP recommendations for prevention and control of influenza go to:
<http://www.cdc.gov/flu/professionals/acip/index.htm>

Vaccination of Healthcare Workers Needs to Improve:

According to the CDC, a national survey reported a vaccination rate of 42% among healthcare providers (CDC, unpublished data). Mortality due to influenza happens in the extremely young population as well as the elderly population. Dr. Gregory Poland of the Mayo Clinic has published many editorials and papers on the ethical responsibility of healthcare workers receiving influenza vaccine. Many of the oaths that healthcare providers accept in the profession address the "first do no harm" principle. Dr. Poland emphasizes that by not receiving an

influenza vaccination each year, healthcare workers are putting their patients in harm.

Besides getting an influenza vaccination annually, healthcare workers should remember to practice good hand hygiene.

Debunking the Myths:

There are many myths that people use to avoid getting their annual influenza vaccination. For example, many people state that they do not need to receive an influenza vaccination because they don't get sick with influenza. Despite the strength of your immune system you may unknowingly spread influenza to someone else even without having symptoms.

There is the longtime myth that the influenza vaccine causes influenza. This is not true. The viruses in the influenza vaccination are either killed (inactivated) or weakened (attenuated), so you cannot get the flu from an influenza vaccination. The risk of a flu vaccine causing serious harm, or death, is extremely small. However, a vaccine, like any medicine, may rarely cause serious problems, such as severe allergic reactions. Almost all people who get influenza vaccine have no serious problems from it.

2007-2008 Influenza Season Vaccine:

Annual influenza vaccine is recommended to provide optimum immunity against strains that are most likely to circulate in the current season.

This year influenza vaccine will contain antigen of the following strains:

- A/Solomon Islands/3/2006 (H1N1)-like (new for this season).
- A/Wisconsin/67/2005 (H3N2)-like (or the equivalent A/Hiroshima/52/2005)
- B/Malaysia/2506/2004-like (or the equivalent B/Ohio/1/2005 virus)

Four manufacturers distributing approximately 135 million doses of vaccine in the United States should ensure a good supply of vaccine.

All U.S. inactivated influenza vaccine supply consists only of split virus vaccine. Influenza vaccines have not been approved by FDA for use among children aged 0 – 5 months. Because this group of children is at high risk for flu-related hospitalizations, vaccination is recommended for all of their household contacts and out-of-home caregivers.

Influenza Vaccine Dosage by Age Group for the United States, 2007-2008 Season

Trade Name/Manufacturer	Presentation	Age Group	No. of Doses	Route
Fluzone ®/ sanofi pasteur	0.25 ml prefilled syringe	6-35 months	1 or 2*	Intramuscular
	0.5 ml prefilled syringe	≥ 36 months	1 or 2*	Intramuscular
	0.5 ml vial	≥ 36 mo.	1 or 2*	Intramuscular
	5.0 ml multidose vial	≥ 6 months	1 or 2*	Intramuscular
Fluvirin™/ Novartis	5.0 ml multidose vial	≥ 4 years	1 or 2*	Intramuscular
Fluarix™/ GlaxoSmithKline	0.5 ml prefilled syringe	≥ 18 years	1	Intramuscular
FluLaval™/ GlaxoSmithKline	5.0 ml multidose vial	≥ 18 years	1	Intramuscular
FluMist™/ Medimmune	0.2 ml sprayer	2-49 years	1 or 2**	Intranasal

* Two doses administered at least 4 weeks apart are recommended for children aged 6 months–8 years who are receiving TIV for the first time and those who only received 1 dose in their first year of vaccination should receive 2 doses in the following year.
 **Two doses administered at least 4 weeks apart are recommended for children aged 2–8 years who are receiving LAIV for the first time, and those who received only 1 dose in their first year of vaccination should receive 2 doses in the following year.

What about the preservative vs. preservative-free vaccine?

A few years ago, the AAP made recommendations to decrease the exposure to thimerosal in young children (particularly less than 6 months of age) because of potential concern regarding excess mercury exposure. The only injectable vaccine that is preservative-free is Fluzone® by sanofi pasteur and it is intended for use in young children 6 to 35 months of age. TCH will have a supply of preservative-free vaccine this year. In addition, FluMist™ (LAIV) does not contain any preservative.

What about intranasal flu vaccine?

FluMist™ is approved for use in persons aged 2–49 years of age. It should not be given to pregnant women. Flu Mist™ is an intranasally administered, trivalent, cold-adapted, live attenuated influenza vaccine (LAIV). The attenuated (weakened) virus is adapted to growing at colder temperatures, which means that the live virus vaccine grows in the cooler upper respiratory tract and stimulates immunity without causing disease in the warmer lungs. Children aged 2–8 years who have never received influenza vaccine need two doses of LAIV (4 weeks apart).

With the recipient in the upright position, approximately 0.1mL is sprayed into each nostril.

For the 2007-2008 season, the FluMist™ has been reformulated to a refrigerator stable product and no longer should be stored frozen. The new formulation of FluMist™ is shipped to end users at 35° F - 46° F (2° - 8°C). FluMist™ should be stored at 35° F - 46° F (2° - 8°C) upon receipt and can remain at that temperature until the expiration date is reached.

TCH will have some FluMist™ available for eligible patients and staff. FluMist is not recommended for TCH staff that have close contact with severely immunosuppressed patients. Specifically, FluMist™ is not recommended for healthcare workers caring for patients in BMT, Hematology/Oncology, and solid organ transplant services. If a healthcare worker receives LAIV, the healthcare worker should refrain from contact with these severely immunosuppressed patients for 7 days after vaccine receipt.

Who should be vaccinated?

We recommend that the following people be vaccinated at the beginning of the 2007-2008 influenza season:

- All healthcare workers in hospitals and outpatient / community / homecare settings because they can transmit influenza to vulnerable patients, residents, etc.
- All children ages 6 – 59 months and their household contacts and out of home caregivers.
- All children and adults who have chronic disorders of the pulmonary or cardiovascular systems, including children with asthma.
- All children and adults who require regular medical visits due to chronic metabolic diseases, renal dysfunction, hemoglobinopathies, or immunosuppression, including persons with HIV.
- Children and teens (6 months – 18 years) who are receiving long-term aspirin therapy and might be at risk for Reyes syndrome after influenza infection.
- Household members (including siblings and out-of-home care providers) of persons in high-risk groups.
- Women who will be pregnant during the influenza season.
- Persons 50 years or older.
- Residents and employees of nursing homes and other chronic care facilities housing persons of age with chronic medical problems.
- Anyone wanting to decrease their risk of acquiring influenza infection this year.

Procedure to Provide Influenza Vaccine to Parents and Siblings of Patients (Household Contacts):

A limited amount of free influenza vaccine is available to household members of TCH inpatients and outpatients. Check Planet TCH under “Quick Links” for information on how to obtain vaccine or check if your clinical area has a vaccine book for this.

What are the contraindications to vaccination?

For TIV:

- Hives or severe anaphylactic reaction to eggs, egg proteins, thimerosal or with life-threatening reactions to previous influenza vaccinations. Most patients do not develop reactions even when patch or intradermal tests for thimerosal indicate

hypersensitivity. When reported, hypersensitivity to thimerosal has usually consisted of local, delayed-type hypersensitivity reactions.

For LAIV:

- Hives or severe anaphylactic reaction to eggs, egg proteins, gentamicin, gelatin, or arginine or with life-threatening reactions to previous influenza vaccinations.
- Children or adolescents on long-term aspirin therapy.

What are the side effects of influenza vaccine?

Inactivated injectable influenza vaccine contains only non-infectious (inactivated) viruses; it therefore cannot cause influenza. The most frequent side effect of vaccination reported by less than one third of vaccines is soreness at the vaccination site that lasts for up to 2 days. Fever, malaise, myalgia, and other systemic symptoms occur infrequently and most often affect persons who have had no prior exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin six to twelve hours after the vaccination and may persist for 1 to 2 days. The most common side effects associated with LAIV include nasal congestion, scratchy throat and cough. Symptomatic relief can be obtained by using non-aspirin containing analgesics. **Aspirin should not be used due to the association of Reyes Syndrome with wild-type influenza infection in children.**

Immediate (presumably allergic) reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) occur rarely and probably result from hypersensitivity to some vaccine component – a majority of which are most likely related to residual egg protein.

Can influenza vaccine be administered with other childhood vaccines?

Children may receive influenza vaccine at the same time they receive other routine vaccinations.

Can pregnant women be immunized?

Because of the increased risk for influenza-related complications, it is recommended that women who will be pregnant during the influenza season should be vaccinated with inactivated influenza vaccine. Vaccination can occur in any trimester. One study of influenza vaccination of more than 2,000 pregnant women demonstrated no adverse fetal effects associated with influenza vaccine.

TCH Employee Health will administer the vaccine to pregnant staff. Reminder: LAIV is contraindicated for pregnant women.

Note: Lactating Mothers. “Inactivated influenza vaccine is safe for mothers who are breastfeeding and their infants. Because excretion of LAIV in human milk is unknown and because of the possibility of shedding vaccine virus given the close proximity of a nursing mother and her infant, caution should be exercised if LAIV is administered to nursing mothers. Breastfeeding does not adversely affect the immune response and is not a contraindication for vaccination”.

What is the appropriate isolation for influenza?

For children hospitalized with symptomatic or confirmed influenza, Droplet Precautions (mask, gown, and gloves) are recommended for the duration of the illness.

What about Avian Influenza?

The current seasonal influenza vaccine probably does not provide protection against the H5N1 avian influenza circulating in birds elsewhere in the world. While there has been some human-to-human spread of H5N1, it has been limited, inefficient and not sustained. No human illness caused by H5N1 avian influenza has been seen in this country to date. Key components to prevention of influenza infection still hold for prevention of "bird flu": good hand hygiene, respiratory etiquette (cover your mouth and nose when you cough or sneeze), droplet precautions for patients in healthcare settings, influenza vaccination and laboratory based viral surveillance. Regularly updated information can be obtained on the CDC website <http://www.cdc.gov/flu/avian/> and <http://pandemicflu.gov/>.



Laboratory Testing

How does TCH test for influenza?

There will be two laboratory tests available at TCH this season for influenza virus detection:

1. Respiratory virus DFA and Culture:

The DFA (or direct fluorescent antibody assay) is performed by staining specimens with virus-specific monoclonal antibodies labeled with fluorescent compounds. These substances cause infected cells to glow under the microscope when viral proteins are inside. Sensitivity of the DFA is about 85% for influenza A and 75% for influenza B compared to culture. Two helpful features of DFA are that specimen adequacy can be determined, and 8 viruses (RSV, parainfluenza, influenza A, influenza B, adenovirus, and human metapneumovirus) can be detected simultaneously. This latter feature is especially helpful because symptoms of influenza virus in children frequently resemble infections caused by other viruses.

The DFA is performed at least twice a day on weekdays, and once a day on weekends, year-round. It can be ordered one of three ways:

- As a stand-alone test for ED or short-stay hospitalized patients who will benefit only from rapid results;
- With backup culture if the DFA is negative for admitted patients who can benefit from more complete and sensitive results;
- With concurrent culture for very high risk patients (e.g., individuals with HIV or organ transplant) who need all viruses detected.

Culture detects several viruses not revealed by DFA, including cytomegalovirus (CMV), rhinovirus, enterovirus. It also detects influenza virus in specimens with an insufficient quantity of cells for DFA, or in specimens that contain low levels of influenza antigen undetectable by DFA.

2. Influenza A+B IA:

A rapid, influenza immunoassay (IA) is available during "flu season." This test is most useful to screen suspected "flu" cases seen in the ED late afternoons, evenings, and nights when the respiratory virus DFA is not available. Unfortunately the IA can miss 10-20% of pediatric DFA-positive influenza cases.

Order the flu IA when a rapid diagnosis of influenza A or influenza B will impact patient care, e.g., when decisions about administering antiviral medications or withholding antibiotics are being made. If the IA is negative and a more comprehensive and complete answer is needed, respiratory virus DFA can be performed on the same sample the following day. Results for the Flu IA are available in less than an hour any time of the day or night.



Treatment and Chemoprophylaxis

1. Neuraminidase Inhibitors:

Zanamivir (Relenza®) and oseltamivir (Tamiflu®) are approved for the chemoprophylaxis and treatment of influenza A and B. Treatment has been shown to decrease the duration of flu-related symptoms by 1 to 1.5 days. Oseltamivir has been approved for chemoprophylaxis and treatment of patients older than one year old. Zanamivir has been approved for treatment in patients 7 years and older and chemoprophylaxis of patients age 5 years and older.

Limitations of Both Medications:

- Must be administered within 48 hours of onset of symptoms.
- Not shown to prevent disease transmission.
- Have not been adequately studied in patients with serious health conditions, with renal or hepatic impairment.

a. Zanamivir (Relenza®):

Available as a dry powder administered via oral inhalation with a plastic device. The dose is two breath-activated inhalations (one 5mg blister per inhalation = 10mg) BID for 5 days.

Note: The product will be packaged in a foil pack (Roto Disk) containing 4 blisters of the drug. Five Roto Disks will be packaged in a tube (equals entire treatment course). The package also includes one Diskhaler device.

Contraindications / Precautions:

Zanamivir is not recommended for use in patients with underlying airway disease including asthma or COPD

because of a lack of safety and efficacy data in these patients. **Serious adverse events including bronchospasm and decline in lung function have been reported with zanamivir use, most commonly in patients with underlying airway disease.** (If zanamivir is used in patients with underlying airway disease, they should be instructed to have a fast-acting bronchodilator available.)

b. Oseltamivir (Tamiflu®):

Given twice daily for 5 days, with dose adjustments required in renal impairment. As with zanamivir, oseltamivir therapy should be initiated within 48 hours of onset of influenza symptoms.

Pediatric Dosing:

1 – 12 Years: 2mg/Kg/dose bid x 5 days (max. dose = 75mg).

13 Years & Older: 75mg bid x 5 days.

Additionally, oseltamivir has shown some benefit as a prophylactic agent for seasonal influenza when given once daily for 6 weeks, although the cost may be prohibitive. CDPHE strongly discourages “personal stockpiling” of Tamiflu (<http://www.cdphe.state.co.us/dc/Influenza/avian/index.html>).

2. Amantidine

A second class of influenza antiviral medications known as the adamantanes (amantadine and rimantadine) are licensed in the U.S. for the treatment and prevention of influenza. However a high proportion of circulating influenza viruses in the U.S. in recent years have been resistant to the adamantanes, so CDC now recommends that neither amantadine nor rimantadine be used for the treatment or chemoprophylaxis of influenza in the U.S. during the upcoming influenza season.

References:

CDC: Prevention and Control of Influenza: Recommendation of the Advisory Committee on Immunization Practices (ACIP). **July 13, 2007/ 56(RR06) p1-54**
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5606a1.htm>

Poland, GA, Tosh, P, Jacobsen, RM. Requiring Influenza Vaccination for Health Care Workers: seven truths we must accept. *Vaccine* : 23 (2005)2251-2255.

Bug Watch

Provides up-to-date weekly information on currently circulating respiratory and enteric viruses detected by the TCH Laboratory and *B. pertussis* detected in individuals under 20 years of age statewide. Current editions are posted on the TCH Internet
<http://www.thechildrenshospital.org/pro/publications/bug.pdf>
and/or sent by broadcast FAX. Contact Carolyn Brock by e-mail (brock.carolyn@tchden.org) or phone (720-777-6412) to begin receiving your personal copy.



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