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 hemaglutinin (H) or neuraminidase (N) protein. Infection with one subtype offers little or no protection against viruses 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 2008-09 Season:

The 2008 recommendations include five principal changes or updates:

• Beginning with the 2008-09 influenza seasons, annual vaccination of all children aged 5-18 years is recommended.

• Annual vaccination of all children aged 6 months-4 years (59 months) and older children should be a focus because they are at increased risk for complications from influenza.

• Either trivalent inactivated influenza vaccine (TIV) or live attenuated influenza vaccine (LAIV) can be used when vaccinating healthy persons aged 2-49 years. Children aged 6 months – 8 years should receive 2 doses of vaccine separated by 4 or more weeks if they have not been vaccinated previously at any time to ensure a good immune response.

• LAIV is FDA approved for persons 2-49 years of age. LAIV should not be administered to children aged < 5 years with possible reactive airways disease, such as those who have had recurrent wheezing or a recent wheezing episode.

For the full 2008-09 ACIP recommendations for prevention and control of influenza go to:
http://www.cdc.gov/flu/professionals/acip/index.htm

2008-09 Influenza Season Vaccine:
Annual influenza vaccine is recommended to provide optimum immunity against strains that are most likely to circulate in the current season. Due to the drift that was seen in the vaccine strains in the 2007-08 season, this year’s formulation of influenza vaccine contains three all new strains.

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

• A/Brisbane/59/2007 (H1N1)-like
• A/Brisbane/10/2007 (H3N2)-like
• B/Florida/4/2006-like
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.

TCH will have some FluMist™ available for eligible patients and staff. FluMist is not recommended for TCH staff who 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 2008-09 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 months – 18 years and their household contacts and out of home caregivers
- 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.

The Children’s Hospital Influenza Vaccination Policy for All Staff:

It is recommended that all TCH staff receive influenza immunizations to maintain a healthy safe hospital environment and healthy staff to care for patients and families. New Joint Commission requirements require extensive monitoring of our influenza vaccination program. Employees who receive influenza vaccine elsewhere are required to provide that information to Employee Health and the Department of Epidemiology. Also, for those who decline influenza vaccination, they will be given a declination form to document why they are not receiving an influenza vaccination. If an employee has a medical contraindication to influenza vaccination, there will be a separate form for them to sign.

### Influenza Vaccine Dosage by Age Group for the United States, 2008-09 Season

<table>
<thead>
<tr>
<th>Trade Name/ Manufacturer</th>
<th>Presentation</th>
<th>Age Group</th>
<th>No. of Doses</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluzone ®/ sanofi pasteur</td>
<td>0.25 mL prefilled syringe</td>
<td>6-35 months</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>0.5 mL prefilled syringe</td>
<td>≥ 36 months</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>0.5 mL vial</td>
<td>≥ 36 mo.</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥ 6 months</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Fluvirin ™/ Novartis</td>
<td>5.0 mL multidose vial</td>
<td>≥ 4 years</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>0.5 mL pre-filled syringe</td>
<td>≥ 4 years</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Fluax™/ GlaxoSmithKline</td>
<td>0.5 mL prefilled syringe</td>
<td>≥ 18 years</td>
<td>1</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>FluMist™/ Medimmune</td>
<td>0.2 mL sprayer</td>
<td>2-49 years</td>
<td>1 or 2 **</td>
<td>Intranasal</td>
</tr>
</tbody>
</table>

* 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?

Many 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. All prefilled syringe influenza vaccine is free of preservative. TCH will have a supply of preservative-free vaccine this year. In addition, intranasal 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...
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.

Can influenza vaccine be administered with other childhood vaccines?
Children may receive influenza vaccine at the same time they receive other routine vaccinations.

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 in conjunction with LAIV administration 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 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.

Laboratory Testing

How does TCH test for influenza?
There will be two types of tests available at TCH this season for influenza virus detection:

1. Respiratory virus DFA and Comprehensive Virus Detection:
The DFA (or direct fluorescent antigen assay) is performed by staining specimens with virus-specific monoclonal antibodies labeled with fluorescent compounds which cause infected cells to glow under the microscope. Sensitivity of the DFA is about 85% for influenza A and 75% for influenza B compared to culture. In addition to identifying influenza virus, our DFA also detects RSV, parainfluenza, adenovirus, and human metapneumovirus which can cause influenza-like symptoms in children as well.

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, clinic, or short-stay hospitalized patients who will benefit only from same or next day results;
• With backup comprehensive virus detection* if the DFA is negative. This combination is for admitted patients (e.g. in the ICU) who may benefit from detection of the major viral pathogen, even if results are available days or weeks after specimen collection.

*Laboratory Processing Time: 24 to 48 hours

VOLUME XXIII NUMBER 3 October 2008 Page 3
• With concurrent comprehensive virus detection*. This workup is for high-risk patients (e.g., immunocompromised individuals) who may benefit from detection of single or multiple viral infections, regardless of result turnaround time.

*Comprehensive virus detection includes respiratory virus PCR (RVP) and culture. RVP is more sensitive than DFA and can detect viruses in specimens with insufficient cells for DFA. It also detects the rhinovirus/enterovirus group and provides the subtype (e.g., H1 or H3) of influenza A. Culture is included to detect cytomegalovirus and viruses occasionally missed by RVP (e.g., some adenovirus types). RVP results are available in 2-3 days; negative cultures are finalized after 2 weeks.

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 and clinics. 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 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. During the 2007-08 influenza season, increased resistance to oseltamivir was identified among influenza A (H1N1) in the United States and some other countries. This finding has not lead to a change in the recommendations for influenza treatment since other influenza virus strains remain sensitive.

Limitations of Both Medications:
• Must be administered within 48 hours of onset of symptoms.
• Not shown to prevent disease transmission.

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.

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.


2. Amantidine
A second class of influenza antiviral medications known as the adamantanes (amantadine and rimantadine) is 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) August 8, 2008 / 57(RR07) p1-60 http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5707a1.htm
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 less than 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.