The Children's Hospital

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CONTAGIOUS COMMENTS
Department of Epidemiology

Influenza 2005 – 2006: Vaccinate Children!

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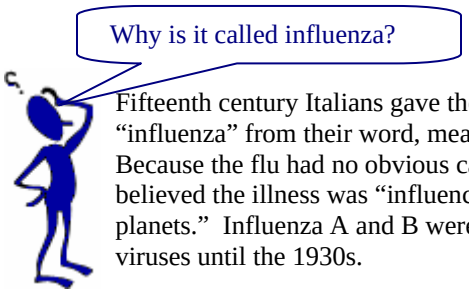
Influenza, the Birds and You:

Influenza loves the media spotlight…from the early deadly season of 2003-04 to the vaccine shortages of last season. This year it seems that seasonal influenza is eclipsed by the threat of the bird flu and concerns about a pandemic.



Fifteenth century Italians gave the disease its name, "influenza" from their word, meaning "to influence." Because the flu had no obvious cause, the people believed the illness was "influenced by the stars and planets." Influenza A and B were not identified as viruses until the 1930s.

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 nasal pharyngeal secretions. The incubation period is short (usually 1 to 4 days) with an average of 2 days.

The illness in adults, older children and adolescents 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.

Influenza virus subtypes are based on their surface hemaglutinin (H) or neuraminidase (N) proteins. 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 influenza vaccine is updated annually to include viruses that have been in the 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 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 live virus) and chemoprophylaxis or treatment with influenza specific antiviral drugs (i.e., amantadine, rimantadine, oseltamivir, and zanamivir).

Vaccination of persons at risk before each annual influenza season is currently the most effective measure for reducing its impact.

2005-2006 Influenza Season Vaccine:

Annual influenza vaccine is required to refresh immunity to strains of flu that may return. Vaccination each year is also recommended to allow for refinement of the vaccine to closer match strains that are in circulation in the current season. In the spring of 2005, we had a new California strain circulating that was not contained in the 2004-05 vaccine.

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

- A/California/7/2004 (H3N2) - like
- A/New Caledonia/20/99 (H1N1) - like
- B/Shanghai/361/2002- like strains

We anticipate a good supply of influenza vaccine this year with the addition of another vaccine manufacturer and reintroduction of the Chiron vaccine after its withdrawal last season secondary to contamination issues in Great Britain.

Influenza Vaccine Dosage by Age Group for the United States, 2005 – 2006 Season

Age Group	Dose	Number of Doses	Route	Product
6 – 35 months	0.25 mL	1 or 2	Intramuscular	FluZone
3 – 8 years	0.50 mL	1 or 2	Intramuscular	FluZone or Fluvirin (More than 4 yrs of age)
More than 9 years	0.50 mL	1	Intramuscular	FluZone or Fluvirin
Healthy people 5-8 yrs	0.5 mL	1 or 2	Intranasal (0.25 mL in each nostril)	FluMist (LAIV)
Healthy people 9-49 yrs	0.5 mL	1	Intranasal (0.25 mL in each nostril)	FluMist (LAIV)

All US inactivated influenza vaccine supply consists only of split virus vaccine. Because influenza vaccines have not been approved

by FDA for use among children aged 0 – 5 months and because this group of children is at high risk for flu-related hospitalizations, vaccination is recommended for their household contacts and out-of-home caregivers.

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. There is a limited supply this year of preservative-free vaccine (FluZone) for use in young children 6 to 35 months of age. FluMist™ (LAIV) does not contain any preservative.

What about intranasal flu vaccine?

FluMist™ is approved for use in healthy persons aged 5–49 years of age. 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 5–8 years who have never received influenza vaccine need two doses of LAIV (6–10 weeks apart).

With the recipient in the upright position, approximately 0.25mL is sprayed into each nostril.

LAIV must be stored frozen (-15°C or colder), but may be thawed in a refrigerator and stored at 2-8°C (36-46°F) for no more than 60 hours prior to use.

TCH will have FluMist™ available for eligible patients and staff. FluMist is not recommended for TCH staff who have close contact with severely immunosuppressed patients. Specifically, we recommend inactivated influenza vaccine for healthcare workers caring for patients in BMT, Hematology/Oncology, Newborn Center and transplant services. If a healthcare worker receives LAIV, the healthcare worker should refrain from contact with severely immunosuppressed patients for 7 days after vaccine receipt. No preference exists for inactivated influenza vaccine use by healthcare workers or other persons who have close contact with persons with lesser degrees of immunosuppression (e.g., persons with asthma taking corticosteroids or persons infected with human immunodeficiency virus), and no preference exists for inactivated influenza vaccine use by healthcare workers or other healthy persons aged 5 – 49 years in close contact with all other groups at high risk.

Who should be vaccinated?

We recommend that the following people be vaccinated at the beginning of the 2005 – 2006 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 – 24 months.
- 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) 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.

What are the contraindications to vaccination?

- Hives or severe anaphylactic reaction to chicken or eggs.
- Acute febrile illness (wait till symptoms have abated).
- Infants less than 6 months of age.
- For inactivated influenza vaccine, an individual with a hypersensitivity to thimerosal (common preservative found in contact lens solution), however, 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.

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 for information on how to obtain vaccine.

TCH Staff Immunizations:

Free immunizations for staff (TCH, UPI, contract, students, etc.) are available in Employee Health Services. For questions, call EHS at x6577.

What are the side effects?

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 influenza 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 inactivated influenza vaccine at the same time they receive other routine vaccinations including pertussis vaccine (DTP or DTaP). Influenza and pneumococcal vaccine may be administered at the same time using different sites without increasing side effects. However, influenza vaccine must be administered each year whereas pneumococcal vaccine is not. For LAIV, refer to package insert.

Can pregnant women be immunized?

Because of the increased risk for influenza-related complications, women who will be pregnant during the influenza season should be vaccinated. 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 after approval from their private obstetrician / physician. LAIV is contraindicated for pregnant women.

Note: Inactivated vaccine and LAIV are safe for lactating mothers.

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 strain circulating in birds in Southeast Asia. At this time there is rare human to human transmission of this strain of influenza. No human illness caused by avian influenza has been seen in this country to date. Key components to prevention of influenza infection still hold: good hand hygiene, respiratory etiquette (cover your mouth when you cough), 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

Christine Robinson, PhD

How does TCH test for influenza?

Two laboratory tests are available at TCH for influenza virus detection:

1. Respiratory virus DFA and Culture:

This test is performed by staining specimens with virus-specific monoclonal antibodies labeled with fluorescent compounds that allow infected cells to glow under a microscope if viral proteins are inside. Sensitivity is about 85% for influenza A and 75% for influenza B relative to culture. Two helpful features of the DFA are that the specimen adequacy can be determined, and 7 viruses (RSV, parainfluenza, influenza A, influenza B, and adenovirus) can be detected simultaneously. 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.

2. Influenza A+B IA:

A rapid, influenza immunoassay (IA) is available during "flu season." This test is most useful for patients seen in the ED during late afternoons, evenings and nights when the respiratory virus DFA, which is slightly more sensitive is not available.

Order the flu IA when a rapid diagnosis of influenza A or influenza B will impact patient care, e.g., when decisions about administering anti-flu drugs or withholding antibiotics are being made. If the IA is negative and a more 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 one hour any time of the day or night.

Chemoprophylaxis

1. Antivirals: (Influenza A Use Only)

Therapy should be started as soon as possible after the onset of symptoms and can be continued for 2 – 7 days depending on clinical improvement. Both Amantadine and Rimantadine are approved by the FDA for use in children and adults for prophylaxis against Influenza A infection. Amantadine is the only currently approved antiviral for treatment of children. Amantadine and Rimantadine are not effective against Influenza B infections.

Dosage Recommendations for Amantadine and Rimantadine for Flu A Only

	Age		
	1 – 9 Years	Children More than 10 Years	
		Weight Less than 40kg	Weight More than 40 kg
Treatment (Amantadine)	5mg/kg/day – maximum 150mg/d in 2 divided doses.	5mg/kg/day in 2 divided doses.	200mg/day in 2 divided doses.
	Duration: 3 – 5 days or for 24 – 48 hours after symptoms disappear.		
Prophylaxis (Amantadine & Rimantadine)	Dosages may be the same as those for treatment. An alternative and equally acceptable dosage for children more than 20kg and adults is 100mg/day. For either regimen, the total daily dosage may be given in one or two divided doses.		
	Duration of prophylaxis varies from daily during community influenza activity to only during peak community activity.		

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2. Neuraminidase Inhibitor: (Influenza A or B Use):

Two newer and more expensive antivirals are available for the treatment of influenza A and B. Zanamivir (Relenza®) and oseltamivir (Tamiflu®) have been shown to decrease the duration of flu-related symptoms by 1 to 1.5 days. Oseltamivir has been approved for prophylaxis of patients older than 13 years old. Zanamivir has been approved for treatment of patients age 7 years and older, while Oseltamivir is approved for children more than 1 year old.

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.

3. 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.)

4. 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).

Reference: CDC: Prevention and Control of Influenza: Recommendation of the Advisory Committee on Immunization Practices (ACIP). **July 29, 2005 / 54(RR08); 1-40** http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5408a1.htm

Bug Watch

Up-to-date information on currently circulating respiratory and enteric viruses and *B. pertussis* detected by the TCH Laboratory provided to you weekly. 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 (303-861-6412) to begin receiving your personal copy.