

# CONTAGIOUS COMMENTS

## Department of Epidemiology

### Influenza 2010-2011:

*Roberta Smith, RN, MSPH, CIC*  
*Christine Robinson, PhD*

#### 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 from exposure to illness 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 viruses of other subtypes. Annual influenza epidemics occur because the type A viruses (and type B viruses to a lesser extent) undergo constant change due to antigenic drift. Major antigenic shifts also occur in influenza A viruses every few decades, resulting in pandemics, characterized by rapid and global spread of the novel virus. Critical to the propagation of an influenza pandemic is the emergence of a new circulating influenza A strain with novel H or N surface proteins, a large susceptible population, and most importantly human-to-human spread.

In 2009-2010 we saw the result of antigenic shift when pandemic 2009 H1N1 (pH1N1) circulated worldwide. The pandemic virus was a mixture of swine, avian, and human influenza A strains and has been called swine-origin 2009 H1N1 or pandemic pH1N1 influenza A. In contrast to infections with seasonal influenza viruses, most serious illnesses due to pH1N1 occurred among school-age children and spared the elderly. Pregnancy and obesity were also associated with severe disease.

#### TCH 2009-2010 H1N1 Experience

From May 1 to November 30, 2009, 307 children with 2009 pH1N1 influenza infection were hospitalized of which 80 (26%) were admitted to the ICU. Most of the children admitted to the ICU were 4 to 5 years of age whereas the inpatients on the floor were less than 2 years of age. Sixty five percent of children admitted to TCH had an underlying medical disorder, of which asthma (26%), neurological disorders (24%), and obesity (19%) were the most common. Eight patients died during their hospital course and one died in the emergency room prior to admission to the hospital. The most common cause of death was respiratory failure. Two of the children who died had no underlying medical conditions and only one child who died was less than 2 years of age.

#### Reducing the Impact of Influenza

In the U.S., two measures are available to 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).

Vaccination is our major defense against infection. The trivalent influenza vaccine is updated annually to include viruses that have been in recent 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.

#### New Advisory Committee on Immunization Practices (ACIP) Recommendations for the 2010-11 Season:

The 2010 recommendations include four principal changes or updates:

- Routine influenza vaccination is now recommended for all persons aged 6 months and older.
- ACIP has published an algorithm for dosing of influenza vaccine for children 8 years of age and younger (see table). This information takes into

account a child's previous influenza vaccination history.

- A newly approved inactive trivalent vaccine containing 60 mcg of H antigen per each vaccine virus strain (Fluzone High-Dose [Sanofi Pasteur]) is an alternative, inactivated vaccine for persons aged 65 years and older.
- Several influenza vaccines were approved by the FDA for expanded age indications in 2009 (see table).

For the full 2010-2011 ACIP recommendations for prevention and control of influenza go to:

[http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5908a1.htm?s\\_cid=rr5908a1\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5908a1.htm?s_cid=rr5908a1_w)

### 2010-2011 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 pH1N1 is included in the vaccine. Many pharmacies are advertising "Triple Protection" flu shots. Influenza vaccine has always contained three strains of the virus and everyone who is vaccinated this year will receive "triple protection".

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

- A/California/7/2009 (H1N1)-like, which is a strain of the pandemic virus
- A/Perth/16/2009 (H3N2)-like
- B/Brisbane/60/2008 –like antigens.

With the new, universal recommendation of influenza vaccination, influenza vaccine supply is projected to be the highest it has ever been.

Influenza vaccines are not 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, 2010-11 Season

Trade Name/Manufacturer	Presentation	Age Group	No. of Doses	Route
Fluzone <sup>®</sup> /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 <sup>™</sup> /Novartis	5.0 mL multidose vial	≥ 4 years	1 or 2*	Intramuscular
	0.5 mL pre-filled syringe	≥ 4 years	1 or 2*	Intramuscular

Agriflu/Novartis	0.5 mL prefilled syringe	≥18 years	1	Intramuscular
Fluarix <sup>™</sup> /GlaxoSmithKline	0.5 mL prefilled syringe	≥ 18 years	1	Intramuscular
FluLuval <sup>™</sup> /GlaxoSmithKline	5.0 mL multidose vial	≥ 18 years	1	Intramuscular
Afluria/CSL Biotherapies	0.5mL prefilled syringe	≥ 9 years	1	Intramuscular
FluMist <sup>™</sup> /Medimmune	0.2 mL sprayer	2-49 years	1 or 2 *	Intranasal
Fluzone High-Dose/sanofi pasteur	0.5mL prefilled syringe	≥65 years	1	Intramuscular

\* Children aged 6 months – 8 years who did not receive at least 1 dose of an influenza A (H1N1) 2009 monovalent vaccine, who have never received a seasonal influenza vaccine before, or who were vaccinated for the first time with the seasonal 2009-10 seasonal vaccine but who received only 1 dose should receive 2 doses of the 2010-11 influenza vaccine formula.

### Recommendations for Afluria produced by CSL Biotherapies.

During the 2010 influenza season in Australia, administration of seasonal influenza TIV manufactured for the Southern Hemisphere by CSL Biotherapies (FluVax Jr. or FluVax) was associated with an increased frequency of fever and febrile seizures in children aged 6 months through 4 years old. There also have been reports of fever in children aged 5 years through 8 years following FluVax compared to previous seasons. Based on this information, ACIP recommends that for the 2010-11 influenza season in the U.S.

- Afluria should not be used in children aged 6 months through 8 years.
- Other age-appropriate, licensed seasonal influenza vaccine formulations should be used for prevention of influenza in children aged 6 months through 8 years.
- If no other age-appropriate, licensed seasonal influenza vaccine is available for a child aged 5 years through 8 years old who has a medical condition that increases their risk for influenza complications, Afluria may be given, and providers should discuss the benefits and risks of influenza vaccination with the parents or caregivers before administering Afluria.

For detailed information, go to [www.cdc.gov/media/pressrel/2010/s100806.htm](http://www.cdc.gov/media/pressrel/2010/s100806.htm).

### What about intranasal flu vaccine?

FluMist<sup>™</sup> is approved for use in persons aged 2–49 years of age. It should not be given to pregnant women. Flu Mist<sup>™</sup> 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. It is administered to recipients in the upright position with approximately 0.1mL sprayed into each nostril.

TCH will have some FluMist™ available for eligible patients and staff. Although there have been no documented reports of vaccine virus transmission person to person, 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.

**If someone had 2009 H1N1 last year do they need to get a flu shot this year?**

We can only know if someone had a true case of 2009 H1N1 last year if it was laboratory confirmed by influenza PCR. Even if an individual had a positive laboratory test result for pH1N1, vaccination with the 2010-11 trivalent influenza vaccine is still needed to be protected against influenza H3N2 and influenza B (see page 1). All 3 types of influenza have been circulating in the Southern Hemisphere during their winter (our summer), so any of these viruses could appear in the US this winter. An individual needs to receive this year's influenza vaccine to be fully protected against the strains we anticipate will circulate this season.

**Which of our pediatric patients will need 2 doses of influenza vaccine for the 2010-11 vaccination season?**

Whether you give injectable vaccine or nasal-spray vaccine or one of each, give 2 doses separated by at least 4 weeks to all children ages 6 months through 8 years who (1) are receiving influenza vaccine for the first time; (2) received their first dose of seasonal vaccine during the 2009-10 season but failed to get their second dose; or (3) failed to get at least 1 dose of 2009 H1N1 vaccine, regardless of their previous influenza vaccination history. If there is uncertainty about the previous season's vaccination history, give 2 doses this season to any child age 6 months through 8 years. CDC has developed a flow chart to aid in making the decision based on the child's previous vaccination history

[www.cdc.gov/vaccines/ed/imzupdate/downloads/doses-algorithm.pdf](http://www.cdc.gov/vaccines/ed/imzupdate/downloads/doses-algorithm.pdf)

The following chart provides a different format of the information in the flow chart.

Guide for determining the number of doses of influenza vaccine to give to children ages 6 months through 8 years during the 2010-11 influenza season

Did the child receive influenza vaccine prior to the 2009-10 season?	How many doses did the child receive in the 2009-10 season?		Number of doses recommended for the 2010-11 season
	H1N1 <sup>1</sup>	Seasonal	
No, yes, or unknown	0 or unknown	0, 1, 2, or unknown	2 <sup>2</sup>
No or unknown	1 or 2	0, 1, or unknown	
No or unknown	1 or 2	2	1
Yes	1 or 2	0, 1, or 2	1

1. Children who had a lab-confirmed 2009 H1N1 virus infection (e.g., reverse transcription-polymerase chain reaction or virus culture specific for H1N1 virus) are likely to be immune to this virus and can be considered to have a "1" in this column.  
 2. Give dose #2 a minimum of 4 weeks after dose #1. Children age 2 years or older can receive 2 injectable doses, 2 nasal-spray doses, or 1 of each.

**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 vaccine?**

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.
- Pregnancy
- People with long term health problems
- Children or adolescents on long term aspirin treatment.
- Children younger than 5 years of age with asthma or one or more episodes of wheezing within the past year.

## 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 Reye 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. N-95 masks should be worn by anyone doing aerosolizing procedures in patients (e.g. nasal wash).

## Laboratory Testing



### When and how should you test for influenza?

There are several tests available at TCH for detection of respiratory viruses. Some of these tests are specific for influenza virus; others detect other viruses that may co-circulate during influenza “season.” We declare “Influenza Season” at TCH once 5 or more specimens are positive for influenza virus within one week.

Testing for respiratory viruses, including influenza virus, should only be ordered if the clinical management of patients will change based on test results. Reasons to order a respiratory virus test include to prescribe antivirals, to limit the use of antibiotics, or to reduce orders for other laboratory tests if influenza virus infection is confirmed.

The type of test ordered should be based on patient factors, severity of the illness, season, and specimen type. There will be comments in EPIC to guide you to the most appropriate order for your patient. This winter, our recommended tests are:

1. For normal patients seen in the Emergency Department or other outpatient settings with mild to moderate acute LRI or URI who will not benefit from treatment: **No test**
2. For patients who will not be hospitalized (e.g. seen only in the ED or Network of Care) but will benefit from testing:
  - When influenza is widely circulating in the community and the patient would benefit from antiviral treatment: **Influenza Virus PCR\***
  - When little or no influenza virus is in the community and the patient would benefit from detection of any virus: **Respiratory Virus DFA**
3. For inpatients or likely admissions whose clinical management will change if any respiratory virus is identified: **Respiratory Virus DFA with Backup Respiratory Viral PCR.** PCR is done if the DFA is negative.
4. For likely critical care or immunocompromised admissions whose clinical management will change if any respiratory virus is identified: **Respiratory Virus DFA with Concurrent Respiratory Virus PCR and CMV/Herpes Culture.** All 3 tests are done.
5. For BAL or lung tissue: **Resp. Virus PCR with CMV/Herpes Culture.**

\*Rapid” influenza immunoassays (IA) will no longer be performed at TCH or in our Network of Care. This change is due to serious concerns raised by the CDC and our internal analysis about the high rate of false negatives and false positives generated by these tests. The new protocols outlined above are now in alignment with the CDC’s current recommendations for influenza virus testing.

The table below lists the tests and information about their use.

Virus Detected	Test & Relative Value			
	Resp. Viral DFA	Resp. Viral PCR (RVP)	Influenza Virus PCR	Influenza Virus IA
<b>Influenza A, B</b>	+++	++++	++++	++
<b>Influenza A Subtype</b>	0	++++ Subtypes seasonal H1 & H3 only. Presence of pH1 is inferred when non-subtype-able influenza A is detected	++++ Subtypes p2009 H1	0
<b>RSV</b>	+++	++++	0	0
<b>Parainfluenza virus</b>	+++ Types 1-3 detected but not differentiated	++++ Differentiates all 4 types	0	0
<b>HMPV</b>	++	++++	0	0
<b>Adenovirus</b>	++	+++	0	0
<b>Rhinovirus</b>	0	++++ Also detects some enteroviruses	0	0
<b>Coronavirus</b>	0	+++ Differentiates 4 common types	0	0
<b>Other Factors</b>				
<b>Acceptable Specimens</b>	Nasal wash tracheal aspirate	Nasal wash tracheal aspirate, BAL, lung tissue	Nasal wash	Nasal wash
<b>Turnaround Time</b>	0.5 day (1 day on weekend)	1.5 – 2 days	4 hours (in season)	15-30 minutes
<b>Relative Cost</b>	\$\$	\$\$\$\$	\$\$	\$

Additional information about laboratory detection of influenza virus is available at:  
<http://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm>

## 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 (but not zanamivir) was identified among influenza A (H1N1) in the United States and some other countries. As of June 2010 in the US, approximately 99% of seasonal influenza A (H1N1) viruses (i.e., H1N1 viruses not associated with the 2009 pandemic) tested have been resistant to oseltamivir. None of the influenza A (H3N2) or influenza B viruses tested were resistant to oseltamivir.

#### Limitations of Both Medications:

- Should be administered within 48 hours of onset of symptoms for maximal efficacy, although some trials with hospitalized patients and severe disease suggest benefit beyond this time-period.
- 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. The Colorado Department of Public Health and the Environment strongly discourages “personal stockpiling” of Tamiflu (<http://www.cdphe.state.co.us/dc/Influenza/avian/Tamiflu%20HAN.pdf>).

### 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.

The following table summarizes the antiviral resistance patterns of the various influenza virus types: (*see next page for chart*)

## Antiviral Resistance of Influenza Viruses in 2009-10

Antivirals		Influenza A			Influenza B
		Pandemic H1	Seasonal H1	H3	
Neuraminidase inhibitors	Oseltamivir	Sensitive	Resistant	Sensitive	Sensitive
	Zanamivir	Sensitive	Sensitive	Sensitive	Sensitive
Amantanes	Amantadine, Rimantadine	Resistant	Sensitive	Resistant	Resistant

### References:

CDC: Prevention and Control of Influenza: Recommendation of the Advisory Committee on Immunization Practices (ACIP) August 6, 2010 / 59 (RR08) p1-62.  
[http://cdc.gov/mmwr/preview/mmwrhtml/rr59e0729a1.htm?s\\_cid=rr59e0729a1\\_w](http://cdc.gov/mmwr/preview/mmwrhtml/rr59e0729a1.htm?s_cid=rr59e0729a1_w)

### Bug Watch



This publication provides up-to-date weekly information on currently circulating respiratory and enteric viruses detected by the TCH Laboratory. Providing as well, updates of *B. pertussis* detected in individuals less than 20 years of age statewide. Current editions are posted on the TCH Internet:

[Publications - The Children's Hospital-Denver Area, Colorado, Rocky Mountain Region](#). Contact Carolyn Brock by e-mail ([brock.carolyn@tchden.org](mailto:brock.carolyn@tchden.org)) or phone (720-777-6412) to begin receiving your personal copy via email.

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Thank you for your interest in our publication.

**CONTAGIOUS COMMENTS**  
**Department of Epidemiology EDITOR:**

Kelly Pearce, Staff Assistant III  
The Children's Hospital, Dept. of Epidemiology, B-276  
13123 E. 16<sup>th</sup> Avenue, Aurora, CO 80045  
Phone: 720-777-6072; FAX: 720-777-7295

[pearce.kelly@tchden.org](mailto:pearce.kelly@tchden.org)  
<http://www.thechildrenshospital.org>

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