**What’s Up with Flu in 2011-2012?**

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**VACCINATION**

The recommendations from the Advisory Committee on Immunization Practices (ACIP) for 2011-12 are relatively unchanged from last winter. The 2011-12 vaccine formulation also remains the same. It contains:

- A/California/7/2009 (H1N1)-like (which is a strain of the pandemic virus and the only currently-circulating H1N1);
- A/Perth/16/2009 (H3N2)-like; and
- B/Brisbane/60/2008—like antigens

*Annual vaccination is still strongly recommended for everyone, even for those who received the vaccine in the previous season. Several studies have demonstrated that post-vaccination antibody titers decline over the course of a year. Although a recent study of children vaccinated against A/Hong Kong/68 (H3N2) virus showed that vaccine efficacy remained high against this strain 3 years later, estimated efficacy of vaccine still decreased over the seasons studied. Thus, annual vaccination is still recommended by the ACIP for optimal protection against influenza for every eligible person.*

Several new items are on the vaccine front. Better guidance for evaluating severe egg allergies is now available.

**Recommendations regarding influenza vaccination for persons who report allergy to eggs - ACIP, 2011-12 influenza 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 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 mos.</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>5 mL multidose vial</td>
<td>≥ 6 months</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Fluvirin ™/Novartis</td>
<td>0.5 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></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluarix ™/GlaxoSmithKline</td>
<td>0.5 mL prefilled syringe</td>
<td>≥ 3 years</td>
<td>1 or 2*</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>FluLaval ™/GlaxoSmithKline</td>
<td>5 mL multidose vial</td>
<td>≥ 18 years</td>
<td>1</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Afluria/CSL Biotherapies</td>
<td>0.5 mL prefilled syringe</td>
<td>≥ 9 years</td>
<td>1</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>5 mL multidose vial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FluMist ™/Medimmune</td>
<td>0.2 mL sprayer</td>
<td>≥ 49 years</td>
<td>1 or 2*</td>
<td>Intranasal</td>
</tr>
<tr>
<td></td>
<td>0.5 mL prefilled syringe</td>
<td>≥ 65 years</td>
<td>1</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>0.1 mL prefilled microinjection system</td>
<td>18-64 years</td>
<td>1</td>
<td>Intradermal</td>
</tr>
</tbody>
</table>

*Children aged 6 months through 8 years who did not receive seasonal influenza vaccine during the 2010-11 influenza season should receive 2 doses at least 4 weeks apart for the 2011-12 season. Those children aged 6 months through 8 years who received ≥1 dose of the 2010-11 seasonal vaccine require 1 dose for the 2011–12 season.*

In addition, this is the first season that an intradermal influenza vaccine from sanofi Pasteur is on the market. In May, the FDA licensed a 0.1mL prefilled microinjection system to administer influenza vaccine intradermally in the deltoid for adults ages 18-64 years of age. New influenza vaccine technology, new formulations and a quadrivalent influenza vaccine are also on the horizon. This upcoming influenza season, six manufacturers will produce approximately 170 million doses of vaccine for the U.S.; five of the six will produce vaccine for children. Since last winter, influenza vaccine is recommended for everyone over the age of 6 months. Influenza vaccines are still not FDA-cleared for use among children age 0 – 5 months. Because this group of very young children are at high risk for flu-related hospitalizations, vaccination is recommended for all of their household contacts and out-of-home caregivers. See the link in the reference list for the full 2011-12 ACIP recommendations about prevention and control of influenza.
If I got a vaccine in 2010-2011, why do I need to get another one this season if the vaccine strains didn’t change?
As mentioned above, your body’s level of immunity from a vaccine received last season has probably declined. You may not have enough immunity to be protected from getting sick this season. You should be vaccinated again to increase your immunity against the three viruses in the vaccine, all of which circulated during the southern hemisphere’s flu season which just ended and will probably appear here as well.

Which pediatric patients will need 2 doses of influenza vaccine for the 2011-12 vaccination season?
In previous seasons, children aged 6 months through 8 years who received only 1 dose of influenza vaccine in their first year of vaccination required 2 doses the following season. However, because the 2011–12 vaccine strains are unchanged from the prior winter, children in this age group who received at least 1 dose of the 2010–11 seasonal vaccine will require only 1 dose of the 2011–12 vaccine. Children in this age group who did not receive at least 1 dose of the 2010–11 seasonal influenza vaccine, or for whom it is not certain whether the 2010–11 seasonal vaccine was received, should receive 2 doses of the 2011–12 seasonal influenza vaccine.

Laboratory Testing

How do we test for influenza?
This winter, laboratory detection of influenza viruses will be straightforward. Only molecular tests will be offered, either an influenza virus-only polymerase chain reaction (PCR) or the full respiratory virus PCR (RVP). Respiratory virus direct stain (DFA) is being discontinued here and in other US laboratories because PCR is a more sensitive and specific technology. Eliminating DFA also reduces costs and simplifies ordering.

Influenza PCR detects any influenza A, influenza A 2009 H1N1 if it is present, and influenza B. The test will be available once influenza appears in Colorado. It will be performed 24/7, with a turnaround time of 5 hours or less once the specimen is received at the main campus laboratory. Nasopharyngeal aspirates are required for this test.

RVP is a more comprehensive assay. It detects any influenza A and influenza B. The influenza A H1N1 2009 virus is detected but not separately identified; the influenza A H3N2 virus is separately reported. In addition, RVP also detects RSV, adenovirus, parainfluenza 1-4, human metapneumovirus, four coronaviruses, and the rhinoviruses/enteroviruses. RVP can be performed on many specimen types, including nasopharyngeal or tracheal aspirates, bronchoalveolar lavage, or tissue. RVP is performed Mon-Fri and on weekends. Specimens received by 6 am will now be resulted by 3 pm.

Who should be tested for influenza?
Tests to detect influenza (or any respiratory virus) should be ordered only if results will affect clinical management. Our recommendations for ordering influenza virus PCR assays in 2011-12 are:

RESPIRATORY VIRUS TEST ALGORITHM

Child with respiratory or flu-like illness

No/ Not sure

Administer 2 doses of 2011–12 seasonal influenza vaccine a minimum of 4 weeks apart

Yes

Administer 1 dose of 2011–12 seasonal influenza vaccine

Will a direct clinical change be made based on a virus result?

E.g. Start or stop antivirals, limit antibiotics and/or ancillary testing, decrease hospitalization

Influenza virus

Yes

If only influenza virus is relevant

Influenza virus PCR

Nasal wash only

Respiratory virus

If any respiratory virus (including influenza) is relevant

Respiratory virus PCR

Nasal wash, tracheal aspirates, BAL, lung tissue

Detects influenza A/B, RSV, MB, parainfluenza 1-4, adenovirus, rhinovirus, and coronaviruses (229E, OC43, NL63, and HKU1)
Neuraminidase Inhibitors
Oseltamivir (Tamiflu®) and zanamivir (Relenza®) are the two neuraminidase inhibitors that are FDA-cleared for treatment and prophylaxis of influenza A and influenza B infections. Oseltamivir has been approved for treatment and prophylaxis of patients older than one year old; zanamivir has been approved for treatment of persons 7 years and older and prophylaxis of persons age 5 years and older. These medications may shorten the duration of fever and symptoms by 1-3.5 days if started within 2 days after onset of symptoms. They may also reduce the risk of complications (e.g. otitis media in young children, pneumonia, respiratory failure, and death).

Persons who may benefit from antiviral treatment for suspected or confirmed influenza are those who are:

- Hospitalized
- Have severe, complicated, or progressive illness; or
- At high-risk for influenza complications, e.g.
  - Children aged <2 years; individuals <19 years receiving long-term aspirin; or adults aged ≥65 years
  - Persons with chronic systemic diseases, or neurologic, neurodevelopmental, or musculoskeletal conditions
  - Persons with immunosuppression
  - Pregnant or recently post-partum women
  - American Indians/Alaska Natives
  - Persons who are morbidly obese
  - Residents of nursing homes or chronic care facilities

Previously healthy, symptomatic outpatients with suspected or confirmed influenza who are not at high risk may also benefit from treatment, if treatment is initiated within 48 hours of onset.

Treatment should not wait for laboratory confirmation of influenza!

Oseltamivir (Tamiflu®) is given orally for 5 days to children 1 year of age or older, with dose adjustments required for renal impairment and weight of child. Recommended dosing for treatment or prophylaxis for children ≥1 year - 12 years old is:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Treatment Dose</th>
<th>Prophylaxis Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 kg</td>
<td>30 mg twice a day</td>
<td>30 mg once daily</td>
</tr>
<tr>
<td>&gt;15-23 kg</td>
<td>45 mg twice a day</td>
<td>45 mg once daily</td>
</tr>
<tr>
<td>&gt;23-40 kg</td>
<td>60 mg twice a day</td>
<td>60 mg once daily</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>75 mg twice a day</td>
<td>75 mg once daily</td>
</tr>
</tbody>
</table>

Treatment dosage for children 13 years of age and adults is 75 mg twice a day. Longer treatment courses can be considered for patients who remain severely ill after 5 days of treatment. Recent data suggest that hospitalized patients may benefit from treatment even if started more than 48 hours after symptoms begin.

Although oseltamivir is not FDA-cleared for children less than a year of age, it was approved under an Emergency Use Authorization for use during the 2009 pandemic. The recommended treatment dose for children under one year of age in this situation was 3mg/kg twice daily. The same dose is given once daily for prophylaxis.

The most common side effects of oseltamivir are nausea or vomiting. Transient neuropsychiatric events (self-injury or delirium) have been reported, mainly among Japanese adolescents and adults.

Zanamivir (Relenza®) is a dry powder administered via oral inhalation. It is not FDA-cleared for treatment in children under 7 years of age. The dose is two breath-activated inhalations twice daily for 5 days. Prophylaxis dose is 2 inhalations once daily for ages 5 yrs and older.

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). Allergic reactions including rashes and oropharyngeal or facial edema are reported. Side effects can be diarrhea, nausea, sinusitis, runny or stuffy nose, bronchitis, cough, headache, dizziness, and ear, nose and throat complaints.

Investigational parenterally-administered zanamivir and peramivir (another neuraminidase inhibitor) were used with variable success for treatment of severely-ill patients during the pandemic. These medications are now in phase 1 and 2 trials, which are still recruiting patients. No outcomes data is available at this time.

Although resistance of influenza viruses to neuraminidase inhibitors is currently less than 1% in the US, this situation could change. Also antiviral resistance can emerge after treatment in certain patients, e.g. the immunosuppressed. For guidance about influenza virus resistance to antivirals, see www.cdc.gov/flu/professionals/antivirals/antiviral-drug-resistance.htm

Amantadine: 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 A infections. However widespread resistance of H3N2 and 2009 H1N1 influenza A viruses, and lack of efficacy against influenza B makes this class of medications less useful than neuraminidase inhibitors. Therefore the CDC does not currently recommend their use.

**Chemoprophylaxis:** The neuraminidase inhibitors are 70-90% effective in preventing influenza. Yet the CDC does not recommend widespread or routine use of chemoprophylaxis due to the possibility that resistant viruses could emerge, thus limiting the usefulness of these medications for high-risk or severely ill persons. Annual vaccination is a better way to prevent influenza because vaccines can be given well before exposures occur and can provide safe and effective immunity throughout the influenza season if the vaccine and circulating strains are well-matched.

To be effective as prophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza, and continued for 7 days after the last known exposure.

Chemoprophylaxis is not recommended if more than 48 hours have elapsed since the last exposure to an infected person. Persons receiving chemoprophylaxis should be encouraged to seek medical attention as soon as they develop a febrile respiratory illness that might indicate influenza.

**References:**

1. CDC: Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) August 26, 2011 /60(33); p1128-1132. [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6033a3.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6033a3.htm)


**Bug Watch**

This publication provides up-to-date weekly information on currently circulating respiratory and enteric viruses and * Bordetella pertussis* detected by Children’s Hospital Colorado Microbiology/Virology Laboratory. Current editions are posted on Planet TCH or the Children’s Colorado external webpage at [http://www.childrenscolorado.org/news/publications/bugwatch.aspx](http://www.childrenscolorado.org/news/publications/bugwatch.aspx).

Contact Carolyn Brock at Carolyn.Brock@childrenscolorado.org, or by phone (720-777-6412) to begin receiving your personal copy via email.

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