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What to do About the Flu

Written By: Kacy Mulligan, Pharm. D. Candidate 2013

Flu season is right around the corner and it's time to get smart about this year's vaccinations. Swine flu, bird flu, the good ole fashioned flu…what's the difference? What does this year's vaccination cover? When should you get it? These are all important questions that you need to consider before getting your annual flu vaccination.

Every year the World Health Organization, Food and Drug Administration, and Centers for Disease C evaluate all of the different influenza strains from around the world. From there, the CDC makes recommendations on which strains are most likely to cause illness in a particular area. For the United States, this season's flu vaccine will contain the following influenza strains: H1N1 (swine flu), influenza A (H3N2), and influenza B. Although the H1N1 strain was incorporated into the 2011-2012 seasonal flu vaccines, the H3N2 and B strains were not. Therefore, it is very important to get vaccinated every year to protect you from new influenza strains.

Everyone aged 6 months or older should receive the flu vaccine. If it is the child's first time receiving the vaccine, he or she should get a two-dose series at least 28 days apart. Flu shots are available at a number of community pharmacies, hospitals, clinics, and physician offices. In the state of Georgia, pharmacists only administer flu shots to adults and children 13 years of age and older (specific company policies may be more strict). Children less than 13 years of age must be vaccinated by a physician.

There are a number of different types of vaccines available: the intramuscular inactivated vaccine approved for everyone 6 months of age and older, the high dose intramuscular inactivated vaccine approved for adults 65 years of age and older, the intradermal inactivated vaccine approved for adults 18 to 64 years old, and the live attenuated intranasal vaccine approved for healthy, non-pregnant people aged 2 to 49 years.

The intradermal vaccine uses a 90% smaller needle to inject the vaccine into the skin, rather than muscle, and also requires less antigen to make the vaccine. This is an option for patients who do not like the regular intramuscular shots, however local injection site reactions such as redness, swelling, toughness, and itching are more common with the intradermal injection. Although the vaccines may be delivered differently, they are all equally effective.

Contrary to popular belief, the flu vaccine cannot *give* you the flu. The flu shots contain inactivated virus and the intranasal formulation contains a live attenuated, or weakened, virus and is only active in the nasal cavity where the temperature is lower. Therefore, it cannot affect other organs, such as the lungs, where the temperature is much warmer. If a person becomes sick after receiving the flu vaccine, it may be due to a number of other reasons. The person may have been exposed to the virus before receiving the flu vaccine or within two weeks post vaccination (the body takes two weeks to develop complete immunity to the virus), the person may have been exposed to strains that are not covered by the vaccine, or the person may be experiencing mild side effects. Al-

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though rare, side effects from the inactivated vaccine include: soreness, redness, or swelling at injection site, low-grade fever, aches, and nausea. Side effects from the live vaccine may include: runny nose, wheezing, headache, vomiting, muscle aches, and fever in children, and runny nose, headache, sore throat, and cough in adults. These side effects are usually very mild and last only one to two days.

Studies have shown that people with weakened immune systems may not develop as many antibodies as healthy people and antibody levels may drop off more quickly.

The CDC recommends getting the flu vaccine as soon as it becomes available in your area. Although the flu season ranges from October to May, it tends to peak around January-February, but this may be different depending on your area. The vaccine takes two weeks to become fully effective and *should* last throughout the entire flu season. However, studies have shown that people with weakened immune systems may not develop as many antibodies as healthy people and antibody levels may drop off more quickly. Therefore, it is important to find the right time to get vaccinated. It may not be as beneficial to get vaccinated too early, such as August, due to the risk of antibody decline, but it is also crucial not to wait too far along into the flu season and put yourself at risk for early infection. Late September/ October seems to be an appropriate vaccination time for most people.

Children in particular have an increased risk for developing complications from the flu. Getting children vaccinated is the single most important precaution against these complications. Children less than 5 more commonly need medical care due to the flu, and children less than 2 are at highest risk for severe complications, including pneumonia and even death. Vaccination is particularly important for high-risk children including those with asthma, diabetes, or disorders of the brain or nervous system.

It is imperative for pharmacists to take an active role in educating the public about the seasonal flu vaccine, especially the importance of getting children vaccinated.

Resources: www.CDC.gov

SSPA members Amanda Frederiksen, Emily Parmer, and Mandy Fruscione volunteering at our booth on childhood immunizations during Dawgtoberfest 2012.

October 17, 2012

Inavir completes phase III clinical trials for prevention of influenza

Written By: Shayla Rose, PharmD Candidate 2013

On August 27, 2012, Biota and Daiichi Sanko, the creators of the anti-influenza agent Inavir (formerly CS-8958), released promising results from a phase III clinical trial examining the drug's ability to protect its users from the influenza virus. Enrollment reached over 1500 patients, made up of single family households in which one member of the family had a confirmed influenza virus infection. The primary endpoint of the study was measured as the proportion of household members who contracted the virus from the infected family member. According to the results of the study reported by Biota, the protective efficacy of the drug exceeded 70%, meeting its primary endpoint with statistical significance. Biota also reports a similar safety profile seen in previous studies.

Inavir, a long acting neuramidase inhibitor, provides benefit over other drugs with similar mechanisms of action because it can be dosed once daily. Once inhaled intranasally, the drug remains in the lungs for a long period of time, at concentrations necessary to inhibit the replication of the influenza virus for up to five days. This presents an advantage over traditional agents, which must be taken twice daily for five days. In addition to treating the H1N1 strain that caused the flu pandemic of 2008, Inavir treats seasonal H3N2 and influenza B viruses at a rate comparable to oseltamivir and zanamivir, as well as a strain resistant to oseltamivir.

Approved for use in Japan, one-time dosing of Inavir is used in both adult and pediatric populations for treatment of the influenza virus. This drug is available as a 20 milligram dry powder inhaler; adults and children over the age of 10 receive a onetime dose for 40 milligrams inhaled intranasally, and children under the age of 10 use a single 20 milligram dose.

Inavir is currently under contract for advanced development in the United States.

In addition to treating the H1N1 strain that caused the flu pandemic of 2008, Inavir treats seasonal H3N2 and influenza B viruses at a rate comparable to oseltamivir and zanamivir.

References:

Kiso, M., Kubo, S., Ozawa, M., Quynh Mai, L., Nidom, C. A., Yamashita, M., & Kawaoka, Y. (2010). Efficacy of the New Neuraminidase Inhibitor CS-8958 against H5N1 Influenza Viruses. Plos Pathogens, 6(2), 1-10. doi:10.1371/journal.ppat.1000786

"Biota Announces Inavir Achieves Primary Endpoint in Phase III Prevention Study ." MarketWire. MarketWire, 22 Aug 2012. Web. 1 Oct 2012.

Preventing Infection: Fall Bugs

Uvette Lou, PharmD. Candidate 2013

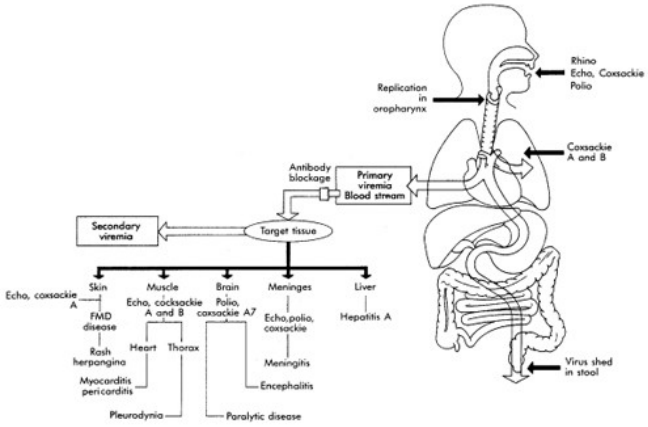
Now that the summer weather is finally cooling down and children are going back to school, healthcare professionals should be mindful of seasonal illnesses. The contagious atmosphere of schools combined with the cooling weather means that everyone will soon be seeing a slew of pediatric infections. Two of the most common pediatric viral infections are discussed below.

Enterovirus

Enterovirus is a family of RNA viruses which include polio and non-polio enteroviruses. In the Western world, poliovirus has been eradicated thanks to diligent vaccination efforts, leaving the non-polio enteroviruses as the main culprits from this family to strike during the summer and fall seasons. The second-most common viral infection after rhinovirus, this virus spreads through fecal-oral or respiratory contact and can survive the acidity of stomach acid and live for several days on surfaces at room temperature.

In healthy adults and even children, enteroviral infection is generally asymptomatic or mild, presenting as a "summer cold". However, in some pediatric patients, especially neonates, because their immune systems are less developed, infections can run a more severe course. Risk factors for severe more infections include prematurity, earlier age at illness onset, history of maternal enteroviral infection, lack of breastfeeding, lower socioeconomic status, Signs and symptoms of infection include sore throat, herpangina (sores in the mouth and throat), hand-foot-and-mouth disease (blisters or sore on the hands, feet and mouth), nausea, diarrhea, aches, chills, and fever. Rarely, more severe problems such as paralysis, myocarditis, encephalitis, or sepsis can develop, especially in the neonatal population.

No specific treatment for enterovirus exists, with supportive care currently being the best option. Therefore, prevention of viral spread to high-risk patients is key; infected surfaces should be cleaned first with soap and water, and then with a ¼:1 dilution of bleach and water. People with known infections should also avoid contact with any susceptible neonates or children.



Path of viral infection, from http://www.meddean.luc.edu/lumen/MedEd/mech/cases/case28/entero.htm

If you would like to contribute to PediaNews, contact Shayla Rose at: PediaNews @gmail.com

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RSV: Respiratory syncytial virus

Respiratory syncytial virus is an RNA virus from the same family of viruses that causes the measles and the mumps. The most common cause of respiratory infections in young children, this virus can cause bronchiolitis and even pneumonia in 4 to 5 million children per year. With the ability to live for up to 5 hours on surfaces, RSV spreads through contact with infected respiratory droplets. Risk factors for contracting this virus include being in daycare, having older siblings in school, having a lower socioeconomic status, exposure to cigarette smoke, less breastfeeding, and multiple birth sets (example, twins or triplets). Premature infants, infants < 3 months of age at infection, and children with congenital abnormalities tend to suffer more severe courses of infection.

Signs and symptoms of RSV infection are usually respiratory in nature, such as wheezing, coughing, tachypnea, cyanosis, and even retractions in severe cases. A fever can also accompany these respiratory symptoms. Treatment of infections is limited to supportive care. However, prevention of RSV infection is possible with good hand hygiene and limiting pediatric patients' exposure to tobacco smoke and people with known infections.

A monoclonal antibody, palivizumab (Synagis®), is also available for prevention of RSV in children less than 24 months of age that meet specific additional criteria that put them at high risk for contracting RSV. Palivizumab is a drug that prevents the viral fusion and entry into cells by attaching to the viral receptor that aids in fusion. It is indicated for patients with bronchopulmonary dysplasia, congenital heart disease, and prematurity as listed in the table below. The intramuscular injection is dosed at 15mg/kg, and starting in November (the beginning of RSV season), given monthly until the end of RSV season (March or April).

Synagis® is indicated for premature infants that fall into BOTH categories

Gestational age at birth		Age at start of RSV season
28 weeks or less	AND	12 months or less
29 to 32 weeks	AND	6 months or less
32 to 35 weeks	AND	3 months or less

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Abzug MJ. Presentation, diagnosis, and management of enterovirus infections in neonates. Paediatr Drugs. 2004;6(1):1-10.
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Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus infections. Pediatrics. 2003;112(6 Pt 1):1442-6.

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Promoting safe and effective pediatric medication therapy through advocacy, education & volunteerism

Management of Pulmonary Arterial Hypertension in Pediatric Patients

Sarah Evans, Pharm.D. Candidate 2013
Jocelyn Owusu-Yaw, Pharm.D. Candidate 2013

Pulmonary arterial hypertension (PAH) is a disorder that affects less than one case per million pediatric patients per year and is associated with a high risk of morbidity and mortality. The pathophysiology of the disease is largely unknown, however some common risk factors for development of PAH include prematurity, certain genetic abnormalities, congenital heart diseases, HIV infection, sleep-disordered breathing, or a combination of factors. Many cases are idiopathic.

PAH is defined as a pulmonary arterial pressure of ≥25 mm Hg at rest, which results in elevated pulmonary vascular resistance and structural changes in the pulmonary vasculature. The most common presenting symptom of PAH is dyspnea, although syncope and failure to thrive (especially in infants) can also occubr. If left untreated, the disease can quickly progress to respiratory failure and death. Treatment is targeted at one or more of three different endothelial signaling pathways, specifically nitric oxide/cGMP, PGI_2 (prostacyclin), and/or ET-1 (endothelin). Mechanisms of several drugs that affect these pathways are discussed in the table below.

Medication	Mechanism of Action	Adverse Drug Reactions	Miscellaneous
Sildenafil (Revatio®) 1st-line treatment (former) **Dosing:** 0.5 mg/kg/dose can increase up to 5 mg/kg/dose	Selective phosphodiesterase type 5 (PDE-5) inhibitor; PDE-5, an enzyme found in high concentrations in the lungs and other areas of the body that normally degrades cGMP, however if PDE-5 is inhibited, cGMP levels increase, which results in vascular smooth muscle relaxation	Urinary tract infections; flushing; dizziness; headache; increased LFTs; myalgia; diarrhea	Cannot be used concomitantly with any other nitrates; watch the use of concomitant CYP34 inhibitors; monitor for decreases in blood pressure and heart rate; administered IV or orally (compounded suspension) **As of 8/30/2012, the FDA recommended sildenafil should NOT be used in patients 1-17 years old due to increased risk of death, especially at high doses.**
Bosentan (Tracleer®) **Dosing**: >2 years: Initial: 0.75-1 mg/kg/dose (maximum: 62.5 mg/dose) twice daily for 4 weeks; increase to maintenance dose of 2 mg/kg/dose	Competitive antagonist of endothelin-1 at the endothelin-A (ET-A) and endothelin-B (ET-B) receptors (higher affinity for ET-A); blocking these receptors causes vasodilation in the lungs	Increased liver aminotransferase levels; headache; edema; respiratory tract infections; decreased hemoglobin	Pregnancy category X; high potential for drug interactions (CYP 2C9/3A4 substrate and inducer); **black box warning** for elevation of transaminases; only available dosage form is oral

Epoprostenol (Flolan®) Last-line treatment **Dosing:** 1-2 ng/kg/minute, increase dose in increments of 1-2 ng/kg/minute every 15 minutes; varies based on respiratory function, age, and weight	Arachidonic acid metabolite and naturally occurring prostaglandin (PGI_2, prostacyclin, or PGX); is a direct-acting and potent vasodilator of pulmonary and systemic arterial vascular beds; also inhibits platelet aggregation by increasing cAMP within platelets	Flushing; hypotension; tachycardia; flu-like syndrome; arthralgias; rash; nausea and vomiting; [rarely: anemia, hepatic failure, **hypersplenism**, pulmonary embolism, thrombocytopenia]	Do not use chronically in patients who develop pulmonary edema during dose initiation; patients should be monitored for bleeding, especially if used concomitantly with other anticoagulants (there are few pediatric studies of patients receiving routine anticoagulation with epoprostenol); can only be reconstituted with product-specific diluent; administered IV or inhalation
Inhaled Nitric Oxide **Dosing:** Based on parts per million; adjusted by respiratory therapist; occasionally used with sildenafil	Endogenous NO relaxes vascular smooth muscle; when inhaled, smooth muscle relaxation is specific to the lungs, improving oxygenation in well-ventilated parts of the lungs	In the circulation, NO combines with hemoglobin and is converted to methemoglobin and nitrate, thus increasing risk for methemoglobinemia; also potential for infection from contaminated ambient air	Very expensive!

While many advances in treatment of PAH have been made in recent decades, there are still many challenges in managing this disease. Because newborns, infants, and children have such variation in drug absorption, distribution, metabolism, and elimination, it can be difficult to predict how newer agents will affect pediatric patients. Dosing of PAH medications in children is often based on small clinical trials and case reports, as currently there are no clinical practice guidelines for pediatric PAH. As pharmacists, we should remain as up-to-date as possible on any new treatment recommendations in order to provide the optimal care for our patients.

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Lexi-Comp. Accessed October 2012.

KID'S CORNER: Time to have some fun!

All about the Flu

G P N B C V H W A Y G E N M D F N Z U J
I I V C V S H G P A E R T Y N B O M T K
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