

THE USE OF VACCINATION TO

Control Influenza

A Report by **Henry H. Bernstein, DO**
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Educating the public about the importance and value of routine influenza (flu) vaccination is essential to decreasing its spread through communities. This past February (2008), the Advisory Committee on Immunization Practices recommended that annual flu vaccinations now be given to all children ages 6 months through 18 years of age. The panel and the Centers for Disease Control and Prevention (CDC) have, in the past, recommended flu shots for people considered to be at highest risk of death or serious illness from the flu. Broader routine influenza vaccination has the potential to reduce the financial costs attributable to the flu among people of all ages, while improving the health of children, families and communities.

In the United States, the annual number of deaths due to influenza exceeds that of all other vaccine-preventable diseases. Estimates suggest more than 36,000 deaths and more than 200,000 hospitalizations due to influenza occur each year in the United States. Although influenza-related deaths are not common in children, those that do occur are often vaccine-preventable. The annual number of influenza-related deaths among children reported to the CDC for the past three influenza seasons has ranged from 44 during 2004–2005 to 68 during 2006–

2007.¹ Many of those who died had not been vaccinated against influenza.

It is currently recommended that the following individuals receive an influenza vaccination:

- All children 6 months of age and older with high-risk conditions, such as asthma, diabetes, kidney disease or weakened immune systems
- All healthy children between 6 months and 5 years of age
- All household contacts and out-of-home caregivers of children with high-risk conditions and of healthy children younger than 5 years of age
- All health care personnel

Young children are at serious risk for influenza infection, hospitalization and complications. The risk of influenza-associated hospitalization in healthy kids younger than 2 years is equal to or greater than the risk in previously recognized high-risk groups. School-age children tend to have the highest risk for influenza during community outbreaks lasting one to two months or longer.^{2,3}

Most childhood cases of influenza are without serious consequences or complications, but an infection

can exacerbate underlying medical conditions like pulmonary or cardiac disease. Influenza infections can be a precursor to more serious illnesses such as pneumonia in children.^{4,5} Antibiotic-resistant pneumonia associated with influenza infection is on the rise. This type of pneumonia has a rapid progression, high fatality rate and occurs in normally healthy children and adults.⁵ Other infrequent complications can include brain damage, heart problems, spinal cord infections and Reye's syndrome, an often fatal illness in children that can result in fever, vomiting, swelling of the kidneys and brain, and liver damage.⁶

What is Influenza?

Influenza viruses are orthomyxoviruses, which cause an acute respiratory illness. This often occurs in epidemics and outbreaks annually throughout the world. The incidence of influenza depends, in part, on whether an individual has



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developed immunity to the virus through previous exposure or through a recent immunization. The influenza immunization contains antigens, which are substances foreign to the body that stimulate a response from the immune system. In this case, the foreign substances are weakened or dead forms of the virus that the immune system recognizes as harmful. In turn, the immune system produces antibodies, which bind to the antigen and neutralize it. Influenza A viruses are grouped into subtypes by two surface antigens, hemagglutinin (HA) and neuraminidase (NA). Immunity to the virus' surface antigens reduces the likelihood of infection and severity of disease when infection occurs.⁷

Each year, the antigenic structure of the virus can vary, causing a variant or a subtype of the same virus. Therefore, antibodies that confer immunity to a previous strain of the flu might not completely protect against the new strain. Often, seasonal epidemics are the result of minor changes in the virus' strain.⁸ Worldwide influenza pandemics are often linked with major antigenic structural shifts, and previously circulating strains offer no protection against the new strain.

Based on global surveillance of circulating virus strains, the influenza vaccine is produced annually and may change from year to year. In fact, all three strains in the vaccine will change for the

2008–2009 season. Only twice in the past sixteen years have three strains in the vaccine remained from the previous year.

This means that health care providers, influenza campaign organizers and public health agencies need to develop plans for expanding outreach programs and infrastructure to vaccinate as many at-risk children and adults as possible. When vaccine supply is limited, vaccination efforts should focus on delivering vaccination to the following:

- Healthy children 6 months through 4 years of age
- All individuals caring for children under 5 years and especially those caring for children under 6 months of age
- Children with medical conditions that place them at high risk for influenza-related complications
- Women who are pregnant

Signs and Symptoms of Influenza

Initial signs and symptoms of the virus may vary, but typically include:

- A sudden onset of fever
- Nonproductive cough, sore throat and nasal congestion
- Chills or rigors
- Headache
- Malaise (*i.e., general feeling of not being well*)
- Diffuse myalgia (*i.e., muscle aches or tenderness*)

Less frequently, conjunctival (*eye*)



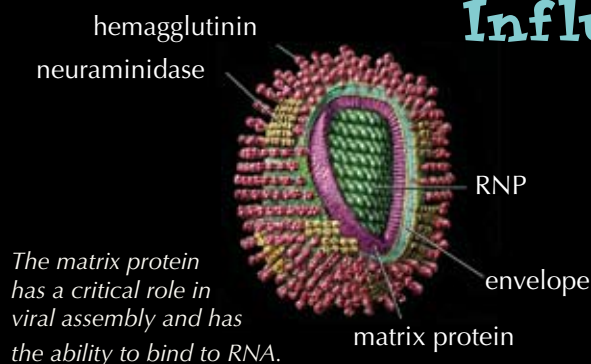
infections, abdominal pain, nausea, vomiting and diarrhea are symptoms reported concurrently with influenza.⁹ Influenza may also appear in children as an upper respiratory tract infection, ear infection or sudden onset of fever with some respiratory tract symptoms.^{6, 9-11}

How is Influenza Spread?

Influenza is spread from person to person primarily by droplets of respiratory secretions from coughing or sneezing. It can also be spread by direct contact with influenza virus-contaminated surfaces. The highest amount of viral shedding (*discharging the virus*) through nasal secretions occurs during the first three days of the illness, but individuals can also spread the virus before they display symptoms.

While adults may spread the virus six days after the onset of symptoms, children can be infectious for up to 10

Influenza Virus Structure

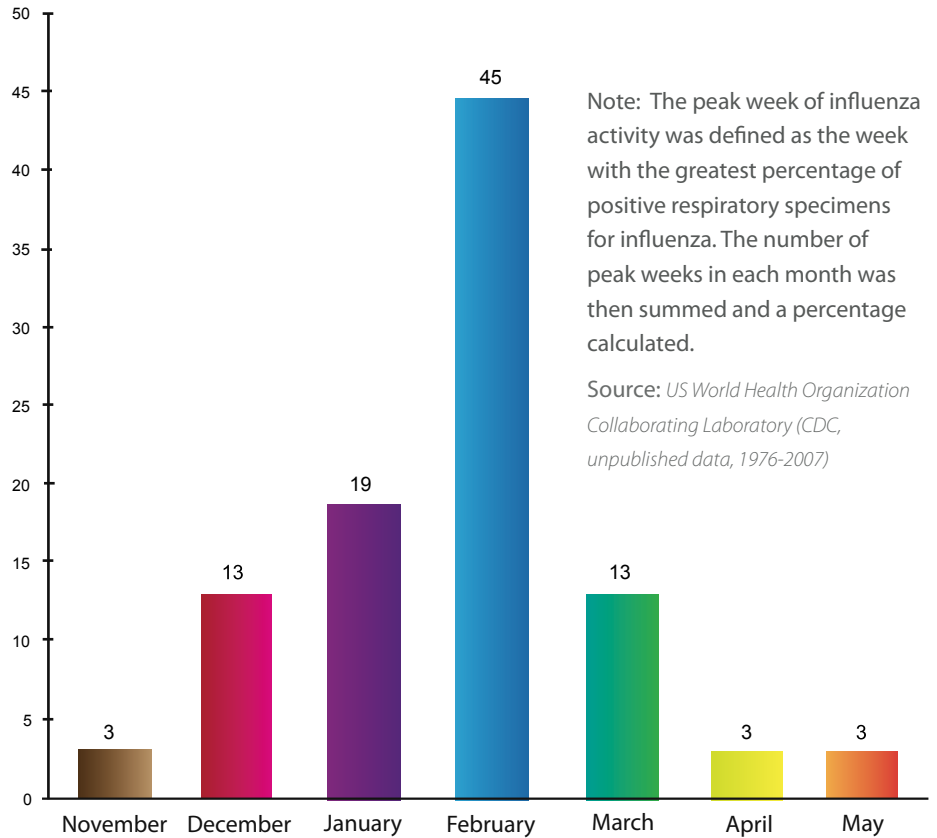


Hemagglutinin is a protein which forms a rod-shaped spike on the surface of the influenza virus.

Neuraminidase is an enzyme which forms a mushroom-shaped projection on the surface of an influenza virus particle.

Ribonucleoprotein (RNP) particle is a combination of ribonucleic acid (RNA) and protein.

Figure 1 - Month of peak influenza activity (%) from 1976-2007



Note: The peak week of influenza activity was defined as the week with the greatest percentage of positive respiratory specimens for influenza. The number of peak weeks in each month was then summed and a percentage calculated.

Source: US World Health Organization Collaborating Laboratory (CDC, unpublished data, 1976-2007)

days afterward.¹² As a result, children can easily spread the virus. To determine if the illness is actually influenza and not another respiratory pathogen, a lab test is often necessary to confirm.

The Facts about Influenza Vaccines

In temperate climates, seasonal influenza epidemics usually occur during winter months, from October until the end of January (see Figure 1). Vaccinations should take place each autumn before the influenza season starts, and as soon as vaccine supplies are available. Vaccination throughout the season, well into March and beyond, helps protect against late influenza outbreaks or a different strain of the virus.

The two types of influenza vaccine currently available in the United States are trivalent inactivated vaccine (TIV) and cold-adapted, live-attenuated influenza vaccine (LAIV). Both TIV and LAIV have demonstrated their effectiveness in preventing influenza infection among children and adults. Limited data suggest that LAIV provides greater protection than TIV for children. These results and other data comparing the efficacy of the two vaccines show LAIV to be superior to TIV in preventing influenza illness because it is well-tolerated in both young children and high-risk groups.¹³

Previously unvaccinated children ages

6 months to younger than 9 years should receive two doses of the influenza vaccine. The vaccine should be administered as soon as locally available during the influenza season.

An alternative to vaccination for individuals with immune deficiencies is chemoprophylaxis, a treatment that uses drugs to prevent infectious diseases, including antiviral drugs such as amantadine and rimantadine. Currently, the CDC recommends that health care providers do not prescribe these two

antivirals because influenza A strains are now resistant to these medications.

Influenza and Immunization

Broader routine influenza vaccination early in life is expected to decrease the incidence of sickness and number of deaths long-term. It may also reduce the financial costs attributable to influenza among all age groups. Evaluations of the impact of influenza vaccination programs must account for year-to-year variations in attack rates, illness severity, hospitalization costs

Thimerosal in Influenza Vaccines Not a problem for Children

Thimerosal is a preservative found in very minute amounts in some licensed forms of the influenza vaccine. Only a limited number of TIV vaccines are thimerosal-free, particularly for children under 4. In recent years, thimerosal has come under scrutiny because it is a mercury-containing preservative, but the CDC reports there is no evidence of harm from using low doses in vaccines.¹⁴ The benefits from influenza vaccination are far greater than the hypothetical risks associated with trace amounts of thimerosal.



and rates, and vaccine effectiveness.

Influenza vaccine schedules and effectiveness depend on how well the vaccine protects against circulating virus strains. Further research is needed to enhance current methods used to predict changes to the virus' strain. Efforts are underway to improve the vaccine development process, allowing for shorter intervals between identification of vaccine strains and vaccine production.

Further developments to improve influenza vaccines will increase the number of people able to receive the annual immunization. It is crucial that all individuals receive the correct type and number of influenza vaccine doses within the specified time period for the vaccination to be effective. Additional studies of other special populations, such as patients who are receiving mild to moderate immunosuppression (*e.g., methotrexate, low-dose corticosteroids*), also warrant further consideration. The development of a vaccine safe for infants under 6 months would also be valuable.

Annual Vaccination for All Children

Expanding the number of individuals vaccinated should be an important goal of universal annual influenza immunization in the United States. The Advisory Committee on Immunization Practices (ACIP), which advises the Centers for Disease Control and Prevention (CDC) on vaccine issues, is now recommending all children from 6 months through 18 years be immunized. This is to take effect no later than the 2009–2010 influenza season. ACIP recommendations become official after they are accepted by the director of the CDC and the Secretary of Health and Human Services and are published in the Morbidity and Mortality Weekly Report.

This latest recommendation targets all school-age children, a population that bears the greatest disease burden and is at a significantly increased risk of



TIV – The “flu shot”

TIV is an inactivated vaccine that contains killed viruses and therefore cannot produce signs or symptoms of the flu. The flu shot can cause only mild symptoms such as soreness in the arm, a low-grade fever and body aches. Both healthy people and those with chronic medical conditions can receive TIV. Since TIV cannot cause influenza illness, it is preferred over LAIV for close family, friends and caregivers of severely immunosuppressed individuals living in protected environments.¹⁵

The most common adverse side effects of TIV are soreness at the administration site and fever. Aspirin or any other over-the-counter medication containing salicylate should not be given as a pain reliever or fever reducer to any child or teen because of the increased risk of developing Reye's syndrome.⁹

LAIV – The nasal-spray flu vaccine

LAIV is a live vaccine, and shedding may occur producing mild symptoms or signs related to influenza. However, it is rare for small amounts of the virus to be transmitted to a non-vaccinated person. In these instances, illness has not been reported.

LAIV is given as a nose spray and is currently licensed as FluMist® for healthy individuals ages 2 through 49. Because LAIV is a live vaccine, the resulting immune response is more likely to achieve a level of immunity that would follow a natural influenza virus infection.

The potential risks and benefits of this vaccine should be considered for patients with compromised immune systems or risk factors that contraindicate the influenza vaccination.

While LAIV is currently licensed for healthy individuals 2 and older, it is not recommended for people with risk factors for influenza-illness-related complications. In a study that compared the effectiveness of the two vaccines in infants and young children, LAIV showed significantly better efficacy and safety than TIV for children between 1–4 years who had no history of wheezing or asthma.¹⁶ ♦

needing influenza-related medical care. In addition, evidence shows that reducing influenza transmission among children may reduce influenza in households and the community as a whole.

This new recommendation poses several challenges that must be addressed. First, the World Health Organization has noted that the 2008–2009 flu vaccine will include three completely new strains, which creates a hurdle to increasing vaccine production.

Overwhelmed health care facilities pose another challenge to immunizing more children. The ACIP has suggested alternative vaccination venues, such as schools and community clinics, but a system of patient record transfer to ensure the maintenance of accurate immunization records is necessary. It has also been suggested that influenza vaccines be given at physician offices without requiring a full medical checkup.

In addition, concerns have been raised about the cost-effectiveness of this new recommendation given the magnitude of coverage and overall cost of vaccines. But the benefits of vaccination would help prevent outpatient visits and antibiotic use resulting from the flu. Reduced absenteeism among students and working parents along with fewer influenza cases and hospitalizations could also be expected. However, more comprehensive outcome data on the direct and indirect economic costs and benefits of childhood immunization are required.

By setting the implementation date for the 2009–2010 season, the CDC hopes to allow sufficient time for implementation and closer examination of logistics of this comprehensive undertaking. ♦

About the Author and his assistants...

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Henry H. Bernstein, D.O. is the chief of General Academic Pediatrics at Children's Hospital at Dartmouth and professor of Pediatrics at Dartmouth Medical School. For the previous 10 years, he served as associate chief of the Division of General Pediatrics at Children's Hospital Boston and associate professor of Pediatrics at Harvard Medical School. Dr. Bernstein is certified by the American Board of Pediatrics.



Dr. Bernstein is a member of the American Academy of Pediatrics' (AAP) Committee on Infectious Diseases and is responsible for developing and revising AAP guidelines for control of infectious diseases in children, including influenza. He is also the AAP liaison to the CDC Advisory Committee on Immunization Practices' Influenza Workgroup.

Dr. Bernstein conducts primary care clinical research while maintaining an active clinical primary care practice. He regularly shares knowledge and expertise by educating the public through writing for academic and health information Web sites as well as regular participation in media interviews on a variety of pediatric topics.

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