ABSTRACT

Influenza is an important cause of morbidity and mortality in the United States and across the globe. Improving influenza vaccination rates among children will help to reduce disease burden, not only by direct effects on vaccine recipients, but also by indirect effects on household contacts, peers, and significant others—some of whom may be at risk for serious complications from influenza. Although influenza infection is responsible for high rates of school and work absenteeism, outpatient visits, hospitalizations, and even deaths, current vaccination rates are suboptimal. Otherwise healthy individuals may fail to appreciate the potential for serious sequelae from influenza infection and may harbor misconceptions about the vaccination. Public health practitioners may be instrumental in educating parents and policy makers to correct these misconceptions and help to achieve target influenza vaccination rates by overcoming barriers to immunization. This article reviews current Advisory Committee on Immunization Practices recommendations for influenza vaccination and various vaccine options, and suggests practical strategies for public health practitioners, including government-sponsored vaccine programs such as the Vaccines for Children Program.

Unlike adult infections, influenza’s infectious period in children can be for 10 or more days after the onset of symptoms. They can also shed virus during the asymptomatic prodrome by 1 day. Symptoms of uncomplicated influenza among children include fever, malaise, headaches and body aches, rhinitis, sore throat, cough, otitis media, nausea, and vomiting. Furthermore, some children can suffer from pneumonia, febrile seizures, and other severe respiratory, cardiac, and neurologic complications, such as encephalitis and encephalopathy.

Several studies show that influenza causes high rates of hospitalizations among children younger than 2 years of age. Most recently, Poehling et al conducted a prospective, population-based investigation of hospitalizations attributable to laboratory-confirmed influenza. A total of 3359 children hospitalized with acute respiratory tract infections or fever were followed—160 of which were confirmed to have influenza. Eighty percent of the children hospitalized for influenza and its complications were younger than 2 years old. The average annual rate of hospitalization associated with influenza was 0.9 per 1000 children. These children sometimes required admission to the intensive care unit, administration of oxygen, chest X-rays, and blood, urine, and/or cerebrospinal fluid cultures. Coinfection with bacteria or noninfluenza viruses also were found on occasion.

A significant disease burden of influenza in children is its potential to cause death, particularly among children younger than 2 years of age. Bhat et al reviewed influenza-associated deaths among children in the United States between 2003 and 2004. The authors found 153 influenza-associated deaths among children reported by 40 state health departments. The median age of the children was 3 years, and 96 (63%) were younger than 5 years old. Forty-seven children (31%) died outside a hospital setting, and 45 (29%) died within 3 days after the onset of illness. Although 33% had an underlying condition recognized to increase the risk of influenza-related complications, nearly half (47%) did not have any underlying condition. The mortality rate was highest among children younger than 6 months of age (0.88 per 100 000 children). In 2004 to 2005, there were 44 deaths and, in 2005 to 2006, there were 48 deaths attributed to influenza. Surveillance data for influenza-related pediatric deaths as of February 15, 2007, includes 15 deaths: 10 children were 5 years of age or older (9 were unvaccinated; 3 had underlying conditions that might have contributed to the severity; 5 had no known underlying conditions; 2 had unknown heath histories).

In short, influenza is the leading cause of vaccine-preventable morbidity and mortality in the United States. It is responsible for up to 60 million infections per year. Influenza results in as many as 95 clinic visits and 27 emergency department visits per 1000 children per year, of which approximately 1 child in 1000 will need to be hospitalized. Furthermore, it should be emphasized that influenza is frequently misdiagnosed or undiagnosed, and is likely responsible for larger numbers of victims. Improved vaccination rates, particularly among children who suffer high complication rates, are needed to stem the tide of disease, disability, and death.

**The Role of Influenza Vaccination**

**Current Vaccination Rates are Suboptimal**

Data collected from the 2004 Behavioral Risk Factor Surveillance System survey, a monthly tele-
phone survey of the US civilian, noninstitutionalized population with an average of 20,000 completed surveys per month show that current influenza vaccination rates for children are suboptimal. For example, 48% of children aged 6 to 23 months received at least 1 dose of influenza vaccine; however, only 37% of children aged 6 to 23 months and 27% of children aged 2 to 17 years with high-risk conditions were vaccinated for the 2005 influenza season by November of 2004, compared to 8.9% of children aged 2 to 17 years with no high-risk condition.\(^1\)\(^8\)\(^9\)

Data obtained from the 2005 National Immunization Survey (NIS), which provides estimates of vaccination coverage among noninstitutionalized children aged 19 to 35 months based on household interviews, via telephone, and their healthcare providers’ immunization records, show that influenza vaccination rates are even lower. Among 17,563 children, 33% received 1 or more doses of influenza vaccine and only 17.8% were fully vaccinated according to guidelines provided by the Centers for Disease Control and Prevention’s (CDC) Advisory Committee on Immunization Practices (ACIP).\(^2\)\(^0\)

**Barriers to Improving Influenza Immunization Rates**

The Behavioral Risk Factor Surveillance System survey participants with an unvaccinated child aged 6 to 23 months gave the following explanations for not vaccinating their children: 63% reported that they thought the vaccine was not needed, 8% reported that they tried but could not obtain vaccination for the child, 1.0% thought the child was ineligible for influenza vaccination, and 0.3% said they were saving the vaccine for those who needed it. Data from parents/caregivers whose children (aged 2–17 years) had a high-risk underlying condition were equally troubling: 38% reported that they thought vaccination was not needed, 14% reported that they tried but could not obtain vaccination, 13% thought their child was not eligible, and 10% said they were saving the vaccine for others.\(^1\)\(^8\) In a study of the effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children, Neuzil et al note that one obstacle to the use of influenza vaccines in children is “the perception that influenza is a benign disease in children.” The authors point out that “data on mortality, commonly used to estimate the effect of influenza on adults, are insensitive indicators of the effect of influenza on children,” and that children have higher attack rates, transmission rates, and suffer more morbidity from cardiopulmonary complications than adults.\(^1\)\(^0\)

Other studies of barriers to childhood immunizations cite a variety of factors, including socioeconomic, operational, and logistics issues (ie, substance abuse, lack of motivation, financial and transportation issues, complex schedules causing forgetfulness or an inability to get children to the clinic for immunizations, childcare and work schedules, past experiences with injections, and knowledge and awareness deficits and misunderstandings about the importance of immunizations). Sometimes parental beliefs lead to active choices not to immunize. These antivaccine beliefs include mistrust of the sources of health information, the impression that the risks of vaccine-preventable diseases are low, or that vaccine-preventable diseases such as influenza are manageable, a preference to utilize alternative medicine, and/or reliance on religious beliefs and interventions. Fears may prevent some parents from vaccinating their children. Parents may harbor fears that their child could contract diseases from vaccines. There may also be fears about side effects, the number of injections, and the trauma of the immunization process itself.\(^2\)\(^1\)

Finally, in their investigation, Niederhauser and Markowitz cite several operational barriers to adequate vaccination of children, including a lack of availability of appointments and vaccines, no reminder systems, insurance issues, and obstructive clinic policies.\(^2\)\(^1\)

In partial response to the financial and organizational barriers to immunization of children and prompted by a large measles epidemic between 1989 and 1991, the Vaccines for Children (VFC) Program was launched in 1994 after its creation by an Act of Congress (the Omnibus Budget Reconciliation Act) in 1993. It is one of several ways that influenza and other childhood vaccines are financed. Health insurance covers most recommended vaccines. Federal grants (authorized by Section 317 of the Public Health Service Act) along

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**Current influenza vaccination rates are suboptimal.** One obstacle is “the perception that influenza is a benign disease in children.” Children have higher attack rates, transmission rates, and suffer more morbidity from cardiopulmonary complications than adults. However, barriers to childhood immunization include socioeconomic, operational, and logistics issues.
with state and local funding help to purchase vaccine for those not covered by insurance or the VFC program.

**Current and Emerging Vaccination Options**

**ACIP Recommendations for Administration of Annual Influenza Vaccine to Children**

The 2006 Recommendations for Prevention and Control of Influenza by the ACIP that relate directly to childhood immunization specify inclusion of children aged 24 to 59 months and their household contacts and out-of-home caregivers and highlight the importance of administering 2 doses of influenza vaccine for children aged 6 months to younger than 9 years who were previously unvaccinated (Table 1). This change extends prior ACIP recommendations to include all children aged 6 to 59 months as being recipients of annual influenza vaccine. In addition, ACIP specifies that all children aged 6 months to younger than 9 years who have not been previously vaccinated at any time with either live, attenuated influenza vaccine (LAIV) or trivalent inactivated influenza vaccine (TIV) should receive 2 doses of vaccine.

If a child aged 6 months to younger than 9 years received influenza vaccine for the first time during a previous season but did not receive a second dose of vaccine within the same season, then only 1 dose of vaccine should be administered in the current season. Prior ACIP recommendations also call for vaccination of children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma; children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by HIV); children who have any condition (eg, cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration; and children and adolescents (aged 6–18 years) who are receiving long-term aspirin therapy and, therefore, might be at risk for experiencing Reye syndrome after developing influenza infection. Inactivated influenza vaccine is recommended for the following broader pediatric group at increased risk for developing severe complications from influenza:

- Children aged 6–23 months

Inactivated influenza vaccine is recommended for the following broader pediatric group because of an increased risk for influenza-associated clinic, emergency department, or hospital visits, particularly if they have a high-risk medical condition:

- Children aged 24–59 months

Inactivated or live, attenuated influenza vaccine is recommended for the following persons who live with or care for persons at high risk for developing influenza-related complications, unless contraindicated, to prevent transmission to persons identified preview:

- Healthy household contacts and caregivers of children aged 0–59 months and persons at high risk for developing severe complications from influenza

**Current Vaccine Options: TIV and LAIV**

Currently, there are both TIV and LAIV options available. TIV and LAIV consist of 3 inactivated

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**Table 1. ACIP Recommendations for Annual Influenza Immunization 2006–2007 Season**

<table>
<thead>
<tr>
<th>Vaccination with inactivated influenza vaccine is recommended for the following special pediatric groups who are at increased risk for developing complications from influenza:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions</td>
</tr>
<tr>
<td>• children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma (hypertension is not considered a high-risk condition)</td>
</tr>
<tr>
<td>• children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by HIV)</td>
</tr>
<tr>
<td>• children who have any condition (eg, cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration</td>
</tr>
<tr>
<td>• children and adolescents (ages 6 months–18 years) who are receiving long-term aspirin therapy and, therefore, might be at risk for experiencing Reye syndrome after developing influenza infection</td>
</tr>
</tbody>
</table>

Inactivated influenza vaccine is recommended for the following broader pediatric group at increased risk for developing severe complications from influenza:

- Children aged 6–23 months

Inactivated influenza vaccine is recommended for the following broader pediatric group because of an increased risk for influenza-associated clinic, emergency department, or hospital visits, particularly if they have a high-risk medical condition:

- Children aged 24–59 months

Inactivated or live, attenuated influenza vaccine is recommended for the following persons who live with or care for persons at high risk for developing influenza-related complications, unless contraindicated, to prevent transmission to persons identified preview:

- Healthy household contacts and caregivers of children aged 0–59 months and persons at high risk for developing severe complications from influenza

- Healthcare workers

Data from Advisory Committee on Immunization Practices et al. Reprinted with permission from Wright PF. Semin Pediatr Infect Dis. 2006;17:200-205.
influenza viruses, 2 different influenza type A strains and 1 strain of influenza type B as recommended by the US Public Health Service. Similarities between the vaccines include their cultivation in hens’ eggs, and their strain variation from year to year based on global surveillance, thus requiring revaccination each season. (Even when the current vaccines contain antigens administered in previous seasons, annual vaccination with the current vaccine is recommended because immunity may decline during the year after vaccination.) However, there are also differences between the 2 vaccine types, including postulated mechanisms of action. The protection afforded by the TIV is related primarily to serum antibodies, with little evidence of induction of mucosal immunity, at least in the absence of prior natural priming. By contrast, LAIV induces an immune response, including mucosal antibodies, via viral replication.

An important difference between the 2 vaccines is that TIV, because it contains killed virus, cannot produce signs and symptoms of influenza, whereas LAIV contains live, attenuated virus and thus can produce mild upper respiratory or systemic symptoms. TIV is approved for use in people older than 6 months by the US Food and Drug Administration (FDA) and recommended for all children aged 24 to 59 months because of their increased risk of influenza-related clinic, emergency room, and/or hospital visits, in addition for children with high-risk conditions as noted earlier in this article. LAIV is approved by the US FDA for use among healthy children aged 5 years and older, and, according to the 2006 MMWR published by the CDC/ACIP, it can be administered as soon as it is available and throughout the season. This early vaccination opportunity may help protect more children and may help improve compliance rates in vaccine-naïve children that require 2 doses. Recently, the US FDA’s advisory board for immunizations, the Vaccines and Related Biological Products Advisory Committee, voted in favor of expanding the indications for use of LAIV to include children younger than 5 years of age. The committee voted that the data demonstrate the efficacy of this vaccine in children 6 to 59 months of age. In addition, the committee voted in favor of the risk-benefit profile of LAIV in children 12 to 59 months of age without a history of wheeze, and also in children 24 to 59 months of age regardless of a history of wheeze. The final decision by the US FDA with regard to approval of this expanded indication for children younger than 5 years of age is still pending. (For more information regarding the status of licensure and recommendations for new vaccines, visit the American Academy of Pediatrics Web site at http://aapredbook.aappublications.org/news/vaccstatus.shtml.)

The other major difference between the 2 vaccine types is the delivery route: TIV is administered via intramuscular injection, whereas LAIV is administered intranasally (Table 2; Sidebar).

Emerging Vaccination Options: CAIV-T

A new formulation of the LAIV that will also be delivered via an intranasal spray has been undergoing clinical trials, and has been approved by the US FDA. Cold adapted influenza vaccine trivalent (CAIV-T) is a refrigerator-stable formulation of influenza virus vaccine live, intranasal, the previous intranasal LAIV that required freezer storage. The US FDA is evaluating CAIV-T for use in children younger than 59 months of age. The results of phase III clinical trials were recently published (Sidebar).

Other influenza vaccine technology is on the horizon. This includes genetically engineered influenza virus vaccines that utilize reverse genetics techniques that will avoid the use of eggs; quadrivalent vaccines to include more strains; novel adjuvants to enhance vaccine response; live virus vaccines with altered non-structural protein 1 genes; replication-defective vaccines; utilizing new modes of delivery such as immunostimulant/transdermal patches; and H5N1 containing vaccines for pandemic influenza, among others. In summary, there are several products on the market and in various stages of development.

Currently, there are both TIV and LAIV options available. A new formulation of LAIV that is refrigerator stable, CAIV-T, is being evaluated by the US FDA for use in individuals younger than 5 years of age.

Overcoming Immunization Barriers: Practical Strategies for Public Health Professionals

Data support the fact that influenza is a significant cause of morbidity and mortality in our society and that most influenza cases arise in children and younger adults, who not only become ill themselves but also transmit the virus to others resulting in illness and lost
productivity. School children have the highest annual attack rates with influenza ranging as high as 30% to 50%;25 however, they respond well to influenza vaccine, which serves not only to reduce illness and school absenteeism but reduce spread of the virus and exposure of high-risk individuals in the community.26 Despite this, reported vaccination rates are low among children (with only 18% receiving ≥1 doses of vaccine, according to the 2004 NIS), and also among healthcare providers themselves (42% report being vaccinated).1 Certainly, these percentages do not point toward levels that would allow achievement of herd immunity. Thus, it is essential for public health officials to communicate the urgency of annual influenza vaccination to parents and healthcare providers alike.

**DISEASE AWARENESS CAMPAIGNS—KEY PARTNERS, KEY TACTICS, AND KEY MESSAGES**

In their recommendations, the ACIP advises healthcare providers, those planning organized campaigns, and state and local health agencies to develop plans for expanding outreach and infrastructure to vaccinate more persons. Aside from raising awareness of the dangers of influenza, education is also essential to dispel

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**Table 2. Comparison of Trivalent Inactivated Influenza Vaccine and Live, Attenuated Influenza Vaccine (LAIV)**

<table>
<thead>
<tr>
<th>Factor</th>
<th>LAIV</th>
<th>Inactivated Influenza Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of administration</td>
<td>Intranasal spray</td>
<td>Intramuscular injection</td>
</tr>
<tr>
<td>Type of vaccine</td>
<td>Live virus</td>
<td>Killed virus</td>
</tr>
<tr>
<td>No. of included virus strains</td>
<td>3 (2 influenza A, 1 influenza B)</td>
<td>3 (2 influenza A, 1 influenza B)</td>
</tr>
<tr>
<td>Vaccine virus strains updated</td>
<td>Annually</td>
<td>Annually</td>
</tr>
<tr>
<td>Frequency of administration</td>
<td>Annually</td>
<td>Annually</td>
</tr>
<tr>
<td>Approved age and risk groups*</td>
<td>Healthy persons aged 5–49 years</td>
<td>Persons aged ≥6 months</td>
</tr>
<tr>
<td>Interval between 2 doses recommended for children aged 6 months to 9 years who are receiving influenza vaccine for the first time</td>
<td>6–10 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Can be administered to family members or close contacts of immunocompromised persons not requiring a protected environment</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Can be administered to family members or close contacts of immunocompromised persons requiring a protected environment (e.g., hematopoietic stem cell transplant recipient)</td>
<td>Inactivated influenza vaccine preferred</td>
<td>Yes</td>
</tr>
<tr>
<td>Can be administered to family members or close contacts of persons at high risk but not severely immunocompromised</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Can be simultaneously administered with other vaccines</td>
<td>Yes†</td>
<td>Yes‡</td>
</tr>
<tr>
<td>If not simultaneously administered, can be administered within 4 weeks of another live vaccine</td>
<td>Prudent to space 4 weeks apart</td>
<td>Yes</td>
</tr>
<tr>
<td>If not simultaneously administered, can be administered within 4 weeks of an inactivated vaccine</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Populations at high risk for complications of influenza infection include persons aged >65 years; residents of nursing homes, and other chronic care facilities that house persons with chronic medical conditions; adults and children with chronic disorders of the pulmonary or cardiovascular systems; adults and children with chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression; children and adolescents receiving long-term aspirin therapy (at risk for Reye syndrome after wild-type influenza infection); pregnant women; and children aged 6–59 months.

†No data are available regarding effect on safety or efficacy.

‡Inactivated influenza vaccine coadministration has been evaluated systematically only among adults with pneumococcal polysaccharide vaccine. Reprinted from Advisory Committee on Immunization Practices et al. MMWR Recomm Rep. 2006;55:1-42.
myths, such as that influenza vaccine can cause illness or that influenza is not a serious illness if contracted by unvaccinated people. Key messages that need to be communicated include the potential deadliness of influenza (among all age groups), and the fact that outbreaks are disruptive and costly compared to vaccinations that are cost effective, safe, and effective (Table 3).

Public health practitioners can utilize a number of tactics and key partners in the community to raise awareness and achieve higher vaccination rates. Key partners include medical and professional societies (eg, the American Academy of Pediatrics), school systems, faith and community-based organizations, members of the business community, VFC providers, and public health agencies themselves. Through these organizations, community outreach and continuing education programs may be developed and implemented. Efforts may be made to emphasize the importance of seasonal influenza vaccination on the agenda of appropriate community and governmental organizations. To assure funding, these must include city councils and/or state legislatures to educate policy makers.

VACCINES FOR CHILDREN PROGRAM

The VFC program provides free doses of influenza vaccine to qualifying children who visit a VFC-enrolled provider. VFC is overseen at the national level by the CDC, Coordinating Center for Infectious Disease, Immunization Services Division, and at the state level by state public health agencies. States establish enrollment, manage vaccine supply and distribution, and oversee providers, including making site visits. Vaccine doses are provided free to enrolled healthcare providers

Table 3. Disease Awareness Key Messages

- Influenza is deadly
- Influenza causes morbidity and mortality across all age groups
- Outbreaks are disruptive and costly
- The vaccines are safe and effective
- Use of the vaccines is cost effective

continued on page 205
who may charge an administrative fee. (Providers cannot deny vaccine to those unable to pay the administrative fee.) States, territories, the District of Columbia, and eligible programs enroll physicians who serve qualifying patients up to and including age 18 years. Eligible children include those who meet the criteria for Medicaid, have no health insurance, are Native American or Alaskan Native, and, in some settings, those who have health insurance that does not cover immunizations.

If a child has health insurance that does not cover vaccines, he or she must receive the immunization from either a Federally Qualified Health Center (FQHC) or Rural Health Clinic (RHC). FQHCs include community and migrant centers, health facilities that cater to specialized populations such as the homeless, Native Americans, or those located within public housing facilities. There are approximately 1400 designated FQHCs nationwide. RHCs are outpatient primary care programs for rural underserved communities and are staffed by nurse practitioners, certified nurse midwives, and/or physician assistants. The 1600 centers located across the United States provide comprehensive primary health services to medically underserved and disadvantaged populations in regions that experience cultural, financial, or geographic barriers to healthcare access. In addition to FQHCs and RHCs, VFC providers may include private doctor’s offices, private clinics, hospitals, public or community health centers, and some schools with a total of approximately 50,000 locations nationwide.

The ACIP, a federal committee, also plays a role in the VFC Program. ACIP has the sole authority to add vaccines to the program and to make recommendations regarding vaccine administration. According to Vaccine Manufacturers Biologic Surveillance Data for 2005, 43% of all childhood vaccine doses are distributed by the VFC program (Figure 2).

METHODS FOR IMPROVING VACCINATION RATES

Because the VFC program permits most eligible children to receive vaccination services in their “medical home” (the site where they usually receive primary care services) rather than being referred out to public health facilities, the barrier of locating and reaching another facility for services is removed. In addition, children receive immunizations in a setting that parents trust and are familiar. Providers also benefit from participation in the VFC program: they can offer influenza vaccine to their patients when supplies

Continued from page 204

vaccination site that is typically mild and self-limited (lasting <2 days), reported in 10% to 64% of patients.1 Fever, malaise, myalgia, and other systemic symptoms can occur after vaccination with inactivated vaccine and most often affect persons who have had no previous exposure to the influenza virus antigens in the vaccine (eg, young children).36 Furthermore, a population-based study of TIV safety in 8476 children aged 6 to 23 months and 215,600 children aged younger than 18 years indicated no vaccine-associated adverse events that had a plausible relationship to vaccination.39 However, rare, serious adverse events have been reported, including immediate, presumably allergic reactions (hives, angioedema, allergic asthma, and systemic anaphylaxis) that are more likely to have been as a result of a hypersensitivity to eggs rather than thimerosal, a vaccine preservative. Therefore, TIV is contraindicated in children known to have anaphylactic hypersensitivity to eggs or other components of TIV without first consulting their healthcare provider.1 The risk of developing Guillain-Barré syndrome (GBS) as a consequence of TIV is estimated to be approximately 1 in 1 million doses, with no specific data for the pediatric age groups reported; however, the risk of severe influenza outweighs the risk of GBS.3,21

LIVE, ATTENUATED INFLUENZA VACCINE

Live, attenuated influenza vaccine (LAIV) is administered intranasally after being thawed, but must be stored frozen (at or below -15°C).40 LAIV is indicated for healthy children and adolescents aged 5 to 17 years and healthy adults aged 18 to 49 years; therefore, VFC recipients may also receive LAIV up to age 19 years.1 Children aged 5 to younger than 9 years who were previously unvaccinated with either LAIV or TIV should receive 2 doses of LAIV 6 to 10 weeks apart—with the latter dose preferably being administered before the onset of influenza season. Children aged 9 years or older and previously vaccinated children between 5 and 8 years of age should receive 1 dose of LAIV. Similar to TIV, LAIV can be administered to children with minor acute illnesses; however, if there is likelihood that nasal congestion may interfere with vaccine delivery into the nasopharyngeal mucosa then vaccination should be deferred.1

Continued on page 206
The immunogenicity of LAIV in children has been evaluated and, although its mechanism of action is not completely understood, it appears to involve both serum and nasal secretory antibodies.\textsuperscript{1,41-46} Efficacy studies of healthy children include a randomized, double-blind, placebo-controlled trial among 1602 healthy children initially aged 15 to 71 months who were evaluated over 2 influenza seasons to assess the efficacy of trivalent LAIV against culture-confirmed influenza. In season 1, when vaccine and circulating virus strains were well matched, efficacy was 93\% for participants who received 2 doses of LAIV. In season 2, when the influenza A strain was not well matched with circulating virus strains, efficacy was 86\% overall. The vaccine was 92\% efficacious in preventing culture-confirmed influenza during the 2-season study. Other results included a 27\% reduction in febrile otitis media and a 28\% reduction in otitis media with concomitant antibiotic use. Receipt of LAIV also resulted in 21\% fewer febrile illnesses.\textsuperscript{1,45,46}

There have been multiple clinical trials to assess the safety of LAIV, including a population of 4000 healthy children aged 5 to 17 years. The incidence of adverse reactions, including conditions that could be considered possible complications of live, attenuated influenza virus immunization, was not statistically different among vaccine recipients compared with children who received placebo. LAIV does not cause influenza among children. Overall serious adverse events requiring medical attention occurred less than 1\% of the time.\textsuperscript{1} The first dose of the vaccine resulted in a slightly higher incidence (not statistically significant) of minor side effects among vaccine recipients, such as runny nose or nasal congestion, headache, vomiting, fever, and body aches. However, these were self-limited.\textsuperscript{1,41,43,45,46}

Because data indicated an increase in asthma or reactive airway disease events in children between the ages of 1 and 5 years, approval was not initially sought in children younger than age 5 years.\textsuperscript{47,48} Some studies of a new formulation of the vaccine, the cold adapted influenza vaccine trivalent (CAIV-T), seem to indicate that it may be well tolerated among children with asthma.\textsuperscript{49,50} However, because of insufficient data regarding the use of LAIV among high-risk individuals (eg, immunocompromised persons and those with respiratory diseases), the ACIP does not recommend vaccinating these populations with LAIV.\textsuperscript{1}

*See text for potential updated indications and contraindications.
†These persons should receive inactivated influenza vaccine.
GBS = Guillain-Barré syndrome, LAIV = live, attenuated influenza vaccine.
Continued from page 206

COLD ADAPTED INFLUENZA VACCINE TRIVALENT

Cold adapted influenza vaccine trivalent is similar
to LAIV with the exception that it may be stored as a
refrigerated rather than frozen formulation. Its dosage,
schedule, and delivery route resemble that of LAIV.
Phase III clinical studies of CAIV-T evaluated children
6 to 59 months of age, without a recent episode of
wheezing illness or severe asthma, randomly assigning
them to receive either CAIV-T or TIV in a double-
blind manner. Safety data were available for 8352 chil-
dren, and 7852 children completed the study according
to the protocol revealing no statistically significant dif-
fERENCE in the incidence of adverse events between the 2
groups. There were 54.9% fewer cases of cultured-con-
firmed influenza in the group that received CAIV-T
than in the group that received TIV (153 vs 338 cases).
Better efficacy of CAIV-T was observed for both anti-
genically well-matched and drifted viruses.

Among previously unvaccinated children, wheezing
within 42 days after the administration of dose 1 was
more common with CAIV-T than with TIV, primarily
among children 6 to 11 months of age; in this age
group, 12 more episodes of wheezing were noted with-
in 42 days after receipt of dose 1 among recipients of
live attenuated vaccine (3.8%) than among recipients of
inactivated vaccine (2.1%). Rates of hospitalization
for any cause during the 180 days after vaccination were
also higher in this group (CAIV-T recipients 6–11
months of age, 6.1%) than among the recipients of TIV
(2.6%). However, the authors of the study note that
further study is warranted to evaluate the risks and ben-
EFITS of CAIV-T compared to TIV because children 12
months or older who took the live attenuated vaccine
without prior history of wheezing had lower rates of
hospitalization than those children who were immu-
nized with TIV, and children younger than 12 months
of age who were given TIV had lower efficacy than
those given CAIV-T. They suggest future studies to
evaluate a combined schedule of TIV for younger chil-
dren (<1 year old) followed by CAIV-T in older chil-
dren to maximize both safety and protection.51

The VFC program permits most eligible children to
receive vaccination services in their “medical home.”
Ongoing challenges for this and all vaccination pro-
grams include flexibility in scheduling and capacity,
supply delays or shortages, unpredictable public
demand, and communication with the public.17

Researchers have identified various barriers to
immunization, with different barriers existing within
different communities, with different healthcare
providers, and with different healthcare systems. The
first step to reducing these barriers is characterizing
(through surveys and focus groups) and targeting the
unique and specific barriers that exist within a particu-
lar community.21 On the practitioner level, clarifying
misinformation regarding influenza disease and
influenza vaccine will help allay parental fears and
encourage more parents to immunize their children.21
On the policy-maker level, increased funding is neces-
SARY, not only for vaccinations themselves but also for
personnel to implement awareness campaigns, vaccina-
tion programs such as VFC, and their quality assurance
programs such as Assessment, Feedback, Incentives,
and eXchange of Information (AFIX). AFIX is a part of
the VFC program that consists of providing assessment
and feedback of a practitioner’s vaccination coverage
levels, making recommendations and providing incen-
tives for improvement, and exchanging information
among the providers within their community with regard to performance and “best practices.” Programs such as AFIX and VFC, implementing vaccine reminder systems, and partnering with insurance companies for children who are covered for their immunizations will all go a long way to improve influenza vaccination rates and quality of care.

Researchers have identified various barriers to immunization. The first step to reducing these barriers is identifying and targeting the unique barriers that exist within a particular community—on the practitioner and policy-maker levels.

CONCLUSIONS

Overcoming barriers is an important step in keeping with trends that seem to point toward universal vaccination in the near future to reduce overall morbidity and mortality from influenza. However, criteria that need to be considered in expanding current influenza vaccination recommendations include safety, effectiveness, and the indirect benefits of preventing illness among contacts. These benefits must also be balanced against the feasibility of implementation, cost effectiveness, and the vaccine supply available. For example, many older children are already recommended for annual vaccination based on their status as household contacts of younger children, persons at high risk, or the elderly. Opportunities to educate and vaccinate older children and adolescents include back-to-school, adolescent wellness, and/or sports physical visits. Certainly routine vaccination of 5- to 18-year-old children would reduce morbidity and mortality for these children and their contacts, but might create logistical and operational challenges in terms of implementation. This may also stress vaccine supply and distribution systems if shortages or delays are present in that particular season. The VFC program offers a unique opportunity to reach many of these children within an existing infrastructure. 37

Several promising developments seem to be on the horizon in terms of new vaccine technologies that will hopefully enhance supply availability, effectiveness, and make immunization more palatable to those who still resist due to issues such as safety concerns or needing to take an injection. Public health officials, health-care practitioners, researchers, and parents working together could perhaps see influenza go the way of smallpox.

Trends seem to point toward universal vaccination in the near future to reduce overall morbidity and mortality from influenza.

REFERENCES