



Recommendations for Prevention and Control of Influenza in Children, 2015–2016

Committee on Infectious Diseases

abstract

The purpose of this statement is to update recommendations for routine use of seasonal influenza vaccine and antiviral medications for the prevention and treatment of influenza in children. The American Academy of Pediatrics recommends annual seasonal influenza immunization for *all* people 6 months and older, including all children and adolescents. Highlights for the upcoming 2015–2016 season include the following:

1. Annual universal influenza immunization is indicated with either a trivalent or quadrivalent vaccine (no preference).
2. The 2015–2016 influenza A (H3N2) and B (Yamagata lineage) vaccine strains differ from those contained in the 2014–2015 seasonal vaccines.
 - a. Trivalent vaccine contains an A/California/7/2009 (H1N1) pdm09-like virus; an A/Switzerland/9715293/2013 (H3N2)-like virus; and a B/Phuket/3073/2013-like virus (B/Yamagata lineage).
 - b. Quadrivalent vaccine contains an additional B virus (B/Brisbane/60/2008-like virus [B/Victoria lineage]).
3. The dosing algorithm for administration of influenza vaccine to children 6 months through 8 years of age has been updated to reflect that virus strains in the vaccine have changed from last season.

With an increasing number of organizations mandating influenza vaccine, all health care personnel should receive influenza vaccine each season and fully promote influenza vaccine use and infection-control measures. In addition, pediatricians should promptly identify children clinically presumed to have influenza disease for rapid antiviral treatment, when indicated, to reduce morbidity and mortality.

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INTRODUCTION

The American Academy of Pediatrics (AAP) recommends annual seasonal influenza immunization for *all* people 6 months and older, including children and adolescents, during the 2015–2016 influenza season. In

addition, special effort should be made to vaccinate people in the following groups:

- All children, including infants born preterm, who are 6 months and older (based on chronologic age) with conditions that increase the risk of complications from influenza (eg, children with chronic medical conditions, such as asthma, diabetes mellitus, hemodynamically significant cardiac disease, immunosuppression, or neurologic and neurodevelopmental disorders);
- American Indian/Alaska Native children;
- All household contacts and out-of-home care providers of the following:
 - children with high-risk conditions; and
 - children younger than 5 years, especially infants younger than 6 months;
- All health care personnel (HCP);
- All child care providers and staff; and
- All women who are pregnant, are considering pregnancy, are in the postpartum period, or are breastfeeding during the influenza season.

KEY POINTS RELEVANT FOR THE 2015–2016 INFLUENZA SEASON

1. **Annual seasonal influenza vaccine is recommended for all people 6 months and older, including children and adolescents, during the 2015–2016 influenza season.** It is important that household contacts and out-of-home care providers of children younger than 5 years, especially infants younger than 6 months, and children of any age at high risk of complications from influenza (eg, children with chronic medical conditions, such as asthma,

diabetes mellitus, hemodynamically significant cardiac disease, immunosuppression, or neurologic and neurodevelopmental disorders) receive the annual influenza vaccine. In the United States, more than two-thirds of children younger than 6 years and almost all children 6 years and older spend significant time in child care or school settings outside the home. Exposure to groups of children increases the risk of contracting infectious diseases. Children younger than 2 years are at elevated risk of hospitalization and complications attributable to influenza. School-aged children bear a large influenza disease burden and have a significantly higher chance of seeking influenza-related medical care compared with healthy adults. Reducing influenza virus transmission (eg, appropriate hand hygiene and respiratory hygiene/cough etiquette) among children who attend out-of-home child care or school has been shown to decrease the burden of childhood influenza and transmission of influenza virus to household contacts and community members of all ages.

2. The 2014–2015 season was moderately severe, with overall high levels of outpatient illness, influenza-associated hospitalization, and pediatric deaths. Influenza A (H3N2) viruses predominated overall, with 81% being drifted strains. The 2009 influenza A (H1N1) pandemic (pH1N1) viruses and influenza B viruses also were reported in the United States later in the influenza season. As of May 30, 2015, a total of 142 laboratory-confirmed influenza-associated pediatric deaths were reported to the Centers for Disease Control and Prevention (CDC) during the 2014–2015

influenza season. Of the 142 deaths, 109 were associated with influenza A viruses, and 29 deaths were associated with influenza B viruses. Two deaths were associated with an undetermined type of influenza virus, and 1 death was associated with dual infection with both influenza A and B viruses. Although children with certain conditions are at higher risk of complications, 64% of the deaths occurred in children with no high-risk underlying medical condition. Among children hospitalized with influenza and for whom medical chart data were available, ~44% had no recorded underlying condition, whereas 26% had underlying asthma or reactive airway disease (Fig 1). In past years, 90% of pediatric deaths have occurred in unvaccinated children.

3. Pediatric hospitalizations and deaths caused by influenza vary by the predominant circulating strain and often between the previous season and the next (Table 1). When an H3N2 virus predominates, higher rates of influenza hospitalization and deaths have been documented. The impact tends to be magnified when circulating strains do not match vaccine strains, as in the 2014–2015 season. Furthermore, in the past 10 seasons, the rates of hospitalization for children younger than 5 years have always exceeded the rates for children 5 through 17 years of age.
4. Vaccine effectiveness can vary depending on match/mismatch of circulating virus with vaccine strains, vaccine product, and age and immune state of patients. For the 2014–2015 influenza season, vaccine effectiveness for all ages against influenza B viruses, which were mostly well-matched

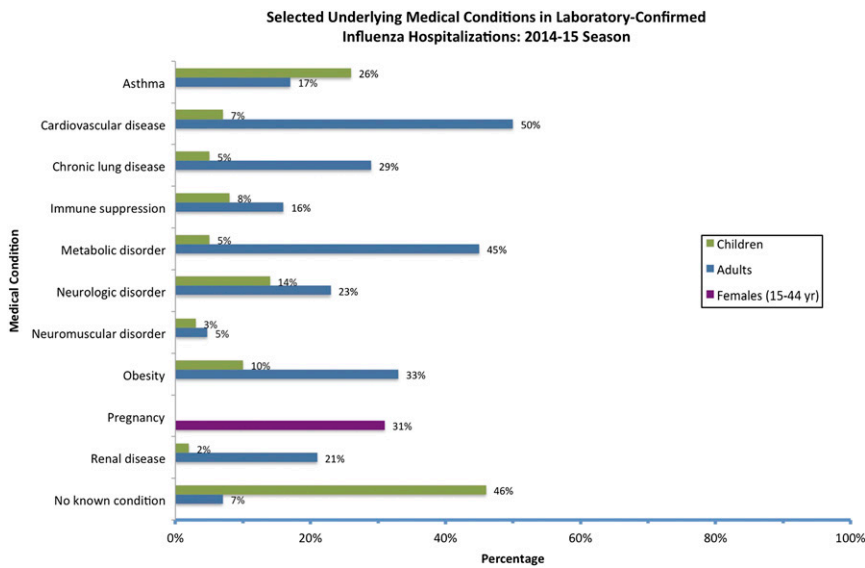


FIGURE 1

Selected underlying medical conditions in patients hospitalized with laboratory-confirmed influenza, FluSurv-NET 2014–2015. Source: Centers for Disease Control and Prevention. FluView 2014–2015 Preliminary Data as of August 13, 2015. Available at: gis.cdc.gov/grasp/fluview/FluHospChars.html

to the vaccine viruses, was 55% (95% confidence interval [CI], 43% to 65%) and 63% (95% CI, 26% to 81%) for the Yamagata and Victoria lineage, respectively. However, data from the US Influenza Vaccine Effectiveness Network indicated that the predominant circulating influenza A (H3N2) viruses were antigenically distinct from the influenza A (H3N2) vaccine viruses, resulting in reduced vaccine effectiveness for all ages against influenza A (H3N2) viruses (13%; 95% CI 2% to 23%). For children 2 through

8 years of age, vaccine effectiveness against H3N2 was 17% (95% CI –13% to 39%) and –11% (95% CI –62% to 23%) for inactivated influenza vaccine (IIV) and live attenuated influenza vaccine (LAIV), respectively. Neither IIV nor LAIV provided significant protection against H3N2 viruses. In particular, LAIV did not offer greater protection than IIV against the drifted H3N2 viruses, as anticipated from previous studies. Furthermore, estimates of vaccine effectiveness during the 2011–2012 and 2012–2013

influenza seasons suggested that the effectiveness of LAIV against influenza A (H3N2) and influenza B viruses was similar to but not superior to that of IIV. Observational data from the US Influenza Vaccine Effectiveness Network and 2 additional studies conducted during the 2013–2014 influenza season unexpectedly showed that LAIV was not effective against the influenza A H1N1 pandemic strain (H1N1 pdm09) virus when compared with IIV in children 2 through 8 years of age. Particular focus should be on the administration of IIV for all children and adolescents with underlying medical conditions associated with an elevated risk of complications from influenza. Additional experience over multiple influenza seasons will help to determine optimal utilization of these 2 vaccine formulations in children.

- Vaccination remains the best available preventive measure against influenza.** Given the unpredictable nature of influenza each season, including the efficacy of a particular vaccine, *any* licensed and age-appropriate influenza vaccine available should be used. The vaccine strains are designed to be well-matched to circulating strains with the intent of providing optimal protection. Immunization is effective in reducing the risk of outpatient medical visits caused by circulating influenza viruses by approximately one-half to three-quarters in most people. Although perhaps less effective against antigenically drifted strains, influenza vaccine may still provide some protection against circulating drifted viruses. During seasons when the vaccine is only moderately effective, influenza vaccine has been shown to reduce illness, antibiotic use, doctor visits, time

TABLE 1 Pediatric Deaths and Hospitalizations by Season and Predominant Strain

| Influenza Season | Predominant Strain | Pediatric Deaths | Hospitalizations (0–4 y old) per 100 000 | Hospitalizations (5–17 y old) per 100 000 |
|------------------------|--------------------|------------------|--|---|
| 2014–2015 ^a | H3N2 | 145 | 57.2 | 16.7 |
| 2013–2014 | pH1N1 | 111 | 47.3 | 9.4 |
| 2012–2013 | H3N2 | 171 | 67 | 14.6 |
| 2011–2012 ^a | H3N2 | 37 | 16 | 4 |
| 2010–2011 | H3N2 | 123 | 49.5 | 9.1 |
| 2009–2010 | pH1N1 | 288 | 77.4 | 27.2 |
| 2008–2009 | H1N1 | 137 | 28 | 5 |
| 2007–2008 | H3N2 | 88 | 40.3 | 5.5 |
| 2006–2007 | H1N1 | 77 | 34.6 | 2.3 |
| 2005–2006 | H3N2 | 46 | 28 | 4 |

Source: Centers for Disease Control and Prevention. FluView 2014–2015. Data as of August 13, 2015. Available at: www.cdc.gov/flu/weekly/fluviewinteractive.htm.

^a Vaccine strains did not change from previous influenza season.

lost from work, hospitalizations, and deaths. The seasonal vaccine is not 100% effective but it still is the best strategy available for preventing illness from influenza.

6. Both trivalent and quadrivalent influenza vaccines are available in the United States for the 2015–2016 season. Neither vaccine formulation is preferred over the other. Both formulations contain an A/California/7/2009 (H1N1)pdm09-like virus, an A/Switzerland/9715293/2013 (H3N2)-like virus, and a B/Phuket/3073/2013-like virus (B/Yamagata lineage). The influenza A (H3N2) and B/Yamagata lineage viruses differ from those contained in the 2014–2015 seasonal vaccines. Quadrivalent influenza vaccines include an additional B virus (B/Brisbane/60/2008-like virus [B/Victoria lineage]) of the other lineage contained in the trivalent products.
7. The number of seasonal influenza vaccine doses to be administered in the 2015–2016 influenza season depends on the child’s age at the time of the first administered dose and his or her vaccine history (Fig 2):
 - Influenza vaccines are not licensed for administration to infants younger than 6 months.
 - Children 9 years and older need only 1 dose.

Number of Seasonal Influenza Doses for Children 6 Months Through 8 Years of Age

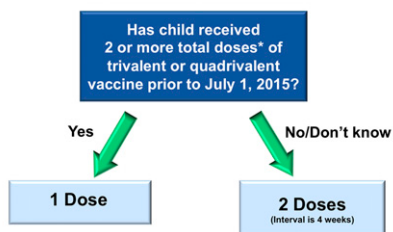


FIGURE 2 Number of 2015–2016 seasonal influenza vaccine doses for children 6 months through 8 years of age. *The 2 doses need not have been received during the same season or consecutive seasons.

- Children 6 months through 8 years of age.
 - Need 2 doses if they have received <2 doses of trivalent or quadrivalent influenza vaccine before July 1, 2015. The interval between the 2 doses should be at least 4 weeks.
 - Require only 1 dose if they have previously received 2 or more total doses of trivalent or quadrivalent influenza vaccine before July 1, 2015. The 2 previous doses need not have been received during the same influenza season or consecutive influenza seasons. Given the continuing circulation of H1N1pdm09 as the predominant influenza A (H1N1) virus since 2009 and its inclusion in all seasonal influenza vaccines since the 2010–2011 season, this virus is no longer believed to be antigenically novel; therefore, special consideration with respect to vaccine policy is no longer recommended.

Vaccination should not be delayed to obtain a specific product for either dose. Any available, age-appropriate trivalent or quadrivalent vaccine can be used; IIV and LAIV are considered interchangeable. A child who receives only 1 of the 2 doses as a quadrivalent formulation is likely to be less primed against the additional B virus.

8. Pediatric offices may choose to serve as an alternate venue for providing influenza immunization for parents and other care providers of children if the practice is acceptable to both pediatricians and the adults who are to be vaccinated.¹ Medical liability issues and medical

record documentation requirements need to be considered before a pediatrician begins immunizing adults (see details at <http://redbook.solutions.aap.org/selfserve/ssPage.aspx?SelfServeContentId=vaccine-policy-guidance>). Pediatricians are reminded to document the recommendation for adult immunization in the vulnerable child’s medical record. In addition, adults still should be encouraged to have a medical home and communicate their immunization status to their primary care provider. Offering adult immunizations in the pediatric practice setting would not be intended to undermine the adult medical home model but could serve as an additional venue for parents and other care providers of children to receive vaccinations. Immunization of close contacts of children at high risk of influenza-related complications (Table 2) is intended to reduce their risk of contagion (ie, “cocooning”). The practice of cocooning also will help protect infants younger than 6 months, because they are too young to be immunized with influenza vaccine. Women can safely receive influenza vaccine at any point during pregnancy, because they are at high risk of complications from influenza. This approach also provides protection for their infants during their first 6 months through transplacental transfer of antibodies.

9. As soon as the seasonal influenza vaccine is available locally, pediatricians or vaccine administrators should immunize HCP, notify parents and caregivers of vaccine availability and the importance of annual vaccination, and immunize children 6 months and older per recommendations, especially

those at high risk of complications from influenza. Health care provider endorsement plays a major role in patient acceptance and vaccine uptake. Prompt initiation of influenza immunization and continuance of immunization throughout the influenza season, whether influenza is circulating (or has circulated) in the community, are important components of an effective immunization strategy. There is no evidence that waning immunity from administering the vaccine early during the influenza season increases the risk of infection.

10. Providers should continue to offer vaccine until June 30 of each year, marking the end of the influenza season, because the influenza season is unpredictable. Protective immune responses persist throughout the influenza season, which can have >1 disease peak and may extend into March or later. Although the peak of influenza activity in the United States tends to occur in January through March, influenza activity can occur in early fall (ie, October) or late spring (eg, influenza circulated through the end of May during the 2014–2015 season). This approach also provides ample opportunity to administer a second dose of vaccine when indicated, as detailed previously in key point 7. In addition, international travel may result in potential exposure to influenza throughout the year.
11. HCP, influenza campaign organizers, and public health agencies should collaborate to develop improved strategies for planning, communication, and administration of vaccines.
 - Plan to make seasonal influenza vaccine easily accessible for all children.

Examples include alerts to families that vaccine is available (eg, e-mails, texts, and patient portals); creating walk-in influenza clinics; extending hours beyond routine times during peak vaccination periods; administering influenza vaccine during both well and sick visits; considering how to immunize parents, adult caregivers, and siblings at the same time in the same office setting as children¹; and working with other institutions (eg, schools, child care programs, and religious organizations) or alternative care sites, such as emergency departments, to expand venues for administering vaccine. If a child receives influenza vaccine outside of his or her medical home, such as at a pharmacy, retail-based clinic, or another practice, appropriate documentation of immunization should be provided to the patient for their medical home and entered into the state immunization registry where possible.

- Concerted efforts among the aforementioned groups, plus vaccine manufacturers, distributors, and payers, also are necessary to prioritize distribution appropriately to the primary care office setting and patient-centered medical home before other venues, especially when vaccine supplies are delayed or limited.
- Vaccine safety, effectiveness, and indications must be communicated often and clearly to the public. Pediatricians can influence vaccine acceptance by explaining the importance of annual influenza vaccination for children and emphasizing

when a second dose of vaccine is indicated.

- HCP should act as role models for both their patients and colleagues by receiving influenza immunization annually and by letting others know that they have received vaccine. Influenza immunization programs for HCP benefit the health of employees, their patients, and members of the community.² Employees of health care institutions are obligated to act in the best interests of the health of their patients and to honor the requirement of causing no harm.
12. Antiviral medications also are important in the control of influenza but are not a substitute for influenza immunization. The neuraminidase inhibitors (NAIs) oral oseltamivir (Tamiflu; Roche Laboratories, Nutley, NJ) and inhaled zanamivir (Relenza; GlaxoSmithKline, Research Triangle Park, NC) are the only antiviral medications that are recommended for chemoprophylaxis or treatment of influenza in children during the 2015–2016 season. Peramivir (Rapivab; Biocryst Pharmaceuticals, Durham, NC), a third NAI, was licensed on December 19, 2014, for use in adults 18 years or older and has not been studied fully in children. Intravenous use of peramivir is approved. Intravenous zanamivir remains investigational but can be used in consultation with infectious diseases specialists. Intravenous zanamivir also may be obtained on a compassionate-use basis for seriously ill children, especially those who are immunocompromised or cannot tolerate or absorb oral or enterically administered oseltamivir. Recent viral surveillance and resistance data

TABLE 2 People at Higher Risk of Influenza Complications Recommended for Antiviral Treatment of Suspected or Confirmed Influenza

| |
|---|
| Children <2 y |
| Adults ≥65 y |
| People with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), or metabolic disorders (including diabetes mellitus) or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury) |
| People with immunosuppression, including that caused by medications or by HIV infection |
| Women who are pregnant or postpartum (within 2 wk after delivery) |
| People <19 y who are receiving long-term aspirin therapy |
| American Indian/Alaska Native people |
| People who are morbidly obese (ie, BMI ≥40) |
| Residents of nursing homes and other chronic care facilities |

Source: Centers for Disease Control and Prevention. Antiviral agents for the treatment and chemoprophylaxis of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(RR-1):1–24

indicate that most currently circulating influenza viruses likely to cause 2015–2016 seasonal influenza in North America continue to be sensitive to oseltamivir, zanamivir, and peramivir. If an oseltamivir- or peramivir-resistant virus is a concern, use of intravenous zanamivir is recommended. In contrast, amantadine and rimantadine should not be used, because circulating influenza A viruses currently have extremely high levels of resistance to these drugs, and they are not effective against influenza B viruses. Because resistance characteristics can change rapidly, especially in severely immunocompromised people, pediatricians should verify susceptibility data at the start of the influenza season and monitor it throughout the season. Up-to-date information can be found on the AAP Web site (www.aap.org or www.aapredbook.org/flu), through state-specific AAP chapter Web sites, or on the CDC Web site (www.cdc.gov/flu/index.htm).

SEASONAL INFLUENZA VACCINES

Before the 2013–2014 influenza season, only trivalent influenza vaccines that included a single influenza B strain were available. However, since the 1980s, 2 antigenically distinct lineages

(ie, Victoria or Yamagata) of influenza B viruses have circulated globally. Vaccination against one B viral lineage confers little cross-protection against the other B viral lineage. Thus, trivalent vaccines offer limited immunity against circulating influenza B strains of the lineage not present in the vaccine. Furthermore, in recent years, it has proven difficult to predict consistently which B lineage will predominate during a given influenza season. Therefore, a quadrivalent influenza vaccine with influenza B strains of *both* lineages would be predicted to offer additional protection.

For the 2015–2016 season, IIVs will be available for injection in both trivalent (IIV3) and quadrivalent (IIV4) formulations. The intranasally administered LAIV is available only in a quadrivalent formulation (LAIV4) and contains the same influenza strains as IIV4. IIVs contain no live virus. IIV3 and IIV4 formulations are available for intramuscular (IM) and intradermal (ID) use. The IM formulation of IIV3 is licensed and recommended for children 6 months and older (Table 3), including those with and without chronic medical conditions. The most common adverse events after IIV administration are local injection site pain and tenderness. Fever may occur within 24 hours after immunization in ~10% to 35% of children younger

than 2 years but rarely in older children and adults. Mild systemic symptoms, such as nausea, lethargy, headache, muscle aches, and chills, may occur after administration of IIV3.

The IM formulation of IIV4 is licensed for use in children as young as 6 months of age. In children, the most common injection site adverse reactions were pain, redness, and swelling. The most common systemic adverse events were drowsiness, irritability, loss of appetite, fatigue, muscle aches, headache, arthralgia, and gastrointestinal tract symptoms. These events were reported with comparable frequency among participants receiving the licensed comparator trivalent inactivated influenza vaccines. IIV4 is an acceptable vaccine for people 6 months or older when otherwise appropriate and may offer broader protection against circulating influenza B strains than IIV3.

An ID formulation of IIV3 and IIV4 is licensed for use in people 18 through 64 years of age. ID vaccine administration involves a microinjection with a shorter needle than needles used for IM administration. The most common adverse events are redness, induration, swelling, pain, and itching, which occur at the site of administration. There is no preference for IM or ID immunization with IIV3 or IIV4 in people 18 through 64 years of age. Therefore, pediatricians may choose to use either the IM or ID product for their young adult patients and for any adults they are vaccinating in their office (ie, as part of a cocooning strategy).

During the 2 influenza seasons spanning 2010 to 2012, there were increased reports of febrile seizures in the United States in young children who received IIV3 and the 13-valent pneumococcal conjugate vaccine concomitantly. A subsequent retrospective analysis of past seasons

has demonstrated a slight increase in the risk of febrile seizures in children 6 through 23 months of age when different vaccines are given concomitantly with IIV. Simultaneous administration of IIV with the 13-valent pneumococcal conjugate vaccine and/or other vaccines for the 2015–2016 influenza season continues to be recommended when these vaccines are indicated.

LAIV4 is a quadrivalent live attenuated influenza vaccine that is administered intranasally. It is licensed by the Food and Drug Administration (FDA) for people 2 through 49 years of age. The most commonly reported reactions in children were runny nose or nasal congestion, headache, decreased activity or lethargy, and sore throat. LAIV4 should not be administered to people with notable nasal congestion because that can impede vaccine delivery. The safety of LAIV in people with a history of asthma, diabetes mellitus, or other high-risk medical conditions associated with an elevated risk of complications from influenza (see Contraindications and Precautions) has not been established. In postlicensure surveillance of LAIV over 7 seasons, the Vaccine Adverse Event Reporting System, jointly sponsored by the FDA and CDC, did not identify any new or unexpected safety concerns even though there were reports of use of LAIV in people with a contraindication or precaution. Although the use of LAIV in young children with chronic medical conditions, including asthma, has been implemented outside of the United States, data are considered insufficient to support a recommendation for such use in the United States.

Two trivalent influenza vaccines manufactured using technologies that do not use eggs also will be available for people 18 years or older during the 2015–2016 season: cell culture–based inactivated influenza

vaccine (ccIIV3) and recombinant influenza vaccine (RIV3). The first vaccine, ccIIV3, is a trivalent cell culture–based IIV that is administered as an IM injection and indicated for people 18 years or older. ccIIV3 has comparable immunogenicity to US-licensed IIV3 comparator vaccines. Although ccIIV3 is manufactured from virus propagated in Madin Darby canine kidney cells rather than embryonated eggs, seed virus strains were created by using the World Health Organization reference virus strains, which have been passaged in eggs. However, only trace amounts of ovalbumin are detectable, and egg allergy is not listed as a contraindication in the package insert. Other contraindications to vaccine delivery are similar to those for other IIVs. The most common solicited adverse reactions included injection site pain, erythema at the injection site, headache, fatigue, myalgia, and malaise. The second vaccine, RIV3, is a recombinant baculovirus-expressed hemagglutinin vaccine produced in cell culture. It is licensed for people 18 years or older and is administered via IM injection. The most frequently reported adverse events were pain, headache, myalgia, and fatigue. There are no egg proteins in this version of influenza vaccine.

Tables 3 and 4 summarize information on the types of 2015–2016 seasonal influenza vaccines licensed for immunization of children and adults. More than 1 product may be appropriate for a given patient. Vaccination should not be delayed to obtain a specific product.

A large body of scientific evidence demonstrates that thimerosal-containing vaccines are not associated with increased risk of autism spectrum disorders in children. Thimerosal from vaccines has not been linked to any other medical condition. As such, the AAP extends its strongest support to the current World Health Organization recommendations to retain the use of

thimerosal as a preservative in multiuse vials in the global vaccine supply. Some people may still raise concerns about the minute amounts of thimerosal in some IIV vaccine formulations (Table 3), and in some states, there is a legislated restriction on the use of thimerosal-containing vaccines. The benefits of protecting children against the known risks of influenza are clear. Therefore, children should receive any available formulation of IIV rather than delaying immunization while waiting for reduced thimerosal-content or thimerosal-free vaccines. Although some formulations of IIV contain a trace amount of thimerosal, thimerosal-free IIV products can be obtained (Table 3). LAIV4 does not contain thimerosal. Vaccine manufacturers are delivering increasing amounts of thimerosal-free influenza vaccine each year.

INFLUENZA VACCINES AND EGG ALLERGY

Although LAIV and most IIV vaccines are produced in eggs and contain measurable amounts of egg protein, recent data have shown that IIV administered in a single, age-appropriate dose is well tolerated by recipients with a history of egg allergy. More conservative approaches in children with a history of egg allergy, such as skin testing or a 2-step graded challenge, no longer are recommended. Studies demonstrating the safety of administering LAIV to egg-allergic recipients have recently been published and future AAP recommendations regarding the use of LAIV in this population will be considered.

The Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology, states that special precautions regarding medical setting and waiting periods

after administration of IIV to egg-allergic recipients beyond those recommended for any vaccine are not warranted. The AAP continues to reevaluate the need for such precautions but currently recommends that pediatricians continue to determine whether the presumed egg allergy is based on a mild (eg, hives alone) or severe (eg, anaphylaxis involving cardiovascular changes, respiratory or gastrointestinal tract symptoms, or reactions that necessitate the use of epinephrine) reaction. Pediatricians should consult with an allergist for children with a history of severe reaction. Most vaccine administration to patients with egg allergy can occur without the need for referral. Data indicate that only ~1% of children have immunoglobulin E-mediated sensitivity to egg, and of those, a rare minority has a severe allergy.

Standard immunization practice should include the ability to respond to acute hypersensitivity reactions. Therefore, it is suggested that influenza vaccine be given to children with mild egg allergy with the following preconditions (Fig 3):

- Appropriate resuscitative equipment must be readily available.³
- The vaccine recipient should be observed in the office for 30 minutes after immunization, the usual observation time for receiving immunotherapy.

Providers may consider use of ccIV3 or RIV3 vaccines produced via non-egg-based technologies for patients 18 years or older with egg allergy in settings in which these vaccines are available and otherwise age appropriate. ccIV3, which does contain trace amounts of ovalbumin, should be administered according to the guidance for other IIVs (Fig 3). RIV3, which contains no ovalbumin, may be administered to people with egg allergy of any severity who are 18 years or older and do not have other contraindications. However, vaccination

of patients with mild egg allergy should not be delayed if RIV3 or ccIV3 is not available. Instead, any licensed, age-appropriate IIV should be used.

VACCINE STORAGE AND ADMINISTRATION

The AAP Storage and Handling Tip Sheet provides resources for practices to develop comprehensive vaccine management protocols to keep the temperature for vaccine storage constant during a power failure or other disaster (www2.aap.org/immunization/pediatricians/pdf/DisasterPlanning.pdf). Any of the influenza vaccines can be administered at the same visit with all other recommended routine vaccines.

Intramuscular Vaccine

IIVs for IM injection are shipped and stored at 2°C to 8°C (35°F–46°F). These vaccines are administered intramuscularly into the anterolateral thigh of infants and young children and into the deltoid muscle of older children and adults. The volume of vaccine is age dependent; infants and toddlers 6 months through 35 months of age should receive a dose of 0.25 mL, and all people 3 years (36 months) and older should receive 0.5 mL/dose.

Intradermal Vaccine

IIVs for ID injection are shipped and stored at 2°C to 8°C (35°F–46°F). These vaccines are administered intradermally only to people 18 through 64 years of age, preferably over the deltoid muscle, and only using the device included in the vaccine package. Vaccine is supplied in a single-dose, prefilled microinjection system (0.1 mL) for adults. The package insert contains the full administration details of this product.

Live Attenuated (Intranasal) Vaccine

The cold-adapted, temperature sensitive LAIV4 formulation currently licensed in the United States must be shipped and stored at 2°C to 8°C (35°F–46°F) and administered

intranasally in a prefilled, single-use sprayer containing 0.2 mL of vaccine. A removable dose-divider clip is attached to the sprayer to administer 0.1 mL separately into each nostril. After administration of any live virus vaccine, at least 4 weeks should pass before another live virus vaccine is administered.

CURRENT RECOMMENDATIONS

Seasonal influenza immunization is recommended for all children 6 months and older. No preference is expressed for IIV or LAIV for people in whom either vaccine is appropriate. Particular focus should be on the administration of IIV for all children and adolescents with underlying medical conditions associated with an elevated risk of complications from influenza, including the following:

- Asthma or other chronic pulmonary diseases, including cystic fibrosis.
- Hemodynamically significant cardiac disease.
- Immunosuppressive disorders or therapy.
- HIV infection.
- Sick cell anemia and other hemoglobinopathies.
- Diseases that necessitate long-term aspirin therapy, including juvenile idiopathic arthritis or Kawasaki disease.
- Chronic renal dysfunction.
- Chronic metabolic disease, including diabetes mellitus.
- Any condition that can compromise respiratory function or handling of secretions or can increase the risk of aspiration, such as neurodevelopmental disorders, spinal cord injuries, seizure disorders, or neuromuscular abnormalities.
- Morbid obesity.
- Pregnancy.

TABLE 3 Recommended Seasonal Influenza Vaccines for Different Age Groups: United States, 2015–2016 Influenza Season

| Vaccine | Trade Name | Manufacturer | Presentation | Thimerosal Mercury Content, microgram of Hg/0.5-mL dose | Age Group |
|-----------------------|----------------------------------|--|---------------------------------|---|--|
| Inactivated | | | | | |
| IIV3 | Fluzone | Sanofi Pasteur | 5.0-mL multidose vial | 25 | ≥6 mo |
| IIV3 | Fluzone Intradermal | Sanofi Pasteur | 0.1-mL prefilled microinjection | 0 | 18–64 y |
| IIV3 | Fluzone HD | Sanofi Pasteur | 0.5-mL prefilled syringe | 0 | ≥65 y |
| IIV3 | Fluvirin | Novartis Vaccines and Diagnostics | 0.5-mL prefilled syringe | ≤1.0 | ≥4 y |
| IIV3 | | | 5.0-mL multidose vial | 25 | ≥4 y |
| IIV3 | Fluarix | GlaxoSmithKline | 0.5-mL prefilled syringe | 0 | ≥36 mo |
| IIV3 | FluLaval | ID Biomedical Corporation of Quebec (distributed by GlaxoSmithKline) | 0.5-mL prefilled syringe | 0 | ≥36 mo |
| | | | 5.0-mL multidose vial | <25 | ≥36 mo |
| IIV3 | Afluria | bioCSL | 0.5-mL prefilled syringe | 0 | ≥9 y ^a |
| | | | 5.0-mL multidose vial | 24.5 | ≥9 y ^a via needle/syringe 18–64 y via jet injector |
| cclIV3 | Flucelvax | Novartis Vaccines and Diagnostics | 0.5-mL prefilled syringe | 0 | ≥18 y |
| IIV4 | Fluzone Quadrivalent | Sanofi Pasteur | 0.25-mL prefilled syringe | 0 | 6–35 mo |
| | | | 0.5-mL prefilled syringe | 0 | ≥36 mo |
| | | | 0.5-mL vial | 0 | ≥36 mo |
| | | | 5.0-mL multidose vial | 25 | ≥6 mo |
| IIV4 | Fluzone Intradermal Quadrivalent | Sanofi Pasteur | 0.1-mL prefilled microinjection | 0 | 18–64 y |
| IIV4 | Fluarix Quadrivalent | GlaxoSmithKline | 0.5-mL prefilled syringe | 0 | ≥36 mo |
| IIV4 | FluLaval Quadrivalent | ID Biomedical Corporation of Quebec (distributed by GlaxoSmithKline) | 0.5-mL prefilled syringe | 0 | ≥36 mo |
| | | | 5.0-mL multidose vial | <25 | ≥36 mo |
| Recombinant RIV3 | FluBlok | Protein Sciences | 0.5-mL vial | 0 | ≥18 y |
| Live attenuated LAIV4 | FluMist Quadrivalent | MedImmune | 0.2-mL sprayer | 0 | 2–49 y |

Implementation guidance on supply, pricing, payment, CPT coding, and liability issues can be found at <http://redbook.solutions.aap.org/selfserve/ssPage.aspx?SelfServeContentId=vaccine-policy-guidance>.

Data sources: American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2014–2015. *Pediatrics*. 2014;134(5):e1503–e1519; and Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2015–2016 influenza season. *MMWR Recomm Rep*. 2015;64(30):818–825.

^a Age indication per package insert is ≥5 years; however, the Advisory Committee on Immunization Practices recommends Afluria not be used in children 6 months through 8 years of age because of increased reports of febrile reactions noted in this age group. If no other age-appropriate, licensed inactivated seasonal influenza vaccine is available for a child 5 through 8 years of age who has a medical condition that increases the child's risk of influenza complications, Afluria can be used; however, pediatricians should discuss with the parents or caregivers the benefits and risks of influenza vaccination with Afluria before administering this vaccine.

Although universal immunization for all people 6 months and older is recommended for the 2015–2016 influenza season, particular immunization efforts with either IIV or LAIV should be made for the following groups to prevent transmission of influenza to those at risk, unless contraindicated:

- Household contacts and out-of-home care providers of children younger than 5 years and of at-risk children of all ages (healthy contacts 2 through 49 years of age can receive either IIV or LAIV).
- Any woman who is pregnant (IIV only) or considering pregnancy (IIV only), is in the postpartum period, or is breastfeeding during the influenza season. Studies have shown that infants born to immunized women have better influenza-related health outcomes. However, according to Internet panel surveys conducted by the CDC, only 52% of pregnant women reported receiving an influenza vaccine during the 2013–2014 season, even though both pregnant women and their infants are at higher risk of complications. In addition, data from some studies suggest that influenza vaccination in pregnancy may decrease the risk of preterm birth and infants being small for gestational age. Breastfeeding also is recommended to protect against influenza viruses by activating innate antiviral mechanisms, specifically type 1 interferons. Pregnant women can receive influenza vaccine (IIV only) safely during any trimester.
- American Indian/Alaska Native children and adolescents.
- HCP or health care volunteers. Despite the AAP recommendation

Approach to Children With Presumed Egg Allergy

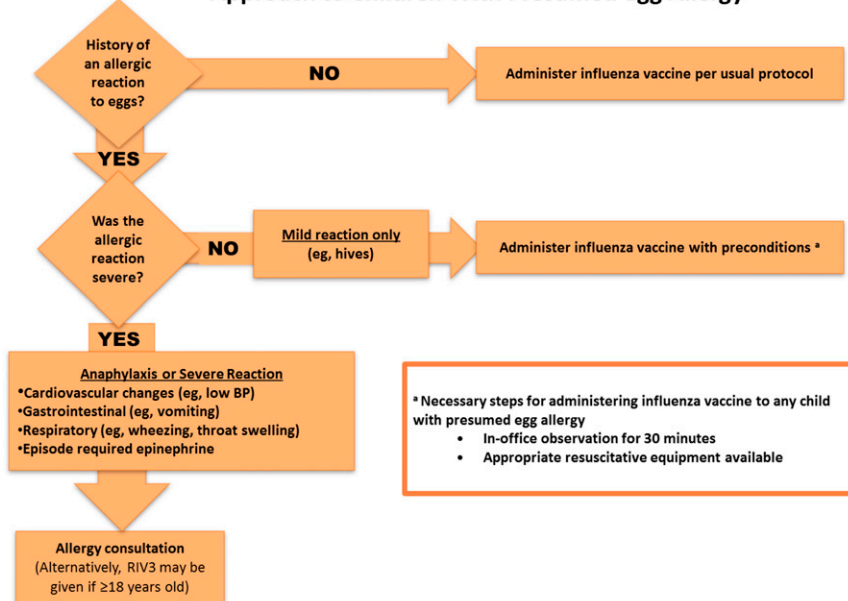


FIGURE 3
Precautions for administering IIV to presumed egg-allergic children.

for mandatory influenza immunization for all HCP,² many remain unvaccinated. With an increasing number of organizations mandating influenza vaccine, coverage among HCP increased to 75% in the 2013–2014 season. Optimal prevention of influenza in the health care setting depends on the vaccination of at least 90% of HCP, which is consistent with the national *Healthy People 2020* target for annual influenza vaccination among HCP. However, overall immunization rates for this group remain consistently below this goal. The AAP recently reaffirmed its support for a mandatory influenza immunization policy for all HCP nationwide.² Mandating influenza vaccine for all HCP can be ethically justified and is necessary to improve patient safety, especially because HCP frequently come into contact with patients at high risk of influenza illness in their clinical settings. For the prevention and control of influenza, all HCP must continue

to put the health and safety of patients first.

- Close contacts of immunosuppressed people.

CONTRAINDICATIONS AND PRECAUTIONS

Minor illnesses, with or without fever, are not contraindications to the use of influenza vaccines, particularly among children with mild upper respiratory infection symptoms or allergic rhinitis.

Children Who Should Not Be Vaccinated With IIV

- Infants younger than 6 months.
- Children who have a moderate to severe febrile illness, based on the judgment of the clinician.

Children Who Should Not Be Vaccinated With LAIV

- Children younger than 2 years.
- Children who have a moderate to severe febrile illness.
- Children with an amount of nasal congestion that would notably impede vaccine delivery.

- Children 2 through 4 years of age with a history of recurrent wheezing or a medically attended wheezing episode in the previous 12 months because of the potential for increased wheezing after immunization. In this age range, many children have a history of wheezing with respiratory tract illnesses and are eventually diagnosed with asthma. Therefore, when offering LAIV to children 24 through 59 months of age, the pediatrician should screen them by asking the parent or guardian, “In the previous 12 months, has a health care professional ever told you that your child had wheezing?” If a parent answers “yes” to this question, IIV rather than LAIV is recommended.

- Children with the diagnosis of asthma.
- Children with a history of egg allergy.
- Children who have received other live virus vaccines within the past 4 weeks; however, other live virus vaccines can be given on the same day as LAIV.
- Children who have known or suspected immunodeficiency disease or who are receiving immunosuppressive or immunomodulatory therapies.
- Children who are receiving aspirin or other salicylates.
- Any female who is pregnant or considering pregnancy.
- Children with any condition that can compromise respiratory function or handling of secretions or can increase the risk for aspiration, such as neurodevelopmental disorders, spinal cord injuries, seizure disorders, or neuromuscular abnormalities.
- Children taking an influenza antiviral medication (oseltamivir or zanamivir), until 48 hours after stopping the influenza antiviral therapy. If a child recently received

LAIV but has an influenza illness for which antiviral agents are appropriate, the antiviral agents should be given. If antiviral agents are necessary for treatment within 5 to 7 days of LAIV immunization, reimmunization may be indicated because of the potential effects of antiviral medications on LAIV replication and immunogenicity.

- Children with chronic underlying medical conditions that may predispose to complications after wild-type influenza infection, including metabolic disease, diabetes mellitus, other chronic disorders of the pulmonary or cardiovascular systems, renal dysfunction, or hemoglobinopathies. The safety of LAIV in these populations has not been established. These conditions are not contraindications but are listed under the “Warnings and Precautions” section of the LAIV package insert. A precaution is a condition in a recipient that might increase the risk or seriousness of an adverse reaction or complicate making another diagnosis because of a possible vaccine-related reaction. A precaution also may exist for conditions that might compromise the ability of the vaccine to produce immunity. Vaccination may be recommended in the presence of a precaution if the benefit of protection from the vaccine outweighs any risk.

IIV is the vaccine of choice for anyone in close contact with a subset of severely immunocompromised people (ie, those in a protected environment). IIV is preferred over LAIV for contacts of severely immunocompromised people because of the theoretical risk of infection attributable to LAIV strain in an immunocompromised contact of an LAIV-immunized person. Available data indicate a very low risk of transmission of the virus in both children and adults vaccinated with

LAIV. HCP immunized with LAIV may continue to work in most units of a hospital, including the NICU and general oncology ward, using standard infection-control techniques. As a precautionary measure, people recently vaccinated with LAIV should restrict contact with severely immunocompromised patients for 7 days after immunization, although there have been no reports of LAIV transmission from a vaccinated person to an immunocompromised person. In the theoretical scenario in which symptomatic LAIV infection develops in an immunocompromised host, oseltamivir or zanamivir could be prescribed, because LAIV strains are susceptible to these antiviral medications.

SURVEILLANCE

Information about influenza surveillance is available through the CDC Voice Information System (influenza update, 888-232-3228) or at www.cdc.gov/flu/index.htm. Although current influenza season data on circulating strains do not necessarily predict which and in what proportion strains will circulate in the subsequent season, it is instructive to be aware of 2014–2015 influenza surveillance data and use them as a guide to empirical therapy until current seasonal data are available from the CDC. Information is posted weekly on the CDC Web site (www.cdc.gov/flu/weekly/fluactivitysurv.htm).

VACCINE IMPLEMENTATION

These updated recommendations for prevention and control of influenza in children will have considerable operational and fiscal effects on pediatric practice. Therefore, the AAP has developed implementation guidance on supply, payment, coding, and liability issues; these documents can be found at <http://redbook.solutions.aap.org/selfserve/ssPage.aspx?SelfServeContentId=vaccine-policy-guidance>.

In addition, the AAP’s Partnership for Policy Implementation has developed a series of definitions using accepted health information technology standards to assist in the implementation of this guideline in computer systems and quality measurement efforts. This document is available at www2.aap.org/informatics/PPI.html.

USE OF ANTIVIRAL MEDICATIONS

Oral oseltamivir remains the antiviral drug of choice for the management of influenza infections. Inhaled zanamivir is an equally acceptable alternative but is more difficult to administer. Antiviral resistance to either drug can emerge, necessitating continuous population-based assessment. If local or national influenza surveillance data indicate a predominance of a particular influenza strain with a known antiviral susceptibility profile, then empirical treatment can be directed toward that strain. For example, all of the influenza A (H3N2) and influenza B viruses tested since October 1, 2014, were sensitive to oseltamivir, zanamivir, and peramivir during the 2014–2015 influenza season. Among the pH1N1 viruses tested for resistance, only 1.6% were found to be resistant to oseltamivir, 1.6% were found to be resistant to peramivir, and none were found to be resistant to zanamivir. In contrast, high levels of resistance to amantadine and rimantadine exist, so these drugs should not be used in the upcoming season unless resistance patterns change significantly.

- Current treatment guidelines for antiviral medications (Table 4) are applicable to both infants and children with suspected influenza when strains are known to be circulating in the community or when infants or children are tested and confirmed to have influenza.
- Oseltamivir is available in capsule and oral suspension formulations.

TABLE 4 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis for the 2015–2016 Influenza Season: United States

| Medication | Treatment | Chemoprophylaxis |
|--|---|--|
| Oseltamivir ^a | | |
| Adults | 75 mg twice daily × 5 days | 75 mg once daily × 10 days |
| Children ≥12 mo | | |
| Body weight | | |
| ≤15 kg (≤33 lb) | 30 mg twice daily × 5 days | 30 mg once daily × 10 days |
| >15 kg–23 kg (33 lb–51 lb) | 45 mg twice daily × 5 days | 45 mg once daily × 10 days |
| >23 kg–40 kg (>51 lb–88 lb) | 60 mg twice daily × 5 days | 60 mg once daily × 10 days |
| >40 kg (>88 lb) | 75 mg twice daily × 5 days | 75 mg once daily × 10 days |
| Infants 9–11 mo ^b | 3.5 mg/kg per dose twice daily × 5 days | 3.5 mg/kg per dose once daily × 10 days |
| Term infants 0–8 mo ^b | 3 mg/kg per dose twice daily × 5 days | 3 mg/kg per dose once daily × 10 days for infants 3–8 mo; not recommended for infants <3 mo old, unless situation judged critical, because of limited safety and efficacy data in this age group |
| Preterm infants | See details in footnote ^c | |
| Zanamivir ^d | | |
| Adults | 10 mg (two 5-mg inhalations) twice daily × 5 days | 10 mg (two 5-mg inhalations) once daily × 10 days |
| Children (≥7 y for treatment, ≥5 y for chemoprophylaxis) | 10 mg (two 5-mg inhalations) twice daily × 5 days | 10 mg (two 5-mg inhalations) once daily × 10 days |

^a Oseltamivir is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available as Tamiflu in 30-mg, 45-mg, and 75-mg capsules and as a powder for oral suspension that is reconstituted to provide a final concentration of 6 mg/mL. For the 6-mg/mL suspension, a 30-mg dose is given with 5 mL of oral suspension, a 45-mg dose is given with 7.5 mL oral suspension; a 60-mg dose is given with 10 mL oral suspension, and a 75-mg dose is given with 12.5 mL oral suspension. If the commercially manufactured oral suspension is not available, a suspension can be compounded by retail pharmacies (final concentration also 6 mg/mL), based on instructions that are present in the package label. In patients with renal insufficiency, the dose should be adjusted on the basis of creatinine clearance. For treatment of patients with creatinine clearance 10–30 mL/min: 75 mg, once daily, for 5 d. For chemoprophylaxis of patients with creatinine clearance 10–30 mL/min: 30 mg, once daily, for 10 d after exposure or 75 mg, once every other day, for 10 d after exposure (5 doses). See www.cdc.gov/flu/professionals/antivirals/antiviral-drug-resistance.htm.

^b Approved by the FDA for children as young as 2 weeks of age. Given preliminary pharmacokinetic data and limited safety data, oseltamivir can be used to treat influenza in both term and preterm infants from birth because benefits of therapy are likely to outweigh possible risks of treatment.

^c Oseltamivir dosing for preterm infants. The weight-based dosing recommendation for preterm infants is lower than for term infants. Preterm infants may have lower clearance of oseltamivir because of immature renal function, and doses recommended for full-term infants may lead to very high drug concentrations in this age group. Limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provides the basis for dosing preterm infants using their postmenstrual age (gestational age + chronological age): 1.0 mg/kg per dose, orally, twice daily × 5 days, for those <38 weeks postmenstrual age; 1.5 mg/kg per dose, orally, twice daily × 5 days, for those 38 through 40 weeks postmenstrual age; 3.0 mg/kg per dose, orally, twice daily × 5 days, for those >40 weeks postmenstrual age. For extremely preterm infants (<28 wk), please consult a pediatric infectious diseases physician.

^d Zanamivir is administered by inhalation using a proprietary “Diskhaler” device distributed together with the medication. Zanamivir is a dry powder, not an aerosol, and should not be administered using nebulizers, ventilators, or other devices typically used for administering medications in aerosolized solutions. Zanamivir is not recommended for people with chronic respiratory diseases, such as asthma or chronic obstructive pulmonary disease, which increase the risk of bronchospasm.

Sources: Centers for Disease Control and Prevention. Antiviral agents for the treatment and chemoprophylaxis of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(RR-1):1–24; Kimberlin DW, Acosta EP, Prichard MN, et al. National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Oseltamivir pharmacokinetics, dosing, and resistance among children aged <2 y with influenza. *J Infect Dis*. 2013;207(5):709–720.

The commercially manufactured liquid formulation has a concentration of 6 mg/mL. If the commercially manufactured oral suspension is not available, the capsule may be opened and the contents mixed with simple syrup or Ora-Sweet SF (sugar-free) by retail pharmacies to a final concentration of 6 mg/mL (Table 4).

- Continuous monitoring of the epidemiology, change in severity, and resistance patterns of influenza strains may lead to new guidance.

Regardless of influenza immunization status and whether the onset of

illness has been <48 hours, treatment should be offered as early as possible for the following:

- Any hospitalized child clinically presumed to have influenza disease or with severe, complicated, or progressive illness attributable to influenza.
- Influenza infection of any severity in children at high risk of complications of influenza infection (Table 2).

Treatment should be considered for the following:

- Any otherwise healthy child clinically presumed to have

influenza disease for whom a decrease in duration of clinical symptoms is felt to be warranted. The greatest effect on outcome will occur if treatment can be initiated within 48 hours of illness onset but still should be considered if later in the course of illness.

- Children clinically presumed to have influenza disease and whose siblings either are younger than 6 months or have underlying medical conditions that predispose them to complications of influenza.

Reviews of available studies by the CDC, the World Health Organization, and independent investigators have

consistently found that timely oseltamivir treatment can reduce the duration of fever and illness symptoms and the risks of complications, including those resulting in hospitalization and death. However, treatment efficacy has not yet been evaluated among hospitalized children or children with comorbid conditions in randomized trials. Although no prospective comparative data exist to date, multiple retrospective studies and meta-analyses have been conducted to determine the role of NAIs in treating severe influenza. Most experts support use of NAIs to reduce complications and hospitalizations, but these conclusions were not universal. A recent 2014 Cochrane review identified unresolved discrepancies in the data presented in published trial reports. The review authors found that the use of either oseltamivir or zanamivir as prophylaxis reduces the risk of developing symptomatic influenza, but not asymptomatic infection. However, this review suggested that there was no evidence to demonstrate an effect on complications, hospitalizations, or death. The Cochrane findings agree with the conservative conclusions on both oseltamivir and zanamivir drawn by the FDA, which described the overall performance of both NAIs as “modest.”

Importantly, treatment with oseltamivir for children with presumed serious, complicated, or

progressive disease, irrespective of influenza immunization status or whether illness began >48 hours before admission, continues to be recommended by the AAP, CDC, and Infectious Diseases Society of America (www.idsociety.org/Influenza_Statement.aspx). Earlier treatment provides better clinical responses. However, treatment after 48 hours of symptoms in adults and children with moderate to severe disease or with progressive disease has been shown to provide some benefit and should be strongly considered. In previous years, the use of double-dose oseltamivir, particularly for those hospitalized with severe illness caused by pH1N1, was believed to provide better outcomes. However, published data from a randomized, prospective trial with 75% of subjects younger than 15 years documented no benefit of double-dose therapy over standard-dose therapy.

Dosages for antiviral agents for both treatment and chemoprophylaxis in children can be found in Table 4 and on the CDC Web site (www.cdc.gov/flu/professionals/antivirals/index.htm). Children younger than 2 years are at an increased risk of hospitalization and complications attributable to influenza. The FDA has licensed oseltamivir for children as young as 2 weeks of age. Given preliminary pharmacokinetic data and limited safety data, AAP believes that oseltamivir can be used to treat influenza in both term and preterm infants from birth

because benefits of therapy are likely to outweigh possible risks of treatment.

In adverse event data collected systematically in prospective trials, the only oseltamivir-attributable adverse effect that was greater in 1- through 13-year-old children was vomiting (ie, 15% of treated versus 9% receiving placebo). In addition, following reports from Japan of oseltamivir-attributable neuropsychiatric adverse effects, a review of controlled clinical trial data and ongoing surveillance has failed to establish a link between this drug and neurologic or psychiatric events. Information is available at: www.gene.com/download/pdf/tamiflu_prescribing.pdf and www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/pediatricadvisorycommittee/ucm302449.pdf.

Clinical judgment (on the basis of underlying conditions, disease severity, time since symptom onset, and local influenza activity) is an important factor in treatment decisions for pediatric patients who present with influenza-like illness. Antiviral treatment should be started as soon as possible after illness onset and should not be delayed while waiting for a definitive influenza test result, because early therapy provides the best outcomes. Influenza diagnostic tests vary by method, availability, processing time, sensitivity, and cost (Table 5), which should be considered in making the

TABLE 5 Comparison of Types of Influenza Diagnostic Tests

| Influenza Diagnostic Test | Method | Availability | Typical Processing Time | Sensitivity | Distinguishing Subtype Strains of Influenza A | Cost |
|--|-------------------|--------------|-------------------------|-------------|---|--------|
| Rapid influenza diagnostic tests | Antigen detection | Wide | <30 min | 10%–80% | No | \$ |
| Direct and indirect immunofluorescence assays | Antigen detection | Wide | 1–4 h | 70%–100% | No | \$ |
| Viral cell culture | Virus isolation | Limited | 3–10 d | 100% | Yes | \$\$ |
| Rapid cell culture (shell vials and cell mixtures) | Virus isolation | Limited | 1–3 d | 100% | Yes | \$\$ |
| Nucleic acid amplification tests (including rRT-PCR) | RNA detection | Limited | 1–6 h | 86%–100% | Yes | \$\$\$ |
| Rapid influenza molecular assays | RNA detection | Wide | <15 min | 86%–100% | No | \$\$\$ |

Adapted from the Centers for Disease Control and Prevention (CDC). Guidance for clinicians on the use of rapid influenza diagnostic tests. Available at: www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm. Accessed June 30, 2015.

best clinical judgment. Decisions on treatment and infection control can be made on the basis of positive rapid antigen test results. However, because of the suboptimal sensitivity and potential for false-negative results with rapid tests, negative results should not be used to make treatment or infection-control decisions or to rule out influenza virus infection. Positive results of rapid influenza tests are helpful, because they may reduce additional testing to identify the cause of the child's influenza-like illness. Polymerase chain reaction (PCR) confirmation should be considered in hospitalized patients. Presumptive treatment in high-risk patients should be started before receiving PCR results. Early detection, prompt antiviral treatment, and control interventions can lead to better individual patient outcomes and allow for effective cohorting and disease containment.

People with suspected influenza who present with an uncomplicated febrile illness typically do not require treatment with antiviral medications unless they are at higher risk of influenza complications (Table 2). Antiviral treatment also should be considered for children clinically presumed to have influenza disease whose siblings either are younger than 6 months or have underlying medical conditions that predispose them to complications of influenza. If there is a local shortage of antiviral medications, local public health authorities should provide additional guidance about testing and treatment. In past years, local shortages have occurred because of uneven drug distribution, but national shortages have not occurred.

Randomized placebo-controlled studies showed that oseltamivir and zanamivir were efficacious when administered as chemoprophylaxis to household contacts after a family member had laboratory-confirmed influenza. During the 2009 pandemic, the emergence of oseltamivir resistance was noted

among people receiving postexposure prophylaxis, highlighting the importance of resistance testing in this population. Decisions on whether to administer antiviral chemoprophylaxis should take into account the exposed person's risk of influenza complications, vaccination status, the type and duration of contact, recommendations from local or public health authorities, and clinical judgment. Optimally, postexposure chemoprophylaxis should be used only when antiviral agents can be started within 48 hours of exposure; the lower dose used for prophylaxis should not be used for symptomatic children. Early, full treatment doses provided to high-risk patients without waiting for laboratory confirmation is an alternate strategy.

Although immunization is the preferred approach to prevention of infection, chemoprophylaxis during an influenza outbreak, as defined by the CDC, is recommended

- For children at high risk of complications from influenza for whom influenza vaccine is contraindicated.
- For children at high risk during the 2 weeks after influenza immunization (IIV only).
- For family members or HCP who are unimmunized and are likely to have ongoing, close exposure to the following:
 - unimmunized children at high risk; or
 - unimmunized infants and toddlers who are younger than 24 months.
- For control of influenza outbreaks for unimmunized staff and children in a closed institutional setting with children at high risk (eg, extended-care facilities).
- As a supplement to immunization among children at high risk, including children who are immunocompromised and may not respond to vaccine.

- As postexposure prophylaxis for family members and close contacts of an infected person if those people are at high risk of complications from influenza.
- For children at high risk and their family members and close contacts, as well as HCP, when circulating strains of influenza virus in the community are not matched with seasonal influenza vaccine strains, on the basis of current data from the CDC and local health departments.

These recommendations apply to routine circumstances, but it should be noted that guidance may change on the basis of updated recommendations from the CDC in concert with antiviral availability, local resources, clinical judgment, recommendations from local or public health authorities, risk of influenza complications, type and duration of exposure contact, and change in epidemiology or severity of influenza. Chemoprophylaxis is not recommended for infants younger than 3 months, unless the situation is judged critical, because of limited safety and efficacy data in this age group.

Chemoprophylaxis Should Not Be Considered a Substitute for Immunization

Influenza vaccine should always be offered when not contraindicated, even after influenza virus has been circulating in the community. Antiviral medications currently licensed are important adjuncts to influenza immunization for control and prevention of influenza disease. Toxicities may be associated with antiviral agents; indiscriminate use might limit availability. Pediatricians should inform recipients of antiviral chemoprophylaxis that risk of influenza is lowered but still remains while taking the medication, and susceptibility to influenza returns when medication is

discontinued. Oseltamivir use is not a contraindication to immunization with IIV (unlike LAIV). For recommendations about treatment and chemoprophylaxis against influenza, see Table 4. Among some high-risk people, both vaccination and antiviral chemoprophylaxis may be considered. Updates will be available at www.aapredbook.org/flu and www.cdc.gov/flu/professionals/antivirals/index.htm.

FUTURE DIRECTIONS

For the 2015–2016 season, postmarketing safety and real-time vaccine effectiveness data will be analyzed as they become available. Continued evaluation of the safety, immunogenicity, and effectiveness of influenza vaccine, especially for children younger than 2 years, is important. The risk of febrile seizures when IIV is administered with other vaccines to children 6 through 23 months of age needs further investigation. The potential role of previous influenza vaccination on overall vaccine effectiveness by vaccine formulation, virus strain, and subject age in preventing outpatient medical visits, hospitalizations, and deaths continues to be evaluated. Furthermore, complete analysis of quadrivalent vaccines is needed as the number of formulations of IIV4 increase. Additionally, the routine use of LAIV in children with certain respiratory and nonrespiratory chronic medical conditions warrants further consideration. If, as expected, safety monitoring continues to show no increased risk of anaphylactic reactions in egg-allergic recipients of IIV, special precautions regarding allergy consultation and waiting periods after administration to egg-allergic recipients beyond those recommended for any vaccine may no longer be recommended. In addition, with limited data on the use of NAIs in hospitalized children or in children with comorbid conditions, prospective randomized clinical trials in this

population are warranted. Furthermore, to administer antiviral therapy optimally in hospitalized patients with influenza who cannot tolerate oral or inhaled antiviral agents, FDA-approved intravenous NAIs for children also are needed.

Immunizing all HCP, a crucial step in efforts to reduce health care–associated influenza infections, serves as an example to patients, highlighting the safety and effectiveness of annual immunization. Future efforts should include broader implementation and evaluation of mandatory immunization programs. Further investigation into the extent of offering to immunize parents and adult child care providers in the pediatric office setting; the level of family contact satisfaction with this practice; how practices handle the logistic, liability, legal, and financial barriers that limit or complicate this service; and most importantly, how this practice will affect disease rates in children and adults is needed. There is also a need for more systematic health services research on influenza vaccine uptake and refusal, as well as identification of methods to enhance uptake.

Efforts should be made to create adequate outreach and infrastructure to facilitate the optimal distribution of vaccine so that more people are immunized. Pediatricians also should become more involved in pandemic preparedness and disaster planning efforts. A bidirectional partner dialogue between pediatricians and public health decision makers assists efforts to address children's issues during the initial state, regional, and local plan development stages. Additional information can be found at www.aap.org/disasters/resourcekit.

With the increased demand for immunization during each influenza season, the AAP and the CDC recommend vaccine administration at any visit to the medical home during influenza season when it is not contraindicated, at specially arranged

vaccine-only sessions, and through cooperation with community sites, schools, and child care centers to provide influenza vaccine. If alternate venues, including pharmacies and other retail-based clinics, are used for immunization, a system of patient record transfer is beneficial in maintaining the accuracy of immunization records. Immunization information systems should be used whenever available. Two-dimensional barcodes have been used to facilitate more efficient and accurate documentation of vaccine administration with limited experience to date. Additional information concerning current vaccines shipped with 2-dimensional barcodes can be found at www.cdc.gov/vaccines/programs/iis/2d-vaccine-barcodes/. Access to care issues, lack of immunization records, and questions regarding who can provide consent may be addressed by linking children (eg, those in foster care or refugee, immigrant, or homeless children) with a medical home, using all health care encounters as vaccination opportunities, and more consistently using immunization registry data.

Development efforts continue for a universal influenza vaccine that induces broader protection and eliminates the need for annual immunization. In addition, development of a safe, immunogenic vaccine for infants younger than 6 months is essential. Studies on the effectiveness and safety of influenza vaccines containing adjuvants that enhance immune responses to influenza vaccines are ongoing. Finally, efforts to improve the vaccine development process to allow for a shorter interval between identification of vaccine strains and vaccine production continue. Pediatricians can remain informed during the influenza season by following the AAP *Red Book* Online Influenza Resource Page (www.aapredbook.org/flu).

^a Vaccine strains did not change from previous influenza season.

COMMITTEE ON INFECTIOUS DISEASES, 2015–2016

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CONTRIBUTORS

Stuart T. Weinberg, MD, FAAP – Partnership for Policy Implementation
Catherina Yang, BA – Research Assistant, Cohen Children's Medical Center of NY
Rebecca J. Schneyer, BA – Research Assistant, Cohen Children's Medical Center of NY
Patriot Yang, BA – Research Assistant, Cohen Children's Medical Center of NY
John M. Kelso, MD, FAAP – Division of Allergy, Asthma, and Immunology, Scripps Clinic, San Diego, CA

LIAISONS

Douglas Campos-Outcalt, MD, MPH – American Academy of Family Physicians
Karen M. Farizo, MD – Food and Drug Administration
Marc Fischer, MD, FAAP – Centers for Disease Control and Prevention
Bruce Gellin, MD, MPH – National Vaccine Program Office
Richard L. Gorman, MD, FAAP – National Institutes of Health

Natasha B. Halasa, MD, MPH, FAAP – Pediatric Infectious Disease Society
Joan L. Robinson, MD – Canadian Pediatric Society
Marco Aurelio Palazzi Safadi, MD – Sociedad Latinoamericana de Infectología Pediátrica
Jane F. Seward, MBBS, MPH, FAAP – Centers for Disease Control and Prevention
Geoffrey Simon, MD, FAAP – Committee on Practice Ambulatory Medicine
Jeffrey R. Starke, MD, FAAP – American Thoracic Society

STAFF

Jennifer M. Frantz, MPH

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ABBREVIATIONS

AAP: American Academy of Pediatrics
cclIV3: trivalent cell culture-based inactivated influenza vaccine
CDC: Centers for Disease Control and Prevention
CI: confidence interval
FDA: US Food and Drug Administration
HCP: health care personnel
ID: intradermal
IIV: inactivated influenza vaccine
IIV3: trivalent inactivated influenza vaccine
IIV4: quadrivalent inactivated influenza vaccine
IM: intramuscular
LAIV: live attenuated influenza vaccine
LAIV4: quadrivalent live attenuated influenza vaccine
NAIs: neuraminidase inhibitors
pH1N1: influenza A (H1N1) pandemic virus
RIV3: trivalent recombinant influenza vaccine

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