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Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

POLICY STATEMENT

Recommendations for Prevention and Control of Influenza in Children, 2011–2012

COMMITTEE ON INFECTIOUS DISEASES

KEY WORDS

influenza, immunization, live-attenuated influenza vaccine, trivalent inactivated influenza vaccine, vaccine, children, pediatrics

ABBREVIATIONS

AAP—American Academy of Pediatrics
HCP—health care personnel
CDC—Centers for Disease Control and Prevention
TIV—trivalent inactivated influenza vaccine
LAIV—live-attenuated influenza vaccine

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abstract

The purpose of this statement is to update recommendations for routine use of trivalent seasonal influenza vaccine and antiviral medications for the prevention and treatment of influenza in children. The key points for the upcoming 2011–2012 season are that (1) the influenza vaccine composition for the 2011–2012 season is *unchanged* from the 2010–2011 season, (2) annual universal influenza immunization is indicated, (3) a *simplified* dosing algorithm for administration of influenza vaccine to children 6 months through 8 years of age has been created, (4) most children presumed to have egg allergy can safely receive influenza vaccine in the office without need for an allergy consultation, and (5) an intradermal trivalent inactivated influenza vaccine has been licensed for the 2011–2012 season for use in people 18 through 64 years of age. Pediatricians, nurses, and all health care personnel have leadership roles in the prevention of influenza through vaccine use and public education. In addition, pediatricians should promptly identify influenza infections to enable rapid treatment, when indicated, to reduce childhood morbidity and mortality. *Pediatrics* 2011;128:813–825

INTRODUCTION

The American Academy of Pediatrics (AAP) recommends annual trivalent seasonal influenza immunization for all children and adolescents 6 months of age and older during the 2011–2012 influenza season. Special outreach efforts should be made to vaccinate people in the following groups:

- All children, including infants born prematurely, 6 months of age and older with conditions that increase the risk of complications from influenza.
- All household contacts and out-of-home care providers of
  - children with high-risk conditions and
  - children younger than 5 years.
- All health care personnel (HCP).
- All women who are pregnant, considering pregnancy, or breastfeeding during the influenza season.

KEY POINTS RELEVANT FOR THE 2011–2012 INFLUENZA SEASON

1. All people 6 months of age and older should receive trivalent seasonal influenza vaccine each year, especially those who are at high

risk of influenza complications (eg, children with chronic medical conditions such as asthma, diabetes mellitus, immunosuppression, or neurologic disorders). In the United States, more than two-thirds of children younger than 6 years and almost all children older than 6 years spend significant time in child care and school settings outside the home. Exposure to groups of children increases the risk of infectious diseases. Children younger than 2 years are at an increased 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. Therefore, reducing influenza transmission among children who attend child care or school should decrease the burden of childhood influenza and transmission of influenza to household contacts and community members. Most egg-allergic children can now receive influenza vaccine safely.

2. Annual trivalent seasonal influenza vaccine is recommended for household members and out-of-home care providers of children and adolescents at high risk of complications of influenza and healthy children younger than 5 years, especially infants younger than 6 months. Pediatric offices should consider serving as an alternate venue for parents and other adults who care for children to receive influenza vaccine, if this approach is acceptable to both the pediatrician and the adult to be immunized. Clinicians should still encourage adults to have a medical home and communicate their immunization status to the primary care provider. Immunization of close contacts of children at high risk of influenza-related complications is intended to reduce their risk of contagion (ie, "cocooning"). The concept of cocooning is particularly important for helping to protect infants younger than 6 months, because they are too young to be immunized with influenza vaccine. The risk of influenza-associated hospitalization in healthy children younger than 24 months has been shown to be greater than the risk of hospitalization in previously recognized high-risk groups such as the elderly. Children 24 through 59 months of age have had increased rates of outpatient visits and antimicrobial use.
3. The 2009 pandemic influenza A (H1N1) virus emerged in March 2009 and was associated with 2 significant waves of influenza activity during 2009 and 2010, as defined by the World Health Organization. This virus strain disproportionately affected the pediatric population compared with the usual seasonal influenza strains. It was 1 of 3 circulating influenza viruses during the 2010–2011 influenza season, and it is expected to circulate again during the 2011–2012 influenza season in combination with 1 or more of the other seasonal influenza strains. During the 2010–2011 season, influenza A (H3N2) was the predominant circulating strain, but weekly virus subtype activity varied regionally.
4. Although the number of hospitalizations for younger persons and outpatient visits for influenza-like illness overall was lower during the 2010–2011 season compared with the influenza A (H1N1) pandemic period, at least 114 laboratory-confirmed influenza-associated pediatric deaths were recorded during the 2010–2011 season. Seventy-one deaths were associated with influenza A virus subtypes: 30 influenza A (2009 H1N1), 21 influenza A (H3N2), and 20 undetermined subtypes. Forty-three deaths were associated with influenza B viruses. More than half of all hospitalized pediatric patients (51.8%) did not have any known underlying conditions (Fig 1). Although children with certain conditions are at higher risk of complications, substantial proportions of seasonal influenza morbidity and mortality occur among healthy children.
5. The recommended trivalent vaccine for the 2011–2012 influenza season contains the following 3 virus strains:
   - A/California/7/2009 (H1N1)–like antigen (derived from 2009 pandemic influenza A [H1N1] virus);
   - A/Perth/16/2009 (H3N2)–like antigen; and
   - B/Brisbane/60/2008–like antigen.
6. On the basis of ongoing global surveillance data, for only the fourth time in 25 years there is no need to change any of the influenza vaccine strains (Fig 2). The number of trivalent seasonal influenza vaccine doses to be administered this year depends on the child's age at the time of the first administered dose and his or her vaccine history (Fig 3):
   - Infants younger than 6 months are too young to be immunized with influenza vaccine.
   - Children 9 years of age and older need only 1 dose.
   - Children 6 months through 8 years of age should receive 2 doses of vaccine if they did not receive any dose of vaccine last

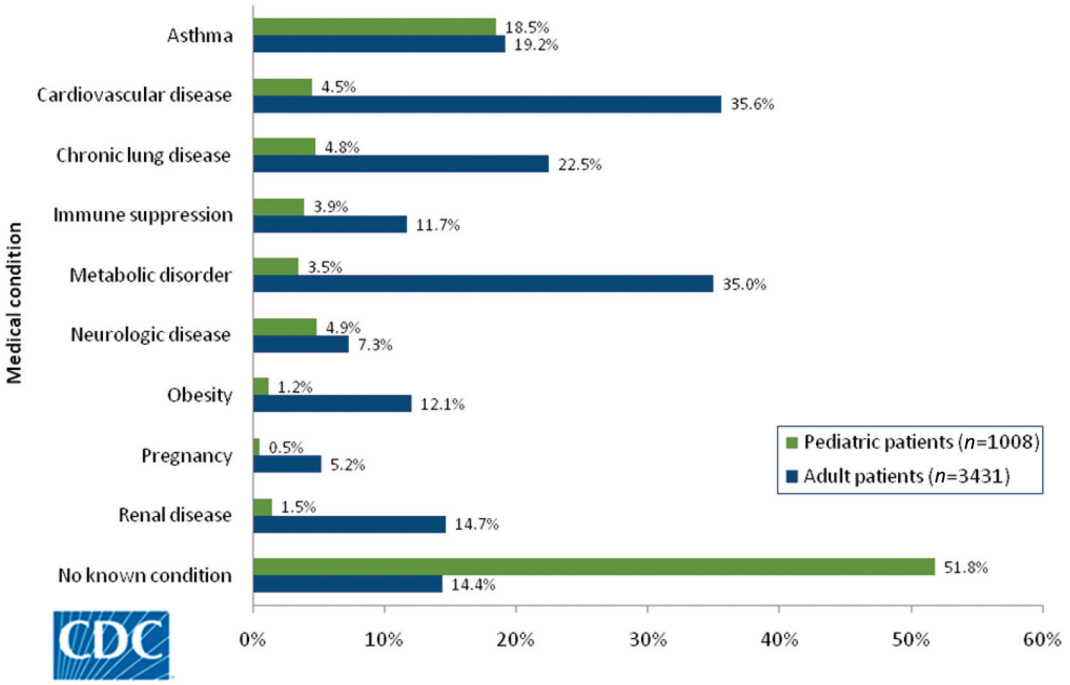

FIGURE 1
Selected underlying medical conditions in patients hospitalized with influenza, FluSurv-NET 2010–2011. Reprinted from: Centers for Disease Control and Prevention. FluView 2010–2011 influenza season week 15 ending April 16, 2010. Available at: www.cdc.gov/flu/weekly.

	H1N1-like strain	H3N2-like strain	B-like strain
1986-'87	A/Chile/1/83 and A/Singapore/6/86	A/Christchurch/4/85-A/Mississippi/1/85	B/Ann Arbor/1/86
1987-'88	A/Singapore/6/86	A/Leningrad/360/1986	B/Ann Arbor/1/86
1988-'89	A/Singapore/6/86	A/Sichuan/2/87	B/Beijing/1/87
1989-'90	A/Singapore/6/86	A/Shanghai/11/87	B/Yamagata/16/88
1990-'91	A/Singapore/6/86	A/Guizhou/54/89	B/Yamagata/16/88
1991-'92	A/Singapore/6/86	A/Beijing/353/89	B/Yamagata/16/88
1992-'93[a]	**A/Singapore/6/86**	**A/Beijing/353/89**	**B/Yamagata/16/88**
1993-'94	A/Singapore/6/86	A/Beijing/32/92	B/Panama/45/90
1994-'95	A/Singapore/6/86	A/Shangdong/9/93	B/Panama/45/90
1995-'96	A/Singapore/6/86	A/Johannesburg/33/94	B/Beijing/184/93
1996-'97	A/Singapore/6/86	A/Wuhan/359/95	B/Beijing/184/93
1997-'98	A/Bayern/7/95	A/Wuhan/359/95	B/Beijing/184/93
1998-'99	A/Beijing/262/95	A/Sydney/5/97	B/Beijing/184/93
1999-2000[a]	**A/Beijing/262/95**	**A/Sydney/5/97**	**B/Beijing/184/93**
2000-'01	A/New Caledonia/20/99	A/Moscow/10/99	B/Beijing/184/93
2001-'02	A/New Caledonia/20/99	A/Moscow/10/99	B/Sichuan/379/99
2002-'03	A/New Caledonia/20/99	A/Moscow/10/99	B/Hong Kong/330/2001
2003-'04[a]	**A/New Caledonia/20/99**	**A/Moscow/10/99**	**B/Hong Kong/330/2001**
2004-'05	A/New Caledonia/20/99	A/Fujian/411/2002	B/Shanghai/361/2002
2005-'06	A/New Caledonia/20/99	A/California/7/2004	B/Shanghai/361/2002
2006-'07	A/New Caledonia/20/99	A/Wisconsin/67/2005	B/Malaysia/2506/2004
2007-'08	A/Solomon Islands/3/2006	A/Wisconsin/67/2005	B/Malaysia/2506/2004
2008-'09	A/Brisbane/59/2007	A/Brisbane/10/2007	B/Florida/4/2006
2009-'10	A/Brisbane/59/2007	A/Brisbane/10/2007	B/Brisbane/60/2008
Pandemic	A/California/07/2009		
2010-'11	A/California/07/2009	A/Perth/16/2009	B/Brisbane/60/2008
2011-'12[a]	**A/California/07/2009**	**A/Perth/16/2009**	**B/Brisbane/60/2008**

FIGURE 2
World Health Organization vaccine composition recommendations 1986 to present. [a] No change in influenza vaccine strains from previous influenza season. Data source: World Health Organization, Global Alert and Response. Recommendations for influenza vaccine composition. Available at: www.who.int/csr/disease/influenza/vaccinerecommendations1/en/index.html (for data from 1998 to present; previous years' data were obtained from *Weekly Epidemiologic Record*).

season. The second dose should be administered at least 4 weeks after the first dose.

- Children 6 months through 8 years of age who received at least 1 dose of the 2010–2011 trivalent seasonal influenza vaccine last season need only 1 dose of the 2011–2012 influenza vaccine this season.

In most influenza seasons, children who received influenza vaccine for the *first time* the previous season but who received only 1 dose are recommended to receive 2 doses of vaccine in the current season, because the first vaccine dose primes the immune system, but no significant protection against disease is achieved until 1 week after the second dose. However, because the vaccine strains for the 2011–2012 season are *unchanged* from last season, 1 dose this season coupled with the 1 dose of last season will provide adequate protection (Fig 4). Previous recommendations for 2 doses of vaccine will resume for seasons in which 1 or more of the vaccine strains change.

7. Optimal protection is achieved through annual immunization. Antibody titers wane to 50% of their

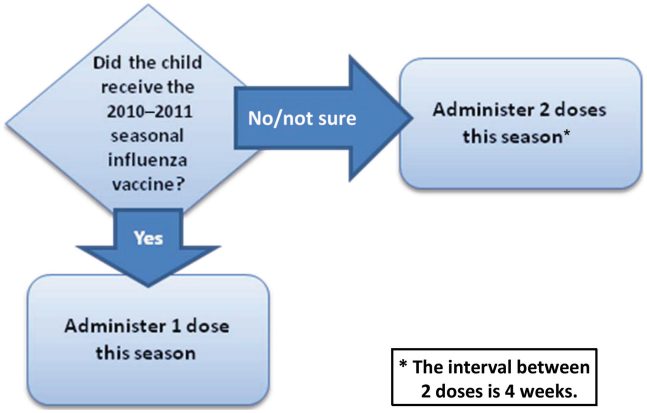

FIGURE 3

Number of 2011–2012 seasonal influenza vaccine doses for children 6 months through 8 years of age.

- This simplified approach is only possible because the 2011–2012 influenza vaccine contains the identical 3 influenza virus strains used last year in the 2010–2011 vaccine.
- The number of doses to be given is determined on the basis of the child's age at the time of the first dose.

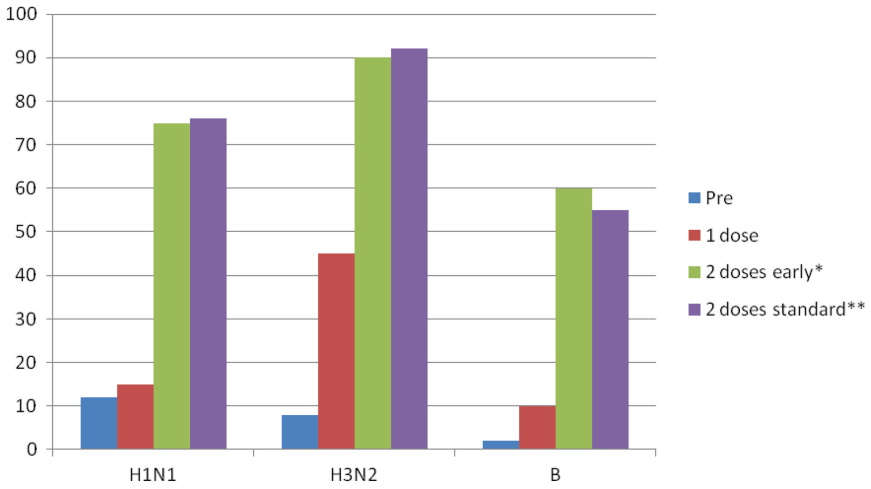

FIGURE 4

Percentage of children with titers greater than 1:32 during seasons with no change in vaccine antigen. * One dose administered in the spring; the second dose administered in the fall. ** Two doses administered 4 weeks apart in the fall. (Reprinted with permission from Englund JA, Fairchok MP, Monto AS, Neuzil KM. *Pediatrics*. 2005;115[4]:1039–1047.)

original levels 6 to 12 months after vaccination. Because the vaccine strains for the 2011–2012 season are unchanged from last season, a repeat dose this season is critical for maintaining protection in all populations.

8. As soon as the trivalent seasonal influenza vaccine is available locally, health care personnel (HCP) should be immunized, publicize vaccine availability to parents and caregivers, and begin immunization of all children 6 months of age and older, especially children at high risk of complications from influenza. HCP endorsement plays a major role in vaccine uptake. A strong correlation exists between HCP endorsement of influenza vaccine and patient acceptance. Providers should continue to offer vaccine through the vaccine expiration date. Protective immune responses persist throughout the influenza season, which can have >1 disease peak and often extends into March or later. Prompt initiation of influenza immunization and continuance of immunization throughout the influenza season, regardless of whether influenza is circulating (or has circulated) in the community, are critical components of an effective immunization strategy. This approach provides ample opportunity to administer a second dose of vaccine, because children younger than 9 years might require 2 doses to confer optimal protection.
9. HCP, influenza campaign organizers, and public health agencies should collaborate to develop improved strategies for planning, communication, and administration of vaccines.
   - Plan to make trivalent seasonal influenza vaccine easily accessible for all children. Examples of such action include creating walk-in influenza clinics, extending office hours beyond routine times during peak vaccination periods, considering how to immunize parents and adult caregivers at the same time in the same office setting as children, and working with other institutions (eg, schools, child care centers, and religious organizations) or alternative care sites, such as emergency departments, to expand venues for administering vaccine while providing appropriate documentation of immunization for the child's medical home.
   - Concerted efforts among the aforementioned groups, plus vaccine manufacturers, distributors, and payers, are also necessary to

TABLE 1 Antiviral Drug Sensitivities of Influenza Strains Expected to Circulate During the 2011–2012 Influenza Season

Seasonal Influenza Vaccine Strain (2011–2012)	Amantadine (Symmetrel[a])/ Rimantadine (Flumadine[b])	Oseltamivir (Tamiflu[c])	Zanamivir (Relenza[d])
Seasonal influenza A (H1N1) virus (derived from 2009 pandemic influenza A [H1N1] virus)	Resistant	Susceptible	Susceptible
Seasonal influenza A (H3N2) virus	Resistant	Susceptible	Susceptible
Seasonal influenza B virus	Resistant	Susceptible	Susceptible

For current recommendations about treatment and chemoprophylaxis of influenza, see www.cdc.gov/flu/professionals/antivirals/index.htm or www.aapredbook.org/flu. Circulating strains in local communities may vary from those found in the vaccine; antiviral sensitivities of these strains are reported weekly at www.cdc.gov/flu/weekly/summary.htm.

[a] Endo Pharmaceuticals (Chads Ford, PA).

[b] Forest Pharmaceuticals (St Louis, MO).

[c] Roche Laboratories (Nutley, NJ).

[d] GlaxoSmithKline (Research Triangle Park, NC).

appropriately prioritize distribution to the primary care office setting, especially when vaccine supplies are delayed or limited.

- Vaccine safety, effectiveness, and indications must be communicated properly to the public. HCP should act as role models by receiving influenza immunization annually and recommending annual immunizations to both their colleagues and patients.

10. The neuraminidase inhibitors oseltamivir (Tamiflu [Roche Laboratories, Nutley, NJ]) and zanamivir (Relenza [GlaxoSmithKline, Research Triangle Park, NC]) are the only antiviral medications routinely recommended for chemoprophylaxis or treatment during the 2011–2012 season. All strains of influenza currently anticipated to circulate are susceptible to neuraminidase inhibitors but have high rates of resistance to amantadine and rimantadine (Table 1). Resistance characteristics might change rapidly; clinicians should verify susceptibility information at the start of the influenza season and monitor it during the season through either the AAP Web site (www.aap.org or http://aapredbook.aappublications.org/flu) or the Centers for Disease Control and Prevention (CDC) Web site (www.cdc.gov/flu/index.htm).
11. As the 2011–2012 influenza season unfolds, it is critically important for HCP to be aware of new or changing recommendations from the CDC or their local and state health departments. Up-to-date information can be found on the AAP Web site (www.aap.org or http://aapredbook.aappublications.org/flu), through state-specific AAP chapter Web sites, or on the CDC Web site (www.cdc.gov/flu/index.htm).

TRIVALENT SEASONAL INFLUENZA VACCINES

Tables 2 and 3 summarize information on the 2 types of 2011–2012 trivalent seasonal influenza vaccines licensed for immunization of children and adults: injectable trivalent inactivated influenza vaccine (TIV) and intranasally administered live-attenuated influenza vaccine (LAIV). Both vaccines contain the identical strains of influenza A subtypes (ie, H1N1 and H3N2) and influenza B anticipated to circulate during the 2011–2012 influenza season.

TIV is an inactivated vaccine that contains no live virus and cannot produce a viral infection. TIV formulations are now available for intramuscular and intradermal use. The intramuscular formulation of TIV is licensed and recommended for children 6 months of age and older and adults, including people with and without chronic medical conditions. The most common adverse events after administration are local injection-site pain and tenderness. Fever might occur within 24 hours after immunization in approximately 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 might occur after administration of TIV.

An intradermal formulation of TIV has been licensed for the 2011–2012 season for use in people 18 through 64 years of age. This method of delivery involves a microinjection with a needle 90% shorter than needles used for intramuscular administration. The most common adverse events are redness, induration, swelling, pain, and itching at the site of administration at a slightly higher rate than occurs with the intramuscular formulation of TIV. Headache, myalgia, and malaise might occur and tend to occur at the same rate as that with the intramuscular formulation of TIV. There is no preference for intramuscular or intradermal immunization in people 18 years of age or older; therefore, pediatricians may choose to use either the intramuscular or intradermal product in their late adolescent and young adult patients.

Increased reports of febrile seizures in the United States were noted by the Vaccine Adverse Event Reporting System (VAERS) and were associated with TIV manufactured by Sanofi Pasteur (Fluzone), mainly in children in the 12- through 23-month age group (the peak age for febrile seizures), and included some who concurrently had received 13-valent pneumococcal conjugate vaccine (PCV13). All children fully recovered. On the basis of current data, prophylactic use of antipyretic agents in TIV-immunized children is not indi-

TABLE 2 Recommended Trivalent Seasonal Influenza Vaccines for Different Age Groups: United States, 2011–2012 Influenza Season

Vaccine	Trade Name	Manufacturer	Presentation	Ovalbumin Content, μg of Ovalbumin per 0.5-mL Dose	Thimerosal Mercury Content, μg of Hg per 0.5-mL Dose	Age Group
Inactivated						
TIV	Fluzone	Sanofi Pasteur, Swiftwater, PA	0.25-mL prefilled syringe	~0.1[a]	0.0	6–35 mo
			0.5-mL prefilled syringe	~0.1[a]	0.0	≥36 mo
			0.5-mL vial	~0.1[a]	0.0	≥36 mo
			5.0-mL multidose vial	~0.1[a]	25.0	≥6 mo
TIV	Fluzone intradermal	Sanofi Pasteur, Swiftwater, PA	0.1-mL prefilled microinjection	Not cited	0.0	18–64 y
TIV	Fluzone HD	Sanofi Pasteur, Swiftwater, PA	0.5-mL prefilled syringe	~0.1[a]	0.0	≥65 y
TIV	Fluvirin	Novartis, East Hanover, NJ	0.5-mL prefilled syringe	≤1.0[b]	<1.0	≥4 y
			5.0-mL multidose vial	≤1.0[b]	25	≥4 y
TIV	Fluarix	GlaxoSmithKline, King of Prussia, PA	0.5-mL prefilled syringe	≤0.05[b]	0.0	≥3 y
TIV	FluLaval	GlaxoSmithKline, King of Prussia, PA	5.0-mL multidose vial	≤1.0[b]	25.0	≥18 y
TIV	Afluria	CSL Biotherapies, King of Prussia, PA	0.5-mL prefilled syringe	≤1.0[b]	0	≥9[c]
			5-mL multidose vial	≤1.0[b]	25.0	≥9[c]
Live-attenuated						
LAIV	FluMist	MedImmune, Gaithersburg, MD	0.2-mL sprayer	Not cited	0.0	2–49 y

[a] Data obtained from Sanofi Pasteur (personal communication, 2011) suggests that the residual egg protein (expressed as ovalbumin) in Fluzone vaccine or in Fluzone High-Dose vaccine is typically on the order of 0.1 μg per dose.

[b] Data are from the package inserts, many of which have been updated for the 2011–2012 season.

Data sources: American Academy of Pediatrics, Committee on Infectious Diseases. *Pediatrics.* 2010;126(4):816–826; Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 2010;59(RR-8):1–62; and Centers for Disease Control and Prevention. *Morb Mortal Wkly Rep.* 2011;60 (Early Release):1–6.

[c] Age indication per package insert is ≥5 years; however, the ACIP recommends Afluria not be used in children aged 6 months through 8 years 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 aged 5 through 8 years of age who has a medical condition that increases the child's risk for influenza complications, Afluria can be used; however, providers should discuss with the parents or caregivers the benefits and risks of influenza vaccination with Afluria before administering this vaccine.

cated, and current AAP and Advisory Committee on Immunization Practices (ACIP) recommendations for administration of TIV in this age group are unchanged. Febrile seizures can occur anytime a child has a fever, but the typical child who has a febrile seizure recovers quickly and fully.

Previous febrile seizures or seizure disorders are not a contraindication to use of TIV or LAIV in otherwise eligible children. Use of antipyretic agents in febrile children does not reduce the incidence of febrile seizures; therefore, routine use of antipyretic agents for avoiding febrile seizures in children who receive influenza vaccine is not recommended. Approximately 2% to 5% of children 6 months through 5 years of age will have at least 1 febrile seizure not associated with vaccines in their lifetime.

LAIV is a live-attenuated influenza vaccine that is administered intranasally and is licensed by the US Food and Drug Administration for healthy people 2 through 49 years of age. It is not recommended for people with a history of asthma or other high-risk medical conditions associated with an increased risk of complications from influenza (see "Contraindications and Precautions"). LAIV has the potential to produce mild symptoms including rhinitis, headache, wheezing, vomiting, muscle aches, and fever. LAIV should not be administered to people with copious nasal congestion that would impede vaccine delivery.

Both TIV and LAIV are cost-effective strategies for preventing influenza among children and their families when circulating and vaccine strains are matched closely, but efficacy varies according to the age of the recipient. Current data from direct comparisons of the efficacy or effectiveness of these 2 vaccines are limited, because the studies were conducted in a variety of settings and in populations using several different clinical end points. In 1 study that compared LAIV with TIV in infants and young children without severe asthma or a recent history of wheezing, LAIV showed significantly better efficacy than TIV; results of other studies suggest that TIV might be more effective in young adults.

A large body of evidence demonstrates that thimerosal-containing vaccines are not associated with increased risk of autism spectrum disorders in children. However, some people might raise concerns about the minute amounts of thimerosal in TIV vaccines, and in some states, there is a legislated restriction on the use of thimerosal-containing vaccines for infants and/or children. The benefits of protecting children against the known risks of influenza are clear. Therefore, children should receive any available formulation of TIV rather than delay immunization while waiting for vaccines with reduced thimerosal content or for

TABLE 3 LAIV Compared With TIV

Vaccine Characteristic	LAIV	TIV
Route of administration	Intranasal spray	Intramuscular or intradermal injection[a]
Type of vaccine	Live virus	Killed virus
Product	Attenuated, cold-adapted	Inactivated subvirion or surface antigen
No. of included virus strains	3 (2 influenza A, 1 influenza B)	3 (2 influenza A, 1 influenza B)
Vaccine virus strains updated	Annually	Annually
Frequency of administration[b]	Annually	Annually
Approved age groups	All healthy persons aged 2–49 y	All persons aged ≥6 mo (intradermal 18–64 y)
Interval between 2 doses in children	4 wk	4 wk
Can be given to persons with medical risk factors for influenza-related complications	No	Yes
Can be given to children with asthma or children aged 2–4 y with wheezing in the previous year	No[c]	Yes
Can be simultaneously administered with other vaccines	Yes[d]	Yes[d]
If not simultaneously administered, can be administered within 4 wk of another live vaccine	No, prudent to space 4 wk apart	Yes
Can be administered within 4 wk of an inactivated vaccine	Yes	Yes

[a] The preferred site of TIV intramuscular injection for infants and young children is the anterolateral aspect of the thigh.
[b] See Fig 4 for decision algorithm to determine the number of doses of 2011–2012 seasonal influenza vaccine recommended for children this year.
[c] LAIV is not recommended for children with a history of asthma. In the 2- through 4-year age group, there are children who have a history of wheezing with respiratory illnesses in whom reactive airways disease is diagnosed and in whom asthma may later be diagnosed. Therefore, because of the potential for increased wheezing after immunization, children 2 through 4 years of age with recurrent wheezing or a wheezing episode in the previous 12 months should *not* receive LAIV. When offering LAIV to children in this age group, a clinician should screen those who might be at higher risk of asthma by asking the parents/guardians of 2-, 3-, and 4-year-olds (24- to 59-month-olds) the question, "In the previous 12 months, has a health care professional ever told you that your child had wheezing?" If the parents answer "yes" to this question, LAIV is *not* recommended for these children.
[d] LAIV coadministration has been evaluated systematically only among children 12 to 15 months of age with measles-mumps-rubella and varicella vaccines. TIV coadministration has been evaluated systematically only among adults with pneumococcal polysaccharide and zoster vaccines.
Data sources: American Academy of Pediatrics, Committee on Infectious Diseases. *Pediatrics*. 2010;126(4):816–826; and Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM; Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2011;60(RR-1):1–24.

thimerosal-free vaccine. Although some formulations of TIV contain only a trace amount of thimerosal, certain types can be obtained with no thimerosal. LAIV does not contain thimerosal. Vaccine manufacturers are delivering increasing amounts of thimerosal-free influenza vaccine each year.

Administration to Egg-Allergic Individuals

Although both TIV and LAIV are produced in eggs, recent data have shown that influenza vaccine administered in a single, age-appropriate dose is well tolerated by nearly all recipients who have egg allergy. More conservative approaches, such as skin testing or a 2-step graded challenge, are no longer recommended.

As a precaution, clinicians should determine if the presumed egg allergy is based on a mild or severe reaction. Mild reactions are defined as hives alone; severe reactions involve cardiovascular changes, respiratory and/or gastrointestinal tract symptoms, or reactions that require the use of epinephrine. Clinicians should consult with an allergist for children with a history of severe reaction. Most vaccine administration to people with egg allergy can happen without the need for referral. Data indicate that only approximately 1% of children have immunoglobulin E–mediated sensitivity to egg, and of those, a very small minority have a severe allergy.

Standard immunization practice should include the ability to respond to acute hypersensitivity reactions. Therefore, influenza vaccine should be given to people with egg allergy with the following preconditions (Fig 5):

- Appropriate resuscitative equipment must be readily available.[1]
- Ovalbumin content up to 0.7 micrograms/0.5 mL per vaccine dose has been well tolerated (Table 2).
- After immunization, the vaccine recipient should be observed in the office for 30 minutes, the standard observation time after receiving immunotherapy.
- For children who need a second dose, the same product brand is preferred, if possible, but it does not need to be from the same lot as the first dose.

VACCINE STORAGE AND ADMINISTRATION

Intramuscular Vaccine

The intramuscular formulation of TIV is shipped and stored at 2°C to 8°C (35°F–46°F). It is 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 older than 6 months but younger than 36 months should receive a dose of 0.25 mL, and all people aged 3 years (36 months) and older should receive 0.5 mL per dose.

Intradermal Vaccine

The intradermal formulation of TIV also is shipped and stored at 2°C to 8°C (35°F–46°F). The package insert

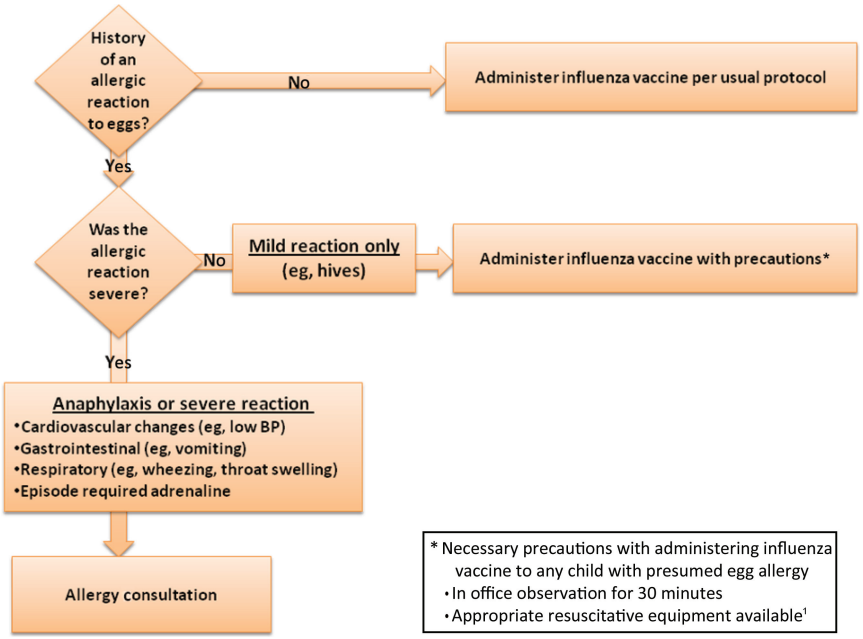

FIGURE 5
Precautions for administering influenza vaccine to presumed egg-allergic recipients.

should be reviewed for full administration details of this new product, which is licensed for the 2011–2012 season for persons 18 through 64 years of age.

Live-Attenuated (Intranasal) Vaccine

The cold-adapted LAIV formulation currently licensed in the United States must be shipped and stored at 2°C to 8°C 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. Any of the influenza vaccines can be administered at the same visit with all other recommended routine vaccines. After administration of any live-virus vaccine, at least 4 weeks should pass before another live-virus vaccine is administered.

CURRENT RECOMMENDATIONS

Trivalent seasonal influenza immunization is recommended for all children 6 months of age and older. Healthy children 2 years of age and older can receive either TIV or LAIV. Particular focus should be on the administration of TIV for all children and adolescents who have underlying medical conditions associated with an increased risk of complications from influenza, including:

- Asthma or other chronic pulmonary diseases including cystic fibrosis.
- Hemodynamically significant cardiac disease.
- Immunosuppressive disorders or therapy.
- HIV infection.
- Sickle cell anemia and other hemoglobinopathies.
- Diseases that require long-term aspirin therapy, including juvenile idiopathic arthritis and 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.

Although universal immunization for all people 6 months of age and older is recommended for 2011–2012, particular immunization efforts with either TIV 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 at-risk children of all ages (healthy contacts 2–49 years of age can receive either TIV or LAIV).
- Any female who is pregnant, considering pregnancy, or breastfeeding during the influenza season (TIV only). Studies have found that infants born to immunized women have better influenza-related health outcomes. However, data suggest that no more than one-half of pregnant women receive seasonal influenza vaccine, although both pregnant women and their infants are at higher risk of complications. In addition, there is limited evidence that influenza vaccination in pregnancy might decrease the risk of preterm birth.
- HCP or health care volunteers. Despite the recent AAP recommendation for mandatory influenza immunization for all HCP,[2] many HCP remain unvaccinated. As of January 2010, the CDC estimated that only 62% of HCP received the seasonal vaccine and only 37% received the 2009 H1N1 monovalent vaccine. HCP frequently come into contact with patients at high risk of influenza illness in their clinical settings, so it is paramount that HCP protect themselves against influenza to remain influenza free, to prevent disease

transmission to patient populations at high risk, and to avoid lost workplace productivity.

- 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 TIV

- Infants younger than 6 months.
- Children who have a moderate-to-severe febrile illness, on the basis of clinical judgment of the provider.
- Children who are known to have experienced Guillain-Barré syndrome (GBS) within 6 weeks after a previous influenza vaccination; whether influenza vaccination specifically might increase the risk of recurrence of Guillain-Barré syndrome is unknown; the decision not to immunize should be thoughtfully balanced against the potential morbidity and mortality associated with influenza for that individual child.

Children Who Should Not Be Vaccinated With LAIV

- Children younger than 2 years.
- Children who have a moderate-to-severe febrile illness.
- Children with copious nasal congestion that would impede vaccine delivery.
- Children who are known to have experienced Guillain-Barré syndrome within 6 weeks after a previous influenza vaccination; whether influenza vaccination specifically might increase the risk of recurrence of Guillain-Barré syndrome is unknown; the decision not to immunize should be balanced against the potential morbidity and mortality associated with influenza for that individual child.
- Children who have received other live-virus vaccines within the previous 4 weeks; however, other live-virus vaccines can be given on the same day as LAIV.
- Children with asthma, children with other chronic disorders of the pulmonary or cardiovascular systems, or children 2 through 4 years of age with a history of recurrent wheezing or a medically attended wheezing episode in the previous 12 months.
- Children with chronic underlying medical conditions including metabolic disease, diabetes mellitus, renal dysfunction, and hemoglobinopathies.
- 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.

PRECAUTIONS

LAIV is not recommended for children with asthma. In the 2- through 4-year age range, many children have a history of wheezing with respiratory tract illnesses and are eventually diagnosed with asthma. Therefore, because of the potential for increased wheezing after immunization, children younger than 5 years with recurrent wheezing or a medically attended wheezing episode in the previous 12 months of age should *not* receive LAIV.

When offering LAIV to children 24 through 59 months of age, the clinician should screen them by asking the parent/guardian the question, "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, LAIV is *not* recommended for the child. TIV would be recommended for the child to whom LAIV is not given.

In addition, TIV is the vaccine of choice for anyone in close contact with a subset of severely immunocompromised people (ie, people in a protected environment). TIV is preferred over LAIV for contacts of severely immunocompromised people (ie, in a protected environment) because of the theoretical risk of infection in an immunocompromised contact of an LAIV-immunized person. Available data indicate that there is 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 wards, while using standard infection-control techniques. As a precautionary measure, people recently vaccinated with LAIV should restrict contact with severely immunocompromised patients (eg, hematopoietic stem cell transplant recipients during periods that require a protected environment) 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.

Information about influenza surveillance is available through the CDC

TABLE 4 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis for the 2011–2012 Influenza Season: United States

Medication	Treatment (5 d)	Chemoprophylaxis (10 d)
Oseltamivir[a]		
Adults	75 mg twice daily	75 mg once daily
Children >12 mo		
Body weight		
≤15 kg (≤33 lb)	30 mg twice daily	30 mg once daily
>15 to 23 kg (33 to 51 lb)	45 mg twice daily	45 mg once daily
>23 to 40 kg (>51 to 88 lb)	60 mg twice daily	60 mg once daily
>40 kg (>88 lb)	75 mg twice daily	75 mg once daily
Children 3 to <12 mo[b]	3 mg/kg per dose twice daily	3 mg/kg per dose once per day
Children 0 to <3 mo[c]	3 mg/kg per dose twice daily	Not recommended unless situation judged critical because of limited data on use in this age group
Zanamivir[d]		
Adults	10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily
Children (≥7 y for treatment, 5 y for chemoprophylaxis	10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily

[a] Oseltamivir is manufactured by Roche Laboratories (Nutley, NJ) and is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available as Tamiflu in 30-, 45-, and 75-mg capsules and as a powder for oral suspension that is reconstituted to provide a final concentration of 6 mg/mL. The volume of oral suspension is being changed from 12 mg/mL to 6 mg/mL this year to reduce frothing when shaken. **Oral suspensions in 12 mg/mL concentrations will remain available until supplies run out. For the 6-mg/mL suspension, a 30-mg dose is given with 5 mL of oral suspension, 45-mg dose is given with 7.5 mL oral suspension, 60-mg dose is given with 10 mL oral suspension, and 75-mg dose is given with 12.5 mL oral suspension**. If the commercially manufactured oral suspension is not available, the capsules may be opened and the contents mixed with a sweetened liquid to mask the bitter taste, or a suspension can be compounded by retail pharmacies (final concentration: 15 mg/mL). For patients with renal insufficiency, the dose should be adjusted on the basis of creatinine-clearance rate. For treatment of patients with a creatinine-clearance rate of 10 to 30 mL/min: 75 mg once daily for 5 days. For chemoprophylaxis of patients with a creatinine-clearance rate of 10 to 30 mL/min: 30 mg once daily for 10 days after exposure or 75 mg once every other day for 10 days after exposure (5 doses). (See www.cdc.gov/flu/professionals/antivirals/antiviral-drug-resistance.htm.)

[b] Weight-based dosing is preferred; however, if weight is not known, dosing according to age for treatment (give 2 doses per day) or prophylaxis (give 1 dose per day) of influenza in term infants younger than 1 year may be necessary: 0 to 3 months (treatment only), 12 mg (2 mL of 6 mg/mL commercial suspension); 4 to 5 months, 17 mg (2.8 mL of 6 mg/mL of commercial suspension); 6 to 11 months, 24 mg (4 mL of 6 mg/mL commercial suspension). Although Emergency Use Authorization recommendations for use of oseltamivir in children younger than 1 y expired on June 23, 2010, this drug remains appropriate for use when indicated.

[c] Current weight-based dosing recommendations are not intended for preterm infants. Preterm infants may have slower clearance of oseltamivir because of immature renal function, and doses recommended for term infants may lead to very high drug concentrations in this age group. Limited data from a cohort of preterm infants who received an average dose of 1.7 mg/kg twice daily revealed drug concentrations higher than those observed with the recommended treatment dose in term infants (3 mg/kg twice daily). Observed drug concentrations were highly variable among preterm infants. These data are insufficient to recommend a specific dose of oseltamivir for preterm infants.

[d] Zanamivir is manufactured by GlaxoSmithKline (King of Prussia, PA) and 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 by using nebulizers, ventilators, or other devices typically used for administering medications in aerosolized solutions. Zanamivir is not recommended for persons with chronic respiratory diseases such as asthma or chronic obstructive pulmonary disease that increase the risk of bronchospasm.
Data source: Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM; Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 2011;60(RR-1):1–24.

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 2010–2011 influenza surveillance data and use them as a guide to empiric therapy until current seasonal data are available from the CDC. Information is posted weekly by the CDC (www.cdc.gov/flu/weekly/fluactivitysurv.htm). During the 2010–2011 season, most activity was attributable to influenza A; approximately 66% was attributable to influenza A (H3N2) activity, and 34% was attributable to 2009 (H1N1) activity. Activity varied widely on a local level.

VACCINE IMPLEMENTATION

These updated recommendations for prevention and control of influenza in children will have considerable operational and fiscal effect on pediatric practice. Therefore, the AAP has developed implementation guidance on supply, payment, coding, and liability issues; these documents can be found at www.aapredbook.org/implementation.

USE OF ANTIVIRAL MEDICATIONS

Antiviral resistance can emerge quickly from one season to the next. If local or national influenza surveillance data indicate a predominance of a particular influenza strain with a known antiviral-susceptibility profile, then empiric treatment can be directed toward that strain. For example, during the 2010–2011 season, only 1.3% of influenza viruses tested were resistant to oseltamivir, and none were resistant to zanamivir. High levels of resistance to amantadine and rimantadine persist, and these drugs should not be used in the upcoming season unless resistance patterns change significantly (Table 1).

- Oseltamivir is available in capsule and oral-suspension formulations. The manufactured liquid formulation has a concentration of 6 mg/mL. Oral suspensions in 12 mg/mL concentrations will remain available until supplies run out. If the commercially manufactured oral suspension is not available, the capsule might be

TABLE 5 Persons at Higher Risk Recommended for Antiviral Treatment for Suspected/Confirmed Influenza

Children <2 y of age
Adults ≥65 y of age
Persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), or metabolic (including diabetes mellitus) disorders or neurologic and neurodevelopmental 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)
Persons with immunosuppression, including that caused by medications or by HIV infection
Women who are pregnant or in the postpartum period (within 2 wk after delivery)
Persons aged <19 y who are receiving long-term aspirin therapy
American Indian/Alaska Native persons
Persons who are morbidly obese (ie, BMI ≥ 40)
Residents of nursing homes and other chronic care facilities

Data source: Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM; Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 2011;60(RR-1):1–24.

opened and the contents mixed with a sweetened liquid by retail pharmacies to a final concentration of 15 mg/mL (Table 4, footnote "a").

- Current treatment guidelines (Table 4) are applicable to infants and children with suspected influenza when known virus strains are circulating in the community or when infants or children are confirmed to have seasonal influenza.
- Continuous monitoring of the epidemiology, change in severity, and resistance patterns of influenza strains might lead to new guidance.

Treatment should be offered for:

- Any child hospitalized with presumed influenza or with severe, complicated, or progressive illness, regardless of influenza immunization status.
- Influenza infection of any severity in children at high risk of complications of influenza infection (Table 5.)

Treatment should be considered for:

- Any otherwise healthy child with influenza infection for whom a decrease in duration of clinical symptoms is felt to be warranted by his or her provider if treatment can be initiated within 48 hours of illness onset.

Earlier treatment provides more optimal clinical responses, although treatment after 48 hours of symptoms in the child with moderate-to-severe disease or with progressive disease might still provide some benefit. Dosages for antiviral agents for both treatment and chemoprophylaxis in children can be found in Table 4 and on the CDC Web site http://www.cdc.gov/flu/professionals/antivirals/index.htm). Children younger than 1 year are at increased risk of influenza-related complications. Although there are no antiviral medications licensed by the Food and Drug Administration for this age group and the 2009 H1N1 pandemic Emergency Use Authorization has expired, recommendations for use of oseltamivir in this young age group can still be followed and are provided in Table 4.

Clinical judgment (based on 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-likeillness. 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. Currently available rapid antigen tests have low sensitivity, particularly for the 2009 pandemic influenza A (H1N1) virus strain and should not be used to rule out influenza. Negative results from rapid antigen tests should not be used to make treatment or infection-control decisions.

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, especially in situations with limited antiviral medication availability. Should there be a shortage of antiviral medications, local public health authorities might provide additional guidance about testing and treatment. Rapid antigen tests are not helpful in the management of children with suspected influenza.

Recommendations for chemoprophylaxis during an influenza outbreak:

- 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.
- For family members or HCP who are unimmunized and are likely to have ongoing, close exposure to:
  - unimmunized children at high risk; or
  - 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 might 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 triva-

lent 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 might change on the basis of updated recommendations from the CDC in concert with antiviral-agent 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 should not be considered a substitute for immunization. Influenza vaccine should always be offered when not contraindicated, even when influenza virus is circulating in the community. Antiviral medications currently licensed are important adjuncts to influenza immunization for control and prevention of influenza disease, but indiscriminate use might promote resistance and/or limit availability (Table 1). Providers should inform recipients of antiviral chemoprophylaxis that risk of influenza is lowered but still remains while taking medication, and susceptibility to influenza returns when medication is discontinued. For recommendations about treatment and chemoprophylaxis against influenza, see Table 4. Updates will be available at www.aapredbook.org/flu and www.cdc.gov/flu/professionals/antivirals/index.htm.

FUTURE NEEDS

Manufacturers anticipate being able to provide adequate supplies of vaccine. Efforts should be made to create adequate outreach and infrastructure to ensure an optimal distribution of vaccine so that more people are immunized. Health care for children should be provided in the child's medical home. However, medical homes might have limited capacity to accommodate all patients (and their families) who seek influenza immunization. Because of 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 are used, a system of patient record transfer is beneficial for ensuring maintenance of accurate immunization records. Immunization-information systems should be used whenever available.

Cost-effectiveness and logistic feasibility of vaccinating everyone continue to be concerns. With universal immunization, particular attention is being paid to vaccine supply, distribution, implementation, and financing. Potential benefits of more widespread childhood immunization among recipients, their contacts, and the community include fewer influenza cases, fewer outpatient visits and hospitalizations for influenza infection, and a decrease in the use of antimicrobial agents, absenteeism from school, and lost parent work time.

Continued evaluation of the safety, immunogenicity, and effectiveness of influenza vaccine, especially for children younger than 2 years, is important. Development of a safe, immunogenic vaccine for infants younger than 6 months is essential. Consideration of how best to offer to immunize parents and adult child care providers in the pediatric office setting continues to be investigated. Mandatory annual influenza immunization has been implemented successfully at pediatric institutions, and future efforts should include broader implementation of mandatory immunization programs. Optimal prevention of influenza in the health care setting depends on coverage of at least 90% of HCP. Finally, efforts are underway to improve the vaccine-development process to allow for a shorter interval between identification of vaccine strains and vaccine production.

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