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

American Academy of Pediatrics
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Recommendations for Prevention and Control of Influenza in Children, 2017–2018

COMMITTEE ON INFECTIOUS DISEASES

abstract

This statement updates the recommendations for routine use of the 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 everyone 6 months and older, including children and adolescents. Highlights for the upcoming 2017–2018 season include the following:

1. Annual universal influenza immunization is indicated with either a trivalent or quadrivalent (no preference) inactivated vaccine;

2. The 2017–2018 influenza A (H1N1) vaccine strain differs from that contained in the 2016–2017 seasonal vaccines. The 2017–2018 influenza A (H3N2) vaccine strain and influenza B vaccine strains included in the trivalent and quadrivalent vaccines are the same as those contained in the 2016–2017 seasonal vaccines:

   a. trivalent vaccine contains an A/Michigan/45/2015 (H1N1)pdm09-like virus, an A/Hong Kong/4801/2014 (H3N2)-like virus, and a B/Brisbane/60/2008-like virus (B/Victoria lineage); and

   b. quadrivalent vaccine contains an additional B virus (B/Phuket/3073/2013-like virus [B/Yamagata lineage]);

3. Quadrivalent live attenuated influenza vaccine (LAIV4) is not recommended for use in any setting in the United States during the 2017–2018 influenza season. This interim recommendation, originally made in 2016, followed observational data from the US Influenza Vaccine Effectiveness Network revealing that LAIV4 performed poorly against influenza A (H1N1)pdm09 viruses in recent influenza seasons;

4. All children with an egg allergy of any severity can receive an influenza vaccine without any additional precautions beyond those recommended for any vaccine;

5. All health care personnel should receive an annual seasonal influenza vaccine, a crucial step in preventing influenza and reducing health care–associated influenza infections, because health care personnel often care for individuals at high risk for influenza-related complications; and

6. Pediatricians should attempt to promptly identify children suspected of having influenza infection for timely initiation of antiviral treatment, when indicated, to reduce morbidity and mortality. Best results are seen when treated within 48 hours of symptom onset.

FREE

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Highlights for the 2017-18 Influenza Season

- Vaccination remains the best available preventive measure against influenza.
- Annual seasonal influenza vaccine is recommended for *everyone* 6 months and older.
- Both trivalent and quadrivalent (no preference) *inactivated* influenza vaccines are available in the US.
- Quadrivalent live attenuated influenza vaccine (LAIV4) is *not* recommended for use in any setting in the US during the 2017-2018 influenza season.
- Children should receive vaccine as soon as possible after it is available in their community, preferably by the end of October.
- The number of recommended doses of influenza vaccine depends on a child's age at the time of the first administered dose and vaccine history.
- All children with egg allergy of any severity can receive influenza vaccine without any additional precautions beyond those recommended for any vaccine.
- Pregnant women may receive influenza vaccine at any time during pregnancy.
- All health care personnel should receive an annual seasonal influenza vaccine, a crucial step in preventing influenza and reducing health care-associated influenza infections.
- Antiviral medications are important in the control of influenza, but are not a substitute for influenza vaccination.

The American Academy of Pediatrics (AAP) recommends annual seasonal influenza vaccination for everyone 6 months and older, including children and adolescents, during the 2017–2018 influenza season. Special effort should be made to vaccinate individuals in the following groups:

- All children, including infants born preterm, 6 months and older (on the basis of chronologic age) with conditions that increase the risk of complications from influenza (eg, children with chronic medical conditions such as pulmonary diseases like asthma, metabolic diseases like diabetes mellitus, hemoglobinopathies like sickle cell disease, hemodynamically significant cardiac disease, immunosuppression, or neurologic and neurodevelopmental disorders);
- All household contacts and out-of-home care providers of children with high-risk conditions or younger than 5 years, especially infants younger than 6 months;
- Children and adolescents (6 months through 18 years of age) receiving an aspirin- or salicylate-containing medication, which places them at risk for Reye syndrome after influenza virus infection;
- American Indian/Alaskan native children;
- 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 2017–2018 INFLUENZA SEASON

1. **The annual seasonal influenza vaccine is recommended for everyone 6 months and older, including children and adolescents, during the 2017–2018 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 for complications from influenza (eg, children with chronic medical conditions such as pulmonary diseases like asthma, metabolic diseases like diabetes mellitus, hemoglobinopathies like sickle cell disease, 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 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

TABLE 1 Pediatric Deaths and Hospitalizations by Season and Predominant Strain

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
2016–2017 (Preliminary data)	H3N2	104	41.4	15.7
2015–2016	H1N1	92	42.4	9.7
2014–2015[a]	H3N2	148	57.2	16.6
2013–2014	pH1N1	111	47.2	9.4
2012–2013	H3N2	171	67	14.6
2011–2012[a]	H3N2	37	16	4
2010–2011	H3N2	124	49.4	9.1
2009–2010	pH1N1	288	77.4	27.2
2008–2009	H1N1	137	28	5
2007–2008	H3N2	88	40.3	5.5

Source: Centers for Disease Control and Prevention. FluView 2016–2017 Data as of August 19, 2017. Available at: www.cdc.gov/flu/weekly/fluviewinteractive.htm.
[a] Vaccine strains did not change from the previous influenza season.

influenza-related medical care compared with healthy adults. Reducing influenza virus transmission (eg, by using appropriate hand hygiene and respiratory hygiene and/or 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 2016–2017 influenza season was moderate overall, and influenza A (H3N2) viruses predominated.** Severity indicators were within the range of what has been observed during previous H3N2-predominant seasons, which have been associated with more severe illness and mortality, especially in older individuals and younger children, compared with seasons during which H1N1 or B viruses predominated. The start of the season was typical in the United States, with increasing activity noted in mid-December 2016 and peak activity in late February. The majority of circulating strains matched vaccine strains well. Pediatric hospitalizations and deaths caused by influenza vary by the predominant circulating strain and from one season to the next (Table 1). Historically, 80% to 85% of pediatric deaths have occurred in unvaccinated children 6 months and older. Influenza vaccination is associated with reduced risk of laboratory-confirmed influenza-related pediatric death. In a recent case-cohort analysis comparing vaccination uptake among laboratory-confirmed influenza-associated pediatric deaths with estimated vaccination coverage among pediatric cohorts in the United States, Flannery et al[1] found that only 26% of cases received a vaccine before illness onset, compared with average vaccination coverage of 48%. In the past 10 seasons, the rates of influenza-associated hospitalization for children younger than 5 years have always exceeded the rates for children 5 through 17 years of age. However, among healthy children hospitalized with influenza B, those 10 to 16 years of age were found to be at the highest risk for admission to the ICU. As of August 19, 2017, the following data were reported by the Centers for Disease Control and Prevention (CDC) during the 2016–2017 influenza season:

- 104 laboratory-confirmed influenza-associated pediatric deaths occurred:
  - 66 of these were associated with influenza A viruses;
  - 37 of these were associated with influenza B viruses; and
  - 1 of these was associated with an undetermined type of influenza virus.

  Flannery et al[1] found that more than half of pediatric deaths from 2010 through 2014 had ≥1 underlying medical condition with an increased risk of severe influenza-related complications; notably, only 1 in 3 of these at-risk children had been vaccinated.

  Although children with certain conditions are at a higher risk of complications, 53.7% of the deaths during the 2016–2017 influenza season occurred in children with no high-risk underlying medical condition. Among children hospitalized with influenza and for whom medical record data were available, ∼41% had no recorded underlying condition, whereas ∼29% had underlying asthma or reactive airway disease (Fig 1). In a recent study of hospitalizations for influenza A versus B, the odds of mortality

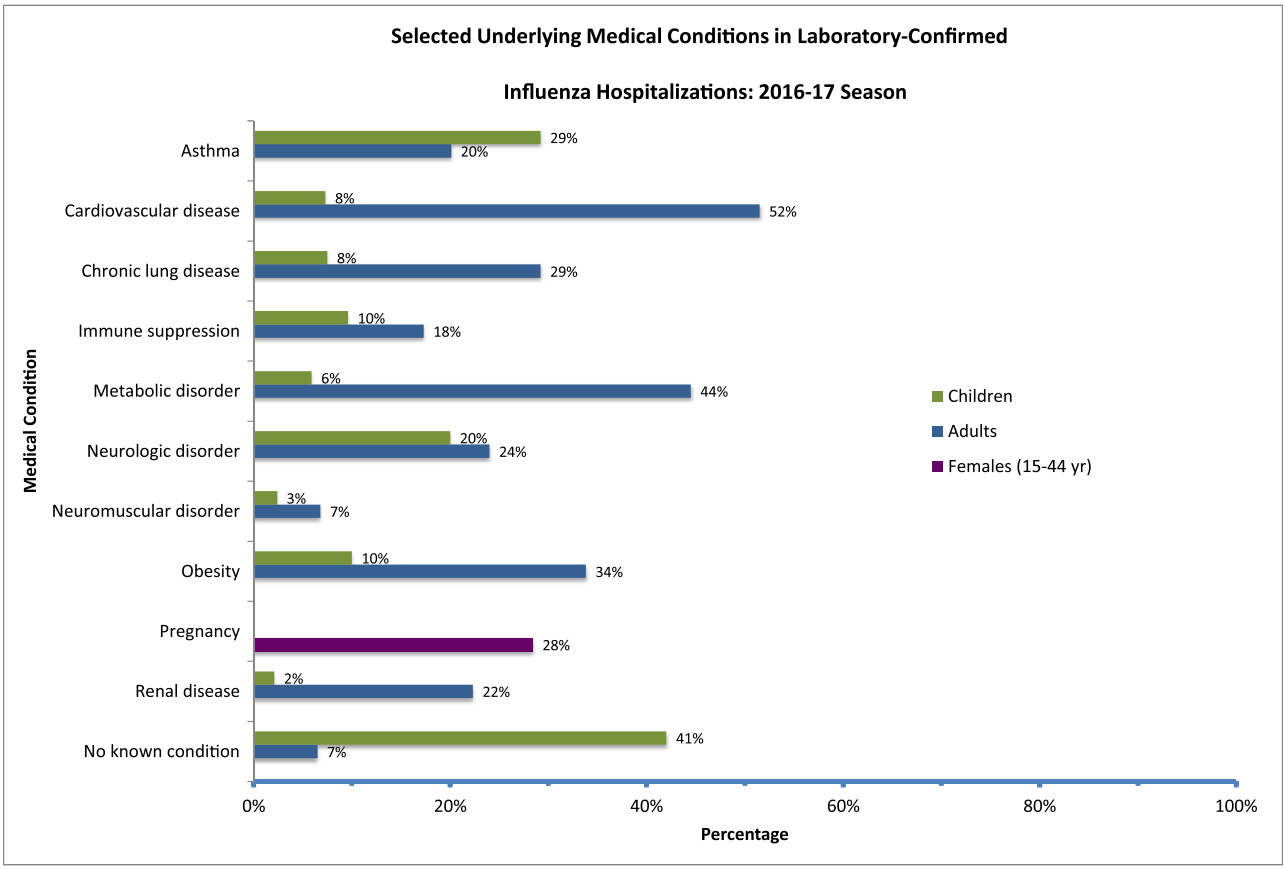

FIGURE 1

Selected underlying medical conditions in patients hospitalized with laboratory-confirmed influenza, FluSurv-NET 2016–2017. Source: Centers for Disease Control and Prevention. FluView 2016–2017 Preliminary Data as of August 19, 2017. Available at: gis.cdc.gov/grasp/fluview/FluHospChars.html. Asthma includes a medical diagnosis of asthma or reactive airway disease. The category of cardiovascular diseases includes conditions such as coronary heart disease, cardiac valve disorders, congestive heart failure, pulmonary hypertension, and aortic stenosis and does not include hypertension only. Chronic lung diseases include conditions such as chronic obstructive pulmonary disease, bronchiolitis obliterans, chronic aspiration pneumonia, and interstitial lung disease. Immune suppression includes conditions such as immunoglobulin deficiency, leukemia, lymphoma, HIV/AIDS, and immunosuppressive medication use. Metabolic disorders include conditions such as diabetes mellitus, thyroid dysfunction, adrenal insufficiency, and liver disease. Neurologic disorders include conditions such as seizure disorders, cerebral palsy, and cognitive dysfunction. Neuromuscular disorders include conditions such as multiple sclerosis and muscular dystrophy. Obesity was assigned if indicated in the patient's medical chart or if the BMI was >30. The pregnancy percentage was calculated by using the number of females aged between 15 and 44 years of age as the denominator. Renal diseases include conditions such as acute or chronic renal failure, nephrotic syndrome, glomerulonephritis, and impaired creatinine clearance. The category "no known condition" indicates that the patient did not have any known underlying medical condition indicated in the medical chart at the time of hospitalization.

were significantly greater with influenza B than with A and were not entirely explained by underlying health conditions.

3. **The AAP continues to recommend that quadrivalent live attenuated influenza vaccine (LAIV4) not be used in any setting during the 2017–2018 season because of low effectiveness against influenza A (H1N1)pdm09 viruses in the United States in recent seasons.** In all pediatric age groups for the influenza seasons from 2013 through 2016, LAIV4 did not have any statistically significant benefit in preventing influenza (all 95% confidence intervals [CIs] cross 0), whereas inactivated influenza vaccine (IIV) provided statistically significant protection, albeit to differing degrees by season (Table 2). Children who received LAIV4 were almost 4 times more likely to become infected with an influenza virus than those who received IIV. No data have been published during the 2016–2017 season regarding laboratory-confirmed influenza to warrant rescinding this recommendation. Additional research will help determine if the interim recommendation that LAIV4 should not be used in any setting will continue for subsequent influenza seasons. Development of alternative live attenuated influenza vaccines is also being investigated. Current efforts should be on the administration of IIV for all children and adolescents, particularly those with underlying medical conditions

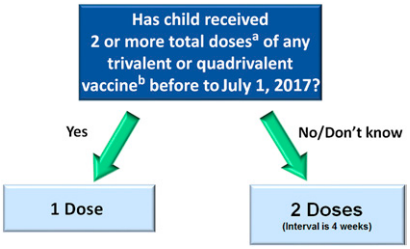

FIGURE 2
Number of 2017–2018 seasonal influenza vaccine doses for children 6 months through 8 years of age. [a] The 2 doses need not have been received during the same season or consecutive seasons. [b] Receipt of LAIV4 in the past is still expected to have primed a child's immune system, despite recent evidence for poor effectiveness. There currently are no data that suggest otherwise.

TABLE 2 Vaccine Effectiveness Against any Influenza in Children, by Age and Vaccine Type

Season (Predominant Strain)	Age Range (y)	Adjusted VE % (95% CI)	
		LAIV4	IIV3/IIV4
2013–2014[a] (H1N1pdm09)	2–17	7 (−46 to 40)	60 (41 to 73)
	2–8	−36 (−151 to 27)	59 (30 to 76)
	9–17	41 (−21 to 72)	61 (27 to 79)
2014–2015[b] (H3N2)	2–17	9 (−18 to 29)	31 (16 to 44)
	2–8	9 (−28 to 35)	26 (2 to 44)
	9–17	17 (−27 to 46)	33 (9 to 51)
2015–2016[c] (H1N1pdm09)	2–17	5 (−47 to 39)	60 (47 to 70)
	2–8	0 (−75 to 43)	56 (42 to 71)
	9–17	17 (−84 to 63)	66 (44 to 80)

VE, vaccine effectiveness.
[a] Gaglani M, Pruszynski J, Murthy K, et al. Influenza vaccine effectiveness against 2009 pandemic influenza A (H1N1) virus differed by vaccine type during 2013–2014 in the United States. *J Infect Dis.* 2016;213(10):1546–1556, Supplemental Table 2.
[b] Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices, presented at June 2015 Meeting.
[c] Jackson L, et al. Influenza vaccine effectiveness in the United States during the 2015-2016 season. *N Engl J Med.* 2017;377:534-543.

associated with an elevated risk of complications from influenza.

4. **Vaccination remains the best available preventive measure against influenza.** Given the unpredictable nature of influenza each season, any licensed and age-appropriate IIV available should be used. The vaccine strains are predicted to match the circulating strains with the intent of providing optimal protection. Vaccination is effective in reducing outpatient medical visits for illness caused by circulating influenza viruses by 50% to 75%. The universal administration of the seasonal vaccine to everyone 6 months and older is the best strategy available for preventing illness from influenza. There is notable room for improvement in influenza vaccination, because overall influenza vaccination rates have been suboptimal during the past 7 seasons in both children (percentages in the mid- to high- 50s) and adults (percentages in the low- to mid- 40s). A child's likelihood of being immunized according to recommendations appears to be associated with the immunization practices of their parents. The authors of 1 study found that children were 2.77 times (95% CI: 2.74 to 2.79) more likely to also be immunized for seasonal influenza if their parents were immunized. When parents who were previously not immunized had received immunization for seasonal influenza, their children were 5.44 times (95% CI: 5.35 to 5.53) more likely to become immunized for influenza.

5. **Both trivalent and quadrivalent IIVs are available in the United States for the 2017–2018 season.** To vaccinate as many people as possible for this influenza season, neither inactivated vaccine formulation is preferred over the other. Although manufacturers anticipate an adequate supply of quadrivalent vaccine, pediatricians should administer whichever formulation is available in their communities. Both formulations contain an A/Michigan/45/2015 (H1N1)pdm09-like virus, an A/HongKong/4801/2014 (H3N2)-like virus, and a B/Brisbane/60/2008-like virus (B/Victoria lineage). Quadrivalent influenza vaccines also contain the B/Phuket/3073/2013-like virus (B/Yamagata lineage). The influenza A (H1N1) virus in both formulations differs from that contained in the 2016–2017 seasonal vaccines.

6. **The number of seasonal influenza vaccine doses to be administered in the 2017–2018 influenza season depends on the child's age at the time of the first administered dose and 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; and
- Children 6 months through 8 years of age:
  - Need 2 doses if they have received fewer than 2 doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV4) before July 1, 2017. The interval between the 2 doses should be at least 4 weeks; and
  - Require only 1 dose if they have previously received 2 or more total doses of any trivalent or quadrivalent

TABLE 3 People at High Risk of Influenza Complications and Thus 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, 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/Alaskan native people
Residents of nursing homes and other chronic care facilities

Source: Adapted from 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.

influenza vaccine (IIV or LAIV4) before July 1, 2017. The 2 previous doses do not need to have been received during the same influenza season or consecutive influenza seasons. Despite recent evidence for poor effectiveness of LAIV4, receipt of LAIV4 in the past is still expected to have primed a child's immune system; there currently are no data that suggest otherwise. Therefore, children who received 2 or more doses of LAIV4 before July 1, 2017 may receive only 1 dose of IIV for the 2017–2018 season.

Vaccination should not be delayed to obtain a specific product for either dose. Any available, age-appropriate trivalent or quadrivalent inactivated vaccine can be used. 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.

7. **Pediatric offices may choose to serve as an alternate venue for providing influenza vaccination for parents and other care providers of children, if the practice is acceptable to both pediatricians and the adults who are to be vaccinated.**[2]

Medical liability issues and medical record documentation requirements need to be considered before a pediatrician begins immunizing adults (see details at www.aapredbook.org/implementation). Pediatricians are reminded to document the recommendation for adult vaccination in the child's medical record. In addition, adults should still be encouraged to have a medical home and communicate their vaccination status to their primary care provider. Offering adult vaccinations 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 influenza vaccines. Vaccination of close contacts of children at high risk of influenza-related complications (Table 3) is intended to reduce children's risk of exposure to influenza (ie, "cocooning"). The practice of cocooning also will help protect infants younger than 6 months who are too young to be immunized with an influenza vaccine.

8. **Pregnant women may receive an influenza vaccine at any time during pregnancy.**

Pregnant women are of special concern because they are at an increased risk for complications from influenza. Any licensed, recommended, and age-appropriate trivalent or quadrivalent inactivated vaccine may be used, including recombinant inactivated vaccines (RIVs). However, experience with the use of RIVs in pregnant women 18 years and older is limited, because RIVs have been available only since the 2013–2014 influenza season. Substantial data indicate that IIV does not cause fetal harm when administered to a pregnant woman, although data on the safety of influenza vaccination in the early first trimester are limited. Assessments of any association with influenza vaccination and preterm birth and small-for-gestational-age infants have yielded inconsistent results, with most studies reporting a protective effect or no association with these outcomes. Vaccination of pregnant women also provides protection for their infants, potentially for as long as 6 months, through the transplacental transfer of antibodies. For example, the authors of 1 recent study documented that infants born to women reporting influenza vaccination during pregnancy had risk reductions of 70% for laboratory-confirmed influenza and 81% for influenza hospitalizations in the first 6 months of life.

9. **As soon as the seasonal influenza vaccine becomes available locally, pediatricians or vaccine administrators should encourage immunization of 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. Vaccination should occur by the end of October, if possible. This is particularly important for children who need 2 doses of the influenza vaccine to achieve optimal protection before the circulation of influenza viruses in the community. Children should receive their first dose as soon as possible after a vaccine becomes available, to allow sufficient time for receipt of the second dose ≥4 weeks later, preferably by the end of October. Provider endorsement plays a major role in patient acceptance and vaccine uptake. Prompt initiation of influenza vaccination and continuing to vaccinate throughout the influenza season, whether influenza is circulating (or has circulated) in the community, are important components of an effective vaccination strategy. Although there is no evidence that waning immunity from early administration of the vaccine increases the risk of infection in children, recent reports raise the possibility that early vaccination of adults, particularly the elderly, might contribute to reduced protection later in the influenza season. Older adults are recognized to have a less robust immune response to influenza vaccines. A recent multiseason analysis from the US Influenza Vaccine Effectiveness Network found that vaccine effectiveness declined by ~7% per month for H3N2 and influenza B and by 6% to 11% per month for H1N1pdm09 in individuals 9 years and older. Vaccine effectiveness remained >0 for at least 5 to 6 months after vaccination. Until there are definitive data that determine if waning immunity influences vaccine effectiveness in children, the administration of the influenza vaccine should not be delayed to a later date, because this increases the likelihood of missing the influenza vaccination altogether. Further evaluation is needed before any policy change in timing is made. An early onset of the influenza season is another concern about delayed vaccination.

10. **Providers may continue to offer vaccines until June 30 of each year, the date marking the end of the influenza season, because influenza is unpredictable.** Protective immune responses generally persist in children throughout the influenza season. Although peak influenza activity in the United States tends to occur from January through March, influenza activity can occur in early fall (October) or late spring (end of May) and may have more than 1 disease peak. This approach also provides ample opportunity to administer a second dose of the vaccine to children 6 months through 8 years of age when indicated, as detailed previously in key point 6. This approach also allows for optimal ability to immunize travelers, particularly international travelers, who may be exposed to influenza year round, depending on destination.

11. **HCP, influenza campaign organizers, and public health agencies are encouraged to collaborate to develop improved strategies for planning, distribution, communication, and administration of vaccines.**

    - Plan to make the seasonal influenza vaccine easily accessible for all children. Examples include sending alerts to families that a vaccine is available (eg, e-mails, texts, letters, and patient portals); creating walk-in influenza vaccination clinics; extending hours beyond routine times during peak vaccination periods; administering influenza vaccines during both well and sick visits, as well as at discharge from the hospital; considering how to immunize parents, adult caregivers, and siblings at the same time in the same office setting as children[2]; and working with other institutions (eg, schools, child care programs, local public health departments, and religious organizations) or alternative care sites, such as emergency departments, to expand venues for administering vaccines. If a child receives an influenza vaccine outside of his or her medical home, such as at a pharmacy, retail-based clinic, or another practice, appropriate documentation of the vaccination should be provided to the patient for his or her medical home and entered into the state or regional immunization information system (ie, registry).

    - Concerted efforts among the aforementioned groups, plus vaccine manufacturers, distributors, and payers, are also 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. Similar efforts should be made to assuage the vaccine supply discrepancy between privately insured patients and those eligible for vaccination through the Vaccines for Children program.

TABLE 4 Recommended Seasonal Influenza Vaccines for Different Age Groups: United States, 2017–2018 Influenza Season

Vaccine	Trade Name	Manufacturer	Presentation	Thimerosal Mercury Content (μg of Hg/0.5-mL dose)	Age Group
Inactivated					
IIV3	Fluzone high-dose	Sanofi pasteur	0.5-mL prefilled syringe	0	≥65 y
IIV3	Fluvirin	Seqirus	0.5-mL prefilled syringe	≤1.0	≥4 y
			5.0-mL multidose vial	25	≥4 y
IIV3	Afluria	Seqirus	0.5-mL prefilled syringe	0	≥5 y
			5.0-mL multidose vial	24.5	≥5 y
aIIV3	Fluad	Seqirus	0.5-mL prefilled syringe	0	≥65 y
ccIIV4	Flucelvax quadrivalent	Seqirus	0.5-mL prefilled syringe	0	≥4 y
			5.0-mL multidose vial	25	≥4 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 ID quadrivalent	Sanofi pasteur	0.1-mL prefilled microinjection	0	18–64 y
IIV4	Fluarix quadrivalent	GlaxoSmithKline	0.5-mL prefilled syringe	0	≥3 y
IIV4	FluLaval quadrivalent	ID biomedical corporation of quebec (distributed by GlaxoSmithKline)	0.5-mL prefilled syringe	0	≥6 mo
			5.0-mL multidose vial	<25	≥6 mo
IIV4	Afluria quadrivalent	Seqirus	0.5-mL prefilled syringe	0	≥18 y
			5.0-mL multidose vial	24.5	≥18 y
Recombinant					
RIV3	Flublok	Protein sciences	0.5-mL vial	0	≥18 y
RIV4	Flublok quadrivalent	Protein sciences	0.5-mL prefilled syringe	0	≥18 y

Data sources: American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2016–2017. *Pediatrics*. 2016;138(4):e20162527; Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2017–18 influenza aeason. *MMWR Recomm Rep*. 2017;66(No. RR-2):1–20. Implementation guidance on supply, pricing, payment, current procedural terminology coding, and liability issues can be found at www.aapredbook.org/implementation. ccIIV4, quadrivalent cell culture-based IIV. RIV3, trivalent recombinant influenza vaccine; RIV4, quadrivalent recombinant influenza vaccine.

- Public health will benefit from pediatricians' discussions about vaccine safety, effectiveness, and indications. Pediatricians can influence vaccine acceptance by explaining the importance of annual influenza vaccination for children, emphasizing when a second dose of the vaccine is indicated and explaining why the intranasal formulation is not available. The AAP and CDC have created communication resources to convey these important messages and to help the public understand influenza recommendations. Resources will be available on *Red Book Online* (https://redbook.solutions.aap.org/ss/influenza-resources.aspx).

- The AAP supports mandatory influenza vaccination programs for all HCP in all settings, including outpatient settings. HCP should act as role models for both their patients and colleagues by receiving influenza vaccination annually and by letting others know that they have received the vaccine, highlighting the safety and effectiveness of annual influenza vaccination. Influenza vaccination programs for HCP benefit the health of employees, their patients, and members of the community. Mandatory influenza immunization for all HCP is considered to be ethical, just, and necessary to improve patient safety.[3] Employees of health care institutions are asked to act in the best interests of the health of their patients and to honor the requirement of causing no harm.

12. Antiviral medications are important in the control of influenza but are not a substitute for influenza vaccination. 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 2017–2018 season. Intravenous peramivir (Rapivab [BioCryst Pharmaceuticals, Durham, NC]), a third NAI, was licensed in December 2014 for use in adults 18 years or older and is being studied in children. Intravenous zanamivir remains investigational and is not approved in the United States. It is not known whether either intravenous zanamivir or intravenous peramivir will be available for compassionate

use during the 2017–2018 influenza season. Intravenous formulations are especially important for those children who cannot absorb orally or enterically administered oseltamivir or tolerate inhaled zanamivir. Recent viral surveillance and resistance data from CDC and the World Health Organization (WHO) indicate that the majority of currently circulating influenza viruses likely to cause influenza in North America during the 2017–2018 season continue to be susceptible to oseltamivir, zanamivir, and peramivir. If a newly emergent oseltamivir- or peramivir-resistant virus is a concern, use of intravenous zanamivir may be appropriate. Resistance characteristics can also change for an individual child over the duration of a treatment course, especially in those who are severely immunocompromised and may receive extended courses because of prolonged viral shedding. Up-to-date information on current recommendations and therapeutic options 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/).

SEASONAL INFLUENZA VACCINES

Before the 2013–2014 influenza season, only trivalent influenza vaccines that included a single influenza B strain were available. Since the 1980s, 2 antigenically distinct lineages (ie, Victoria or Yamagata) of influenza B viruses have circulated globally. Vaccination against 1 B viral lineage generally confers little cross-protection against the other B viral lineages. 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 vaccine with influenza B strains of both lineages would be predicted to offer additional protection, but there is no evidence at this time that a quadrivalent vaccine is more effective.

IIVs

For the 2017–2018 season, IIV will be available for intramuscular (IM) injection in both trivalent (IIV3) and quadrivalent (IIV4) formulations. IIVs do not contain the live virus. The available IIV formulations and age groups for which use is approved are presented in Table 4. IIV formulations can be used in children with and without chronic medical conditions. The most common adverse events after IIV3 administration are local injection site pain and tenderness. Fever occurs 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.

IM formulations of IIV4 are available from several manufacturers with specific age indications, including brands licensed for use in children as young as 6 months. Two licensed IIV4 vaccines are available for use in children 6 through 35 months of age, including one that was approved for use in this age group in November 2016. Of note, as listed in Table 4, the dose volume for children 6 through 35 months of age differs between these 2 vaccines (0.25 and 0.5 mL), as does the approved ages for which these vaccines may be used. Clinical data show comparable immunogenicity and reactogenicity for these 2 vaccines.

In children, the most common injection site adverse reactions after administration of IIV 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 IIV3. IIV4 is, therefore, available for people 6 months or older when otherwise appropriate and may offer broader protection against circulating influenza B strains than IIV3.

An intradermal (ID) formulation of IIV4 is licensed and available 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 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.

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 13-valent pneumococcal conjugate vaccine (PCV13) concomitantly. Subsequent retrospective analyses of past seasons have demonstrated a slight increase in the risk of febrile seizures in children 6 through 23 months of age when PCV13 vaccines are administered concomitantly with IIV. For example, although the authors of 1 study found that IIV3 was not independently associated with a risk of febrile seizures, a small increased risk of febrile seizures was noted when IIV3 was administered on the

same day as either pneumococcal conjugate vaccine or diphtheria-tetanus-acellular-pertussis (DTaP) vaccine. Data on which dose in the series was associated with the small risk of febrile seizures were not documented for either of these vaccines. The concomitant administration of IIV3, pneumococcal conjugate, and DTaP vaccines was associated with the greatest relative risk estimate, corresponding to a maximum additional 30 febrile seizure cases per 100 000 children vaccinated, compared with the administration of the vaccines on separate days. In contrast, data from the Post-Licensure Rapid Immunization Safety Monitoring program of the US Food and Drug Administration (FDA), the largest vaccine safety surveillance program in the United States, revealed that there was no significant increase in febrile seizures associated with concomitant administration of these 3 vaccines in children 6 to 59 months of age during the 2010–2011 season. Although the possibility of increased risk for febrile seizures cannot be ruled out, simultaneous administration of IIV with PCV13 and/or other vaccines for the 2017–2018 influenza season continues to be recommended when these vaccines are indicated. Overall, the benefits of timely vaccination with same-day administration of IIV and PCV13 or DTaP outweigh the risk of febrile seizures, which rarely have any long-term sequelae.

One trivalent and 2 quadrivalent influenza vaccines manufactured by using newer technologies will be available during the 2017–2018 season: trivalent and quadrivalent recombinant hemagglutinin influenza vaccines, available for people 18 years and older, and cell culture-based IIVs, available for people 4 years and older. All of these vaccines are administered intramuscularly. Trivalent and quadrivalent recombinant influenza vaccines are recombinant baculovirus-expressed hemagglutinin vaccines produced in cell cultures. The quadrivalent recombinant influenza vaccine was licensed for people 18 years and older by the FDA in October 2016. The most frequently reported adverse events after administration of the 3 vaccines are pain, headache, myalgia, and fatigue.

The FDA licensed trivalent, MF59-adjuvanted, IIV for people 65 years and older in November 2015, the first adjuvanted influenza vaccine marketed in the United States. Adjuvants elicit a more robust immune response, which could lead to a reduction in the number of doses required for children. The vaccine is currently being studied in children.

Table 4 summarizes information on the types of IIVs licensed for children and adults during the 2017–2018 season. 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 medical condition. As such, the AAP extends its strongest support to the current WHO 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 trace amount of thimerosal in some IIV vaccine formulations (Table 4), and in some states, including California, Delaware, Illinois, Missouri, New York, and Washington, 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, to the extent authorized by state law, children should receive any available formulation of IIV rather than delaying vaccination while waiting for reduced thimerosal-content or thimerosal-free vaccines. Although some IIV formulations contain a trace amount of it, thimerosal-free IIV products can be obtained (Table 4). Vaccine manufacturers are delivering increasing amounts of thimerosal-free influenza vaccine each year.

Vaccine Effectiveness and LAIV4

The AAP continues to support the decision by the CDC to not use LAIV4 in any setting during the 2017–2018 influenza season. This interim recommendation, originally made in 2016, followed observational data from the US Influenza Vaccine Effectiveness Network revealing that LAIV4 performed poorly against influenza A(H1N1)pdm09 viruses in recent influenza seasons. There has not been additional published data during the 2016–2017 season to warrant rescinding this interim recommendation.

INFLUENZA VACCINES AND EGG ALLERGIES

IIV administered in a single, age-appropriate dose is well tolerated by recipients with an egg allergy of any severity. Special precautions for egg-allergic recipients of IIV are not warranted, because the rate of anaphylaxis after IIV administration is no greater in egg-allergic than in non–egg-allergic recipients or from other universally recommended vaccines. Standard vaccination practice for all vaccines in children should include the ability to respond to rare acute hypersensitivity reactions.[4] Patients who refuse to receive an egg-based vaccine may be vaccinated with an age-appropriate recombinant or cell-cultured product.

VACCINE STORAGE AND ADMINISTRATION

The "AAP Storage and Handling Tip Sheet: Disaster Planning" document 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 (https://www.aap.org/en-us/Documents/immunization_disasterplanning.pdf).

Any of the influenza vaccines can be administered at the same visit with all other recommended routine vaccines.

IM Vaccine

IIVs for IM injection are shipped and stored at 2°C to 8°C (36°F–46°F); frozen vaccines should not be used. These split or subunit vaccines are administered intramuscularly into the anterolateral thigh of infants and young children and into the deltoid muscle of older children and adults. Most have variable immune responses in young children. A new vaccine option available for infants and toddlers 6 months through 35 months of age can be administered as 0.5-mL doses for all age groups, a delivery of twice the amount of antigen previously indicated for children 6 through 35 months of age. For this new vaccine, clinical data reveal immunogenicity and reactogenicity comparable to that for the vaccine used in this age group in recent seasons, which was administered as 0.25 mL per dose (Table 4). Although the amount of antigen differs, the number of doses required with either vaccine for this age group is the same. A 0.5-mL unit dose of any IIV should not be split into 2 separate 0.25-mL doses because of safety concerns for lack of sterility, variance with the package insert, and potential compliance difficulties with vaccine excise taxes.

ID Vaccine

IIVs for ID injection are shipped and stored at 2°C to 8°C (36–46°F). These vaccines are administered intradermally only to people 18 through 64 years of age, preferably over the deltoid muscle, and only by using the device included in the vaccine package. The 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.

CURRENT RECOMMENDATIONS

Seasonal influenza vaccination with IIV is recommended for all children 6 months and older. LAIV4 should not be used. Children and adolescents with certain underlying medical conditions, listed below, have an elevated risk of complications from influenza:

- 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 necessitate long-term aspirin therapy or salicylate-containing medication, including juvenile idiopathic arthritis or Kawasaki disease, that may place a child at increased risk of Reye syndrome if infected with influenza;
- 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; and
- pregnancy.

Additional vaccination efforts 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;
- Any woman who is pregnant or considering pregnancy, is in the postpartum period, or is breastfeeding during the influenza season. It is safe to administer the influenza vaccine to pregnant women during any trimester. Any licensed, recommended, and age-appropriate trivalent or quadrivalent IIV or RIV may be used, although experience with the use of RIVs in pregnant women is limited. Studies have revealed that infants born to immunized women have better influenza-related health outcomes than infants of unimmunized women. However, according to Internet-based panel surveys conducted by the CDC, only ∼50% of pregnant women during the 2015–2016 influenza season and 47% of women during the 2016–2017 season (according to preliminary data) reported receiving an influenza vaccine, even though both pregnant women and their newborn infants are at higher risk of complications. More data on the safety of influenza vaccination in the early first trimester are becoming available. In a 5-year retrospective cohort study from 2003 to 2008, which included more than 10 000 women, influenza vaccination in the first trimester was not associated with an increase in the rates of major congenital malformations. Similarly, a systematic review and meta-analysis of studies of congenital anomalies after vaccination during pregnancy, including data from 15 studies (14 cohort studies and 1 case-control study) did not reveal any association between congenital defects and influenza vaccination in any trimester, including the first trimester's gestation. Assessments of any association with influenza

TABLE 5 Summary of Antiviral Treatment of Clinical Influenza During the 2017–2018 Season

Offer Treatment ASAP to Children…	Consider Treatment ASAP for…
Hospitalized with presumed influenza	Any healthy child with presumed influenza
Hospitalized for severe, complicated, or progressive illness attributable to influenza	Healthy children with presumed influenza, who live at home with a sibling or household contact that is <6 mo old or has a medical condition that predisposes him or her to complications
With presumed influenza (of any severity) and at high risk of complications	

ASAP, as soon as possible.

vaccination and preterm birth and small-for-gestational-age infants have revealed inconsistent results, with the authors of most studies reporting a protective effect or no association against these outcomes. Breastfeeding is also recommended to protect against influenza viruses by activating innate antiviral mechanisms, specifically type 1 interferons. In addition, human milk from mothers vaccinated during the third trimester contains higher levels of influenza-specific immunoglobulin A. Greater exclusivity of breastfeeding in the first 6 months of life decreases the episodes of respiratory illness with fever in infants of vaccinated mothers. For infants born to mothers with confirmed influenza illness at delivery, guidance can be found at https://www.cdc.gov/flu/professionals/infectioncontrol/peri-post-settings.htm;

- American Indian/Alaskan native children and adolescents;
- HCP or health care volunteers. Despite the AAP recommendation for mandatory influenza immunization for all HCP,[3] many remain unvaccinated. With an increasing number of organizations mandating influenza vaccination, coverage among HCP increased to 79% in the 2015–2016 season. Early-season 2016–2017 vaccine coverage among HCP was 68.5%, similar to early-season coverage during the 2015–2016 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 vaccination rates for this group remain consistently below this goal. The AAP recently reaffirmed its support for a mandatory influenza vaccination policy for all HCP nationwide, including in outpatient settings.[2] Mandating the influenza vaccine for all HCP is ethical, just, and necessary to improve patient safety, especially because HCP frequently come into contact with patients at a high risk of influenza illness in their clinical settings. For the prevention and control of influenza, all HCP must continue to prioritize the health and safety of patients; and
- 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 diagnosed with a moderate to severe febrile illness, on the basis of the judgment of the clinician, should not be vaccinated with IIV until resolution of the illness. Infants younger than 6 months should also not be vaccinated with IIV. A previous severe allergic reaction to an influenza vaccine (ie, anaphylaxis involving cardiovascular changes, respiratory or gastrointestinal tract symptoms, or reactions that necessitate the use of epinephrine), regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the vaccine.

The estimated risk for Guillain-Barré syndrome (GBS) is low, especially in children. Although influenza infection is recognized to be a cause of GBS, there is no elevated risk of GBS from influenza vaccination. As a precaution, people who are not at high risk for severe influenza and who are known to have experienced GBS within 6 weeks of influenza vaccination generally should not be vaccinated. However, the benefits of influenza vaccination might outweigh the risks for certain people who have a history of GBS and who also are at high risk for severe complications from influenza.

SURVEILLANCE

Information about influenza surveillance is available through the CDC Voice Information System (influenza update at 1-800-232-4636) 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 2016–2017 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). The AAP offers "What's the Latest with the Flu" (https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Pages/What's-the-Latest-with-the-Flu.aspx) messages to

TABLE 6 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis in Children for the 2017–2018 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 by body weight		
≤15 kg (≤33 lb)	30 mg, twice daily	30 mg, once daily
>15–23 kg (33–51 lb)	45 mg, twice daily	45 mg, once daily
>23–40 kg (>51–88 lb)	60 mg, twice daily	60 mg, once daily
>40 kg (>88 lb)	75 mg, twice daily	75 mg, once daily
Infants 9–11 mo[b]	3.5 mg/kg per dose, twice daily	3.5 mg/kg per dose, once daily
Term infants 0–8 mo[b]	3 mg/kg per dose, twice daily	3 mg/kg per dose, once daily 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 (2 5-mg inhalations), twice daily	10 mg (2 5-mg inhalations), once daily
Children (≥7 y for treatment, ≥5 y for chemoprophylaxis)	10 mg (2 5-mg inhalations), twice daily	10 mg (2 5-mg inhalations), once daily

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. —, not applicable.

[a] Oseltamivir 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. 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 of oral suspension; a 60-mg dose is given with 10 mL of oral suspension, and a 75-mg dose is given with 12.5 mL of oral suspension. If the commercially manufactured oral suspension is not available, a suspension can be compounded by retail pharmacies (the final concentration is also 6 mg/mL), on the basis of instructions contained 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 a creatinine clearance of 10–30 mL/min, the following dosage should be provided: 75 mg, once daily, for 5 d. For chemoprophylaxis of patients with a creatinine clearance of 10–30 mL/min, the following dosage should be provided: 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 wk 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 recommendations for preterm infants are as follows. 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 term infants may lead to 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 by using their postmenstrual age (gestational age + chronological age): 1.0 mg/kg per dose, orally, twice daily, for those <38 wk postmenstrual age; 1.5 mg/kg per dose, orally, twice daily, for those 38 through 40 wk postmenstrual age; 3.0 mg/kg per dose, orally, twice daily, for those >40 wk postmenstrual age. For extremely preterm infants (<28 wk), please consult a pediatric infectious diseases physician.

[d] Zanamivir is administered by inhalation by 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 people with chronic respiratory diseases, such as asthma or chronic obstructive pulmonary disease, which increase the risk of bronchospasm.

highlight those details most relevant for AAP members and child care providers on a monthly basis during influenza season.

VACCINE IMPLEMENTATION

The AAP's Partnership for Policy Implementation has developed a series of definitions by 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. In addition, the AAP has developed implementation guidance on supply, payment, coding, and liability issues; these documents can be found at https://redbook.solutions.aap.org/selfserve/sspage.aspx?selfservecontentid=vaccine-policy-guidance.

USE OF ANTIVIRAL MEDICATIONS

Oral oseltamivir remains the antiviral drug of choice for the management of influenza infections. Although more difficult to administer, inhaled zanamivir is an equally acceptable alternative for patients who do not have chronic respiratory disease. Options are limited for children who cannot absorb orally or enterically administered oseltamivir or tolerate inhaled zanamivir. Peramivir, a third NAI, was licensed in December 2014 for use in adults 18 years or older and is being studied in children. Intravenous zanamivir remains investigational and is not approved in the United States. It is not known whether either intravenous zanamivir or intravenous peramivir will be available for compassionate use during the 2017–2018 influenza season. A prospective, open-label pediatric clinical trial has been conducted to investigate pharmacokinetics and the clinical/virologic response to treatment with intravenous zanamivir for children 6 months or older who have a serious influenza infection and could not tolerate oral or inhaled NAIs.

Although intravenous zanamivir has previously been available for compassionate use for seriously ill children, with the support of the FDA through the manufacturer, GlaxoSmithKline, it is not known whether it will be available for compassionate use during the 2017–2018 influenza season.

Antiviral resistance to any drug can emerge, necessitating continuous population-based assessment that is conducted by the CDC. If local or national influenza surveillance data indicate the emergence of an influenza strain with a known antiviral resistance profile, then, according to the CDC, empirical treatment can be directed toward that strain with an effective antiviral agent. During the 2016–2017 season, the vast majority of the tested influenza strains were susceptible to oseltamivir, zanamivir, and peramivir. In contrast, high levels of resistance to amantadine and rimantadine persist among the influenza A viruses currently circulating, and adamantanes are not effective against influenza B viruses, so these drugs should not be used in the upcoming season unless resistance patterns change significantly. Therefore, it is important to note the following:

- Current treatment guidelines for antiviral medications (Table 5) are unchanged for the 2017–2018 season and 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. 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 6); and

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

Regardless of influenza vaccination status and whether the onset of illness has been <48 hours, treatment should be offered as early as possible without waiting for confirmatory influenza testing for the following individuals (Table 5):

- any hospitalized child clinically presumed to have influenza disease or with severe, complicated, or progressive illness attributable to influenza; and

- influenza infection of any severity in children at high risk of complications of influenza infection (Table 3).

Treatment should be considered for the following individuals (Table 5):

- Any otherwise healthy child clinically presumed to have influenza disease. 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 progressive, symptomatic illness; and

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

Reviewers of available studies by the CDC, the WHO, 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. A 2014 Cochrane meta-analysis of randomized, placebo-controlled trials of oseltamivir or zanamivir overwhelmingly performed in outpatient adults and children with confirmed or suspected exposure to naturally occurring influenza revealed that the question of whether the complications of influenza are reduced by NAIs is not settled, so the balance between benefits and harms should be considered when making decisions about use of NAIs for either treatment or prophylaxis of influenza. Unfortunately, treatment efficacy has not yet been adequately evaluated among hospitalized children or children with comorbid conditions in randomized trials. Although limited prospective comparative data exist to date, multiple retrospective observational studies and meta-analyses have been conducted to determine the role of NAIs in treating severe influenza. Most experts support the use of NAIs to reduce complications and hospitalizations, although less agreement exists on the use of NAIs in low-risk populations in whom the benefits are likely modest.

Importantly, treatment with oseltamivir for children with serious, complicated, or progressive disease presumptively or definitively caused by influenza, irrespective of influenza vaccination status or whether illness began >48 hours before admission, continues to be recommended by the AAP, CDC, and Infectious Diseases Society of America/Pediatric Infectious Diseases Society. 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. No benefit exists for double-dose NAI therapy, compared with standard-dose therapy, a

TABLE 7 Influenza Diagnostic Tests

Influenza Diagnostic Test	Method	Availability	Typical Processing Time	Sensitivity %	Distinguishing Subtype Strains of Influenza A	Cost
Rapid influenza diagnostic tests[a]	Antigen detection	Wide	<15 min	10–70	No	$
Rapid influenza molecular assays[b]	RNA detection	Wide	<20 min	86–100	No	$$$
Nucleic acid amplification tests (including RT-PCR)	RNA detection	Limited	1–8 h	86–100	Yes	$$–$$$
Direct and indirect immunofluorescence assays	Antigen detection	Wide	1–4 h	70–100	No	$
Rapid cell culture (shell vials and cell mixtures)	Virus isolation	Limited	1–3 d	100	Yes	$$
Viral cell culture	Virus isolation	Limited	3–10 d	100	Yes	$$$

Adapted from the Centers for Disease Control and Prevention (CDC). Guidance for clinicians on the use of rapid influenza diagnostic tests. Available at: http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm. Accessed July 25, 2017. RT-PCR, reverse transcription polymerase chain reaction.

[a] Most rapid influenza diagnostic tests are waived by the Clinical Laboratory Improvement Amendments.

[b] Some rapid influenza molecular assays are waived by the Clinical Laboratory Improvement Amendments, depending on the specimen.

conclusion based on published data from a randomized, prospective trial with 75% of its subjects of ages younger than 15 years.

Dosages of antiviral agents for both treatment and chemoprophylaxis in children can be found in Table 6 (doses for all ages, including doses for preterm infants that have not been evaluated by the FDA) 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. Given preliminary pharmacokinetic data and limited safety data, the AAP believes that oseltamivir can be used to treat influenza in both term and preterm infants from birth, because the benefits of therapy are likely to outweigh possible risks of treatment.

In adverse event data collected systematically in prospective trials, vomiting was the only adverse effect seen more often with oseltamivir than with placebo when studied in children 1 through 12 years of age (ie, 15% of treated children versus 9% receiving placebo). In addition, after 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 https://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4180b_06_07_Tamiflu%20Executive%20Summary_Oct25.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 7), all of which should be considered in making the best clinical judgment. Influenza test results are influenced by the level of influenza activity in the population being tested, the characteristics of a test compared with a gold standard, pretest probability, whether the influenza virus is actively replicating in the person, proper collection and transport of specimens, and proper test procedures. Testing should be performed when timely results will be available to influence clinical management or infection control measures. Although decisions on treatment and infection control can be made on the basis of positive rapid antigen test results, negative results should not always be used in a similar fashion because of the suboptimal sensitivity and the potential for false-negative results. 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 and promote appropriate antimicrobial stewardship. Available FDA-approved rapid molecular assays are highly sensitive, and specific diagnostic tests are performed in <20 minutes by using RNA detection. These molecular assays or polymerase chain reaction (PCR) test confirmation are preferred in hospitalized patients because they are more sensitive than antigen detection. Presumptive antiviral treatment in high-risk and hospitalized patients should be started before receiving rapid test, molecular assay, or PCR results. Immunofluorescence assays may be an alternative to PCR testing, although the sensitivity is lower. Early detection, prompt antiviral treatment, and infection control interventions can lead to improved individual patient outcomes and allow for effective cohorting and disease containment.

People with suspected influenza who present with an uncomplicated febrile illness should be offered treatment with antiviral medications

if they are at a higher risk of influenza complications (Table 3). Any otherwise healthy children who have a similar uncomplicated presentation should be considered for antiviral medication, particularly if they are in contact with other children who 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 of oseltamivir suspension have occurred because of uneven drug distribution, although national shortages have not occurred since 2009, particularly given the availability of the capsule formulation that can be made into a suspension for young children (Table 6).

Randomized placebo-controlled studies revealed that oral oseltamivir and inhaled 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 need to be aware of the possibility of emerging resistance 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 only be used when antiviral agents can be started within 48 hours of exposure; the lower dose for prophylaxis should not be used for treatment of children symptomatic with influenza. Early, full treatment doses (rather than prophylaxis doses) provided to high-risk symptomatic patients without waiting for laboratory confirmation is an alternate strategy.

Although vaccination is the preferred approach to prevention of infection, chemoprophylaxis during an influenza outbreak, as defined by the CDC (http://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section11.html), is recommended in the following situations:

- for children at high risk of complications from influenza for whom the influenza vaccine is contraindicated;
- for children at high risk during the 2 weeks after influenza vaccination, before optimal immunity is achieved;
- 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 vaccination among children at high risk, including children who are immunocompromised and may not respond with sufficient protective immune responses after vaccination;
- as postexposure prophylaxis for family members and close contacts of an infected person if those people are at high risk of complications from influenza; and
- for children at high risk of complications 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.

The influenza vaccine should always be offered before and within the influenza season when not contraindicated, even after the influenza virus has been circulating in the community. Antiviral medications currently licensed are important adjuncts to influenza vaccination for control and prevention of influenza disease. Toxicities are associated with antiviral agents, and 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 vaccination with IIV. For recommendations about treatment and chemoprophylaxis against influenza, see Table 6. 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 2017–2018 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 vaccines, especially for young children and pregnant women, is important. 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, 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. The interim recommendation that LAIV4 should not be used in children continues to be reevaluated.

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 vaccination. Ongoing efforts should include broader implementation and evaluation of mandatory vaccination programs in both inpatient and outpatient settings. 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.[5] In 2017, only 3 states (ie, CA, MS, and WV) restrict vaccine exemption laws to medical exemptions.[6] However, influenza vaccination is not typically required for school entry.

Efforts should be made to create adequate outreach and infrastructure to facilitate the optimal distribution of the vaccine so that more people are immunized. Pediatricians also might consider becoming 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. Pandemic influenza preparedness of directors of child care centers also needs to improve. Additional information can be found at www.aap.org/disasters/resourcekit.

Pandemic influenza preparedness is of particular interest because of the increase in the number of human infections with Asian H7N9 reported in China. A few human infections of Asian H7N9 have been reported outside of mainland China, but most of these infections have occurred among people who had traveled to China before becoming ill. These Asian H7N9 viruses have not been detected in people or birds in the United States. Although the current risk to the public's health from this virus is low, Asian H7N9 virus is among the nonhuman influenza viruses that are most concerning to public health officials because of their pandemic potential and ability to cause severe disease in infected humans. The current risk to the public's health from the virus remains low; however, the CDC is monitoring the situation carefully and taking routine preparedness measures, including making a candidate vaccine.

With the increased demand for vaccination 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 the influenza vaccine. If alternate venues, including pharmacies and other retail-based clinics, are used for vaccination, a system of patient record transfer is beneficial in maintaining the accuracy of immunization records. Immunization information systems should be used whenever available and prioritized to document influenza vaccination. 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, by using all health care encounters as vaccination opportunities, and by more consistently using immunization registry data. Innovative strategies of capturing those who usually prefer the intranasal formulation would be valuable, given the recent recommendations to not use LAIV4. One new strategy of interest is IIV delivered by a dissolvable microneedle patch, which has

the potential to improve vaccine acceptability, coverage and reduce costs. Data from the first phase-1 human clinical trial (n = 100) found that the microneedle patch immunization was well tolerated and generated robust antibody responses.

Development efforts continue for a universal influenza vaccine that induces broader protection and eliminates the need for annual vaccination. 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).

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ABBREVIATIONS

AAP: American Academy of Pediatrics
CDC: Centers for Disease Control and Prevention
CI: confidence interval
DTaP: diphtheria-tetanus-acellular-pertussis
FDA: US Food and Drug Administration
GBS: Guillain-Barré syndrome
HCP: health care personnel
ID: intradermal
IIV: inactivated influenza vaccine
IIV3: trivalent inactivated influenza vaccine
IIV4: quadrivalent inactivated influenza vaccine
IM: intramuscular
LAIV4: quadrivalent live attenuated influenza vaccine
NAI: neuraminidase inhibitor
PCR: polymerase chain reaction
PCV13: 13-valent pneumococcal conjugate vaccine
RIV: recombinant inactivated vaccines

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