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PRACTICE GUIDE: Influenza Vaccination and Treatment in Primary Care

Learning Objectives

- State the symptoms commonly associated with influenza.
- List the current CDC recommendations for administering influenza vaccine to adults and children, including those with chronic diseases such as asthma or diabetes.
- Describe the composition of the influenza vaccine for the 2012-2013 season.
- Describe current FDA-approved influenza vaccine formulations and their indications.
- State the current CDC recommendations for using antiviral agents to treat influenza in adults and children, including those with chronic illnesses such as asthma and diabetes.
- State the current CDC recommendations for influenza vaccination of healthcare personnel.

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Target Audience

Family Physicians and other primary care clinicians.

Accreditation

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Credit Designation

AMA PRA Category 1–The Illinois Academy of Family Physicians/Family Practice Education Network designates this enduring material, Practice Guide: *Influenza Vaccination and Treatment in Primary Care*, for a maximum of 0.75 AMA PRA Category 1 credit™.
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Kristin Drynan, MD, Renee M. Poole, MD, Charles A. Goldthwaite, Jr., Ph.D (medical writer),
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Influenza is a viral infection transmitted by coughing or sneezing or through direct contact with contaminated surfaces or nasal secretions. In addition to causing short-term discomfort, influenza can promote bacterial pneumonia or ear/sinus infections or aggravate existing chronic illnesses such as congestive heart failure, asthma, or chronic obstructive pulmonary disease. Using data gathered between 1976 and 2007, the Centers for Disease Control and Prevention (CDC) estimates that seasonal flu causes 3,000-49,000 deaths per year in the US, depending on the severity and length of the flu season.[1]

Vaccination is an effective and simple preventive measure against contracting or spreading influenza. However, the CDC reports that for the 2012-2013 flu season, only 36.5% of US children and adults were vaccinated by early to mid-November 2012.[2] Moreover, a recent CDC survey of 2,096 pregnant women indicated that only ~47% reported being vaccinated against influenza during the 2011–12 influenza season, even though the CDC recommends immunizing pregnant women to protect them and their newborns.[3] Women who received both health-care provider recommendations and offers to vaccinate had substantially higher vaccination coverage (73.6%) compared to 47.9% for those with recommendations but no offers and 11.1% for those with neither.

Diagnosing Influenza:

Influenza can be diagnosed through symptoms and/or with rapid influenza tests. Characteristic symptoms, which have rapid onset, include a high fever (100-102 °F) that persists for several days, usually accompanied by fatigue (lasting up to several weeks), body aches and pains, and headache. Other symptoms may include stuffy nose, cough, or sore throat. Confirmation of diagnosis can be made using a rapid flu test, which will produce results typically within 15 minutes. Available flu tests vary in sensitivity and specificity relative to viral culture, with a sensitivity of approximately 50-70% and specificity of 90-95%.[4] Thus, clinical judgment plays a role in diagnosis, especially for high-risk patients.

Current CDC Recommendations for Influenza Vaccination:[5]

General Population. The CDC's Advisory Committee on Immunization Practices (ACIP) currently recommends routine annual influenza vaccination for all persons aged ≥6 months. Given that 2-3 weeks are necessary to develop antibodies to influenza vaccine antigens, providers should offer the vaccine as early in the influenza season as possible (preferably before the onset of influenza activity in the community) and continue to make the vaccine available through the influenza season. The timing of influenza seasons varies somewhat. The CDC reports that influenza-like illness in the United States typically begins to increase in late December or early January and usually peaks in February, although outbreaks have recently occurred as early as October.[6] While patients are encouraged to receive the influenza vaccine when first available, the influenza season may last for months. Thus, it is never too late to benefit from the vaccine during the influenza season, even for individuals who have already been diagnosed with influenza. Furthermore, immunization may lessen symptom severity in individuals who contract a strain of influenza not included in the vaccine.

The CDC currently recommends routine annual influenza vaccination for all persons aged 6 months and older.

Children Aged 6 Months to 8 Years. For the 2012-2013 flu season, ACIP recommends that children ages 6 months through 8 years receive two doses of vaccine (administered at a minimum interval of four weeks) during their first season of vaccination. Children who have received two or more doses of seasonal influenza vaccine since July 1, 2010 should receive only one dose. In cases where the history of the child's flu vaccination is unknown, two doses are recommended. Providers should verify CDC recommendations on age-related flu vaccine dosing each year, as these guidelines may change based on the characteristics of a particular flu season.

Vaccine Strains for the 2012-2013 Influenza Season:

The composition of the influenza vaccine is determined each year by the World Health Organization's (WHO) Global Influenza Surveillance Network, which selects an H1N1, an H3N2, and a Type-B influenza strain to include in the year's vaccine, based on those predicted to be most predominant in the upcoming season. The alphanumeric designations refer to influenza virus A subtypes that contain specific hemagglutinin (H) and neuraminidase (N) antigens. After WHO makes its recommendations, the US FDA Vaccines and Related Biological Products Advisory Committee concurs with or modifies the recommendation for the US. The H1N1 strain used in the 2012-2013 vaccine (see below) derives from the 2009 H1N1 virus and was included in the 2009 H1N1 monovalent pandemic vaccine and the 2010-11 and 2011-12 seasonal vaccines.[5] Given the virus's relatively high mutation rate, seasonal vaccines tend to be effective for a year or so.

A flu vaccine is the primary preventive strategy to minimize the spread of influenza.

Influenza vaccines available in the U.S. for the 2012-2013 season contain the following strains of antigens:[5]

- A/California/7/2009 (H1N1)-like
- A/Victoria/361/2011 (H3N2)-like
- B/Wisconsin/1/2010-like (Yamagata lineage)

Types of Flu Vaccines:

Currently available influenza vaccines are classified based on their preparation. "Flu shots" are trivalent inactivated vaccines (TIV) that engender an immune response

to the antigens present on the inactivated virus strains. Age indications vary among TIV products, and the CDC expresses no preference among TIV formulations within specified age indications.[5] An intranasal formulation composed of a live-attenuated influenza vaccine (LAIV) is also indicated for healthy, non-pregnant persons aged 2 to 49 years, with no preference for LAIV versus TIV in this age group. In this context, "healthy" individuals do not have an underlying medical condition that predisposes them to influenza complications. As an attenuated vaccine, the LAIV formulation contains live virus particles of low virulence. CDC recommends that immunocompromised persons (e.g., those with conditions such as diabetes, asthma, or HIV), persons with an egg allergy, and those who care for severely immunosuppressed persons or infants preferentially receive TIV.[5,7] However, LAIV may be administered to breastfeeding women and to individuals who have contact with others with lesser degrees of immunosuppression (e.g., diabetes, asthma, HIV). For a detailed list of who should not receive LAIV, see Table 1 in reference #7. In February 2012, the US FDA approved a seasonal quadrivalent intranasal LAIV formulation that contains two A and two B influenza strains. This formulation is anticipated to become available in the 2013-2014 season and will replace the current trivalent LAIV formulation.

Currently available flu vaccines are prepared by inoculation into chicken eggs. CDC recommends that persons with egg allergy who report only hives after egg exposure receive a TIV (but not a LAIV) formulation, with a 30-minute observation period following administration.[5] Persons who can eat lightly-cooked (e.g., scrambled) eggs without reaction should receive the flu vaccine. However, individuals who report more severe symptoms, including respiratory distress, angioedema, lightheadedness or recurrent emesis in response to egg exposure should be referred to a physician with expertise in allergy management for risk assessment. In early 2013, the FDA approved a non-egg-based vaccine for use in adults aged 18-49; this product is expected to be widely available in the 2013-14 season.

Individuals with asthma and/or diabetes should receive only a TIV formulation of the influenza vaccine.

High-Dose and Intradermal TIV Formulations:

A branded high-dose TIV formulation is available that contains four times the amount of each flu antigen present in a standard TIV formulation. Available in pre-filled 0.5 mL syringes, the high-dose formulation is indicated for persons aged ≥65 years.[5] ACIP has not expressed a preference for any specific licensed inactivated trivalent influenza vaccine, including the high-dose formulation, for use in persons aged ≥65 years. The high-dose safety profile is similar to those of standard-dose flu vaccines. Data suggest that the high-dose formulation produces higher antibody levels than standard-dose formulations following vaccination, although it is not known at present whether this improved immune response translates into greater protection against influenza. The high-dose formulation costs roughly double that of standard-dose formulations, although both are covered by Medicare. It should be noted that the high-dose formulation is not as widely available as standard-dose formulations.

An FDA-approved intradermal TIV formulation is also indicated for persons aged 18-64 years.[5] Available as a pre-filled, single-dose, 0.1 mL syringe, this formulation is preferably administered over the deltoid muscle. This formulation is more costly than its intramuscular counterpart; providers should consider cost and insurance coverage when recommending this formulation. As with intramuscular flu shots, the intradermal shot is associated with side effects that include redness, swelling, toughness, pain, and itching at the injection site. However, with the exception of pain, these side effects are more commonly reported with the intradermal shot than with intramuscular flu shots.[8]

Antiviral Treatment for Influenza:

Two prescription antiviral agents, oseltamivir and zanamivir, are currently FDA-approved to treat influenza or as a second-line preventive measure following immunization (Tables 1 and 2). If administered within 48 hours of symptom onset, these agents can lessen the severity of symptoms and shorten their duration by 1-2 days. The CDC recommends administering agents as soon as possible to persons with suspected or confirmed influenza, especially those at high risk for complications.[9] To achieve maximum efficacy, agents should be taken for five days. These agents can also prevent complications of influenza and may be useful for persons with high-risk health conditions even if initially administered relatively late after symptom onset. Antiviral agents may also be used for prophylaxis in high-risk patients with known influenza exposure or those living in nursing homes or other communal environments subject to outbreaks, although the dosing varies for these situations. Providers are advised to check for the latest CDC or health department guidelines for antiviral agent use, as these guidelines tend to reflect sensitivity to seasonal flu strains and product availability.

Preventing the Spread of Influenza:

A flu vaccine is the primary preventive strategy to minimize the spread of influenza. However, promoting good hygiene is also helpful. Providers should remind patients that practicing the "Three C's of Good Hygiene"—**Clean** (wash your hands), **Cover** your coughs and sneezes, and **Contain** your germs by staying home if you are sick–will help to keep from spreading the flu.

Patients should be reminded that they can minimize the spread of influenza by practicing the "Three C's of Good Hygiene"—Clean, Cover, and Contain.

Special Considerations for Patients with Chronic Disease:

Persons with chronic illness, including asthma and diabetes, are at high risk for developing complications from influenza.

Asthma. Asthma is a common medical condition among persons hospitalized with influenza. Influenza can exacerbate asthma symptoms and promote pneumonia and

other respiratory complications. Per CDC recommendations, persons with asthma should receive a seasonal flu shot (TIV formulation) as part of an established asthma action plan, although intranasal formulations are contraindicated.[10] Persons with asthma should also receive pneumococcal vaccine as appropriate. The CDC also recommends that persons with asthma and confirmed or suspected influenza receive antiviral treatment as early as possible.[9] Persons with asthma who require antiviral therapy should receive only oseltamivir, as zanamivir is contraindicated.

Diabetes. Diabetes can compromise the immune system, and illness can elevate blood sugar levels. Compared to individuals who do not have diabetes, those with the condition are six times more likely to be hospitalized with flu complications. Each year, influenza and pneumonia are associated with the deaths of 10,000-30,000 individuals with diabetes; persons with diabetes are nearly three times more likely to die with influenza or pneumonia than those who do not have diabetes. Furthermore, deaths among people with diabetes increase 5-15% during influenza epidemics.[11] As such, the CDC classifies diabetes mellitus as a medical risk factor for influenza-related complications.[7] Per CDC recommendations, persons with diabetes should receive a seasonal flu shot (TIV formulation) and pneumococcal vaccination as part of a diabetes management plan, although LAIV formulations are contraindicated.[7] As with asthma patients, the CDC also recommends that persons with diabetes and confirmed or suspected influenza receive antiviral treatment as early as possible.[9]

Vaccination of Healthcare Personnel:

Healthcare personnel (HCP) who are vaccinated protect themselves, their coworkers, and all contacted patients. As such, failure of HCP to receive an influenza vaccine represents a public health concern, especially if the personnel work among patients who, for medical reasons, cannot be immunized. Although low vaccination rates among HCP have been associated with influenza outbreaks in hospitals and long-term–care facilities,[12] a recent CDC survey of 2,342 HCP indicates that only 66.9% of HCP were vaccinated during the 2011-2012 flu season.[13] Coverage was highest among physicians (86.7%) and nurses (78.1%) who worked in hospitals and lowest (50.2%) among other HCP who worked in long-term care facilities.

The CDC recommends that all HCP who have no contraindications receive annual influenza vaccination, preferably as soon as seasonal vaccines become available.[12] HCP who care for severely immunocompromised hospitalized persons who require care in a protective environment, as well as HCP who themselves have a condition that confers high risk for influenza complications, who are pregnant, or who are aged ≥50 years should receive TIV rather than LAIV. CDC further recommends that healthcare facilities regularly measure and document HCP influenza vaccination rates and develop a comprehensive influenza vaccination strategy that includes targeted education about the disease, vaccine, and disease risk among HCP and patients.

Table 1. Dosing Regimen for Oseltamivir (Tamiflu®)

Indication	Infants (2 MONTHS–1 YEAR)	Children (> 1 YEAR)		Adolescents/Adults (> 13 YEARS)
		Body Weight	Dose (5 days)	
Treatment	3 mg/kg; twice daily for 5 days	< 33 lbs	30 mg twice daily	75 mg; 2X daily for 5 days
		33-51 lbs	45 mg twice daily	
		> 51-88 lbs	60 mg twice daily	
		> 88 lbs	75 mg twice daily	
Prophylaxis	Not approved	(same as for Treatment)		75 mg; once daily for 10 days
Source: Genetech; www.tamiflu.com.				

Table 2. Dosing Regimen for Zanamivir (Relenza®)

Indication	Children and Adults
Treatment	10 mg twice daily for 5 days (7 Years and older)
Prophylaxis	10 mg once daily for 10 days (5 Years and older)
Source: Glaxo Smith Kline; www.gsk.com	

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