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MORBIDITY AND MORTALITY WEEKLY REPORT

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## Prevention and Control of Influenza: Part I, Vaccines

### Recommendations of the Advisory Committee on Immunization Practices (ACIP)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Centers for Disease Control  
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# Prevention and Control of Influenza: Part I, Vaccines Recommendations of the Advisory Committee on Immunization Practices (ACIP)

## Summary

*These recommendations update information on the vaccine available for controlling influenza during the 1994–95 influenza season. The recommendations supersede MMWR 1993;42(No. RR-6)1–13.*

*Antiviral agents also have an important role in the control of influenza. Recommendations for the use of antiviral agents will be published later in 1994 as Part II of these recommendations.*

## INTRODUCTION

Influenza A viruses are classified into subtypes on the basis of two surface antigens: hemagglutinin (H) and neuraminidase (N). Three subtypes of hemagglutinin (H1, H2, and H3) and two subtypes of neuraminidase (N1 and N2) are recognized among influenza A viruses that have caused widespread human disease. Immunity to these antigens—especially to the hemagglutinin—reduces the likelihood of infection and lessens the severity of disease if infection occurs. Infection with a virus of one subtype confers little or no protection against viruses of other subtypes. Furthermore, over time, antigenic variation (antigenic drift) within a subtype may be so marked that infection or vaccination with one strain may not induce immunity to distantly related strains of the same subtype. Although influenza B viruses have shown more antigenic stability than influenza A viruses, antigenic variation does occur. For these reasons, major epidemics of respiratory disease caused by new variants of influenza continue to occur. The antigenic characteristics of circulating strains provide the basis for selecting the virus strains included in each year's vaccine.

Typical influenza illness is characterized by abrupt onset of fever, myalgia, sore throat, and nonproductive cough. Unlike other common respiratory illnesses, influenza can cause severe malaise lasting several days. More severe illness can result if either primary influenza pneumonia or secondary bacterial pneumonia occurs. During influenza epidemics, high attack rates of acute illness result in both increased numbers of visits to physicians' offices, walk-in clinics, and emergency rooms and increased hospitalizations for management of lower respiratory tract complications.

Elderly persons and persons with underlying health problems are at increased risk for complications of influenza. If they become ill with influenza, such members of high-risk groups (see Groups at Increased Risk for Influenza-Related Complications under Target Groups for Special Vaccination Programs) are more likely than the general population to require hospitalization. During major epidemics, hospitalization rates for persons at high risk may increase two- to five-fold, depending on the age group. Previously healthy children and younger adults may also require

hospitalization for influenza-related complications, but the relative increase in their hospitalization rates is less than for persons who belong to high-risk groups.

An increase in mortality further indicates the impact of influenza epidemics. Increased mortality results not only from influenza and pneumonia but also from cardiopulmonary and other chronic diseases that can be exacerbated by influenza. It is estimated that >10,000 influenza-associated deaths occurred during each of seven different U.S. epidemics in the period 1977–1988, and >40,000 influenza-associated deaths occurred during each of two of these epidemics. Approximately 90% of the deaths attributed to pneumonia and influenza occurred among persons  $\geq 65$  years of age.

Because the proportion of elderly persons in the U.S. population is increasing and because age and its associated chronic diseases are risk factors for severe influenza illness, the number of deaths from influenza can be expected to increase unless control measures are implemented more vigorously. The number of persons <65 years of age at increased risk for influenza-related complications is also increasing. Better survival rates for organ-transplant recipients, the success of neonatal intensive-care units, and better management of diseases such as cystic fibrosis and acquired immunodeficiency syndrome (AIDS) result in a higher survival rate for younger persons at high risk.

## **OPTIONS FOR THE CONTROL OF INFLUENZA**

In the United States, two measures are available that can reduce the impact of influenza: immunoprophylaxis with inactivated (killed-virus) vaccine and chemoprophylaxis or therapy with an influenza-specific antiviral drug (amantadine or rimantadine). Vaccination of persons at high risk each year before the influenza season is currently the most effective measure for reducing the impact of influenza. Vaccination can be highly cost effective when a) it is directed at persons who are most likely to experience complications or who are at increased risk for exposure and b) it is administered to persons at high risk during hospitalizations or routine health-care visits before the influenza season, thus making special visits to physicians' offices or clinics unnecessary. When vaccine and epidemic strains of virus are well matched, achieving high vaccination rates among persons living in closed settings (e.g., nursing homes and other chronic-care facilities) can reduce the risk for outbreaks by inducing herd immunity.

## **INACTIVATED VACCINE FOR INFLUENZA A AND B**

Each year's influenza vaccine contains three virus strains (usually two type A and one type B) representing the influenza viruses that are likely to circulate in the United States in the upcoming winter. The vaccine is made from highly purified, egg-grown viruses that have been made noninfectious (inactivated). Influenza vaccine rarely causes systemic or febrile reactions. Whole-virus, subvirion, and purified-surface-antigen preparations are available. To minimize febrile reactions, only subvirion or purified-surface-antigen preparations should be used for children; any of the preparations may be used for adults.

Most vaccinated children and young adults develop high postvaccination hemagglutination-inhibition antibody titers. These antibody titers are protective against illness caused by strains similar to those in the vaccine or the related variants that may emerge during outbreak periods. Elderly persons and persons with certain chronic diseases may develop lower postvaccination antibody titers than healthy young adults and thus may remain susceptible to influenza-related upper respiratory tract infection. However, even if such persons develop influenza illness despite vaccination, the vaccine has been shown to be effective in preventing lower respiratory tract involvement or other secondary complications, thereby reducing the risk for hospitalization and death.

The effectiveness of influenza vaccine in preventing or attenuating illness varies, depending primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the virus strains included in the vaccine and those that circulate during the influenza season. When there is a good match between vaccine and circulating viruses, influenza vaccine has been shown to prevent illness in approximately 70% of healthy persons <65 years of age. In these circumstances, studies have also indicated that influenza vaccine is approximately 70% effective in preventing hospitalization for pneumonia and influenza among elderly persons living in settings other than nursing homes or similar chronic-care facilities.

Among elderly persons residing in nursing homes, influenza vaccine is most effective in preventing severe illness, secondary complications, and death. Studies of this population have shown the vaccine to be 50%–60% effective in preventing hospitalization and pneumonia and 80% effective in preventing death, even though efficacy in preventing influenza illness may often be in the range of 30%–40% among the frail elderly. Achieving a high rate of vaccination among nursing home residents has been shown to reduce the spread of infection in a facility, thus preventing disease through herd immunity.

## RECOMMENDATIONS FOR USE OF INFLUENZA VACCINE

Influenza vaccine is strongly recommended for any person  $\geq 6$  months of age who—because of age or underlying medical condition—is at increased risk for complications of influenza. Health-care workers and others (including household members) in close contact with persons in high-risk groups should also be vaccinated. In addition, influenza vaccine may be administered to any person who wishes to reduce the chance of becoming infected with influenza. The trivalent influenza vaccine prepared for the 1994–95 season will include A/Texas/36/91-like (H1N1), A/Shangdong/9/93-like (H3N2), and B/Panama/45/90-like hemagglutinin antigens. Recommended doses are listed in Table 1. Guidelines for the use of vaccine among different groups follow.

Although the current influenza vaccine can contain one or more of the antigens administered in previous years, annual vaccination with the current vaccine is necessary because immunity declines in the year following vaccination. Because the 1994–95 vaccine differs from the 1993–94 vaccine, supplies of 1993–94 vaccine should not be administered to provide protection for the 1994–95 influenza season.

Two doses administered at least 1 month apart may be required for satisfactory antibody responses among previously unvaccinated children <9 years of age; however, studies with vaccines similar to those in current use have shown little or no

improvement in antibody responses when a second dose is administered to adults during the same season.

During the past decade, data on influenza vaccine immunogenicity and side effects have been obtained for intramuscularly administered vaccine. Because there has been no adequate evaluation of recent influenza vaccines administered by other routes, the intramuscular route is recommended. Adults and older children should be vaccinated in the deltoid muscle and infants and young children in the anterolateral aspect of the thigh.

## TARGET GROUPS FOR SPECIAL VACCINATION PROGRAMS

To maximize protection of high-risk persons, they and their close contacts should be targeted for organized vaccination programs.

### Groups at Increased Risk for Influenza-Related Complications:

- Persons  $\geq 65$  years of age
- Residents of nursing homes and other chronic-care facilities that house persons of any age with chronic medical conditions
- Adults and children with chronic disorders of the pulmonary or cardiovascular systems, including children with asthma
- Adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications)
- Children and teenagers (6 months–18 years of age) who are receiving long-term aspirin therapy and therefore may be at risk for developing Reye syndrome after influenza

**TABLE 1. Influenza vaccine\* dosage, by age group — United States, 1994–95 season**

Age group	Product <sup>†</sup>	Dosage	No. doses	Routes <sup>§</sup>
6–35 mos	Split virus only	0.25 mL	1 or 2 <sup>¶</sup>	IM
3–8 yrs	Split virus only	0.50 mL	1 or 2 <sup>¶</sup>	IM
9–12 yrs	Split virus only	0.50 mL	1	IM
>12 yrs	Whole or split virus	0.50 mL	1	IM

\*Contains 15  $\mu$ g each of A/Texas/36/91-like (H1N1), A/Shangdong/9/93-like (H3N2), and B/Panama/45/90-like hemagglutinin antigens in each 0.5 mL. Manufacturers include: Connaught Laboratories, Inc. (Fluzone<sup>®</sup> whole or split); Evans Medical Ltd. (distributed by Adams Laboratories, Inc.) (Fluviron<sup>™</sup> purified surface antigen vaccine); Parke-Davis (Fluogen<sup>®</sup> split); and Wyeth-Ayerst Laboratories (Flushield<sup>™</sup> split). For further product information call Connaught, (800) 822-2463; Adams, (800) 932-1950; Parke-Davis, (800) 223-0432; Wyeth-Ayerst, (800) FLU-SHIELD.

<sup>†</sup>Because of the lower potential for causing febrile reactions, only split-virus vaccines should be used for children. They may be labeled as “split,” “subvirion,” or “purified-surface-antigen” vaccine. Immunogenicity and side effects of split- and whole-virus vaccines are similar among adults when vaccines are administered at the recommended dosage.

<sup>§</sup>The recommended site of vaccination is the deltoid muscle for adults and older children. The preferred site for infants and young children is the anterolateral aspect of the thigh.

<sup>¶</sup>Two doses administered at least 1 month apart are recommended for children <9 years of age who are receiving influenza vaccine for the first time.

### **Groups that Can Transmit Influenza to Persons at High Risk**

Persons who are clinically or subclinically infected and who care for or live with members of high-risk groups can transmit influenza virus to them. Some persons at high risk (e.g., the elderly, transplant recipients, and persons with AIDS) can have low antibody responses to influenza vaccine. Efforts to protect these members of high-risk groups against influenza may be improved by reducing the likelihood of influenza exposure from their care givers. Therefore, the following groups should be vaccinated:

- Physicians, nurses, and other personnel in both hospital and outpatient-care settings;
- Employees of nursing homes and chronic-care facilities who have contact with patients or residents;
- Providers of home care to persons at high risk (e.g., visiting nurses and volunteer workers);
- Household members (including children) of persons in high-risk groups.

## **VACCINATION OF OTHER GROUPS**

### **General Population**

Physicians should administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza. Persons who provide essential community services may be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings, such as those who reside in dormitories, should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.

### **Pregnant Women**

Influenza-associated excess mortality among pregnant women has not been documented except in the pandemics of 1918–19 and 1957–58. However, pregnant women who have other medical conditions that increase their risks for complications from influenza should be vaccinated because the vaccine is considered safe for pregnant women—regardless of the stage of pregnancy. Thus, it is undesirable to delay vaccination of pregnant women who have high-risk conditions and who will still be in the first trimester of pregnancy when the influenza season begins.

### **Persons Infected with Human Immunodeficiency Virus (HIV)**

Limited information exists regarding the frequency and severity for influenza illness among HIV-infected persons, but reports suggest that symptoms may be prolonged and the risk for complications increased for some HIV-infected persons. Because influenza can result in serious illness and complications, vaccination is a prudent precaution and will result in protective antibody levels in many recipients. However, the antibody response to vaccine may be low in persons with advanced HIV-related illnesses; a booster dose of vaccine does not improve the immune response for these persons.

## Foreign Travelers

The risk for exposure to influenza during foreign travel varies, depending on season and destination. In the tropics, influenza can occur throughout the year; in the southern hemisphere, the season of greatest activity is April–September. Because of the short incubation period for influenza, exposure to the virus during travel can result in clinical illness that begins while traveling, an inconvenience or potential danger, especially for persons at increased risk for complications. Persons preparing to travel to the tropics at any time of year or to the southern hemisphere during April–September should review their influenza vaccination histories. If they were not vaccinated the previous fall or winter, they should consider influenza vaccination before travel. Persons in the high-risk categories should be especially encouraged to receive the most current vaccine. Persons at high risk who received the previous season's vaccine before travel should be revaccinated in the fall or winter with the current vaccine.

## PERSONS WHO SHOULD NOT BE VACCINATED

Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine without first consulting a physician (see Side Effects and Adverse Reactions). Use of an antiviral agent (amantadine or rimantadine) is an option for prevention of influenza A in such persons. However, persons who have a history of anaphylactic hypersensitivity to vaccine components but who are also at higher risk for complications of influenza may benefit from vaccine after appropriate allergy evaluation and desensitization. Specific information about vaccine components can be found in package inserts for each manufacturer.

Adults with acute febrile illness usually should not be vaccinated until their symptoms have abated. However, minor illnesses with or without fever should not contraindicate the use of influenza vaccine, particularly among children with mild upper respiratory tract infection or allergic rhinitis.

## SIDE EFFECTS AND ADVERSE REACTIONS

Because influenza vaccine contains only noninfectious viruses, it cannot cause influenza. Respiratory disease after vaccination represents coincidental illness unrelated to influenza vaccination. The most frequent side effect of vaccination reported by fewer than one-third of vaccinees is soreness at the vaccination site that lasts for up to 2 days. In addition, two types of systemic reactions have occurred:

- Fever, malaise, myalgia, and other systemic symptoms occur infrequently and most often affect persons who have had no exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6–12 hours after vaccination and can persist for 1 or 2 days;
- Immediate—presumably allergic—reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) occur rarely after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; the majority of reactions are most likely related to residual egg protein. Although

current influenza vaccines contain only a small quantity of egg protein, this protein may induce immediate hypersensitivity reactions among persons with severe egg allergy. Persons who have developed hives, have had swelling of the lips or tongue, or have experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons with documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs—including those who have had occupational asthma or other allergic responses due to exposure to egg protein—may also be at increased risk for reactions from influenza vaccine, and similar consultation should be considered. The protocol for influenza vaccination developed by Murphy and Strunk may be considered for patients who have egg allergies and medical conditions that place them at increased risk for influenza-associated complications (Murphy and Strunk, 1985).

Hypersensitivity reactions to any vaccine component can occur. Although exposure to vaccines containing thimerosal can lead to induction of hypersensitivity, most patients do not develop reactions to thimerosal when administered as a component of vaccines even when patch or intradermal tests for thimerosal indicate hypersensitivity. When reported, hypersensitivity to thimerosal has usually consisted of local, delayed-type hypersensitivity reactions.

Unlike the 1976–77 swine influenza vaccine, subsequent vaccines prepared from other virus strains have not been associated clearly with an increased frequency of Guillain-Barré syndrome (GBS). However, it is difficult to make a precise estimate of risk for a rare condition such as GBS. In 1990–91, although there was no overall increase in frequency of GBS among vaccine recipients, there may have been a small increase in GBS cases in vaccinated persons 18–64 years of age, but not in those aged  $\geq 65$  years. In contrast to the swine influenza vaccine, the epidemiologic features of the possible association of the 1990–91 vaccine with GBS were not as convincing. Even if GBS were a true side effect, the very low estimated risk for GBS is less than that of severe influenza that could be prevented by vaccine.

## **SIMULTANEOUS ADMINISTRATION OF OTHER VACCINES, INCLUDING CHILDHOOD VACCINES**

The target groups for influenza and pneumococcal vaccination overlap considerably. Both vaccines can be administered at the same time at different sites without increasing side effects. However, influenza vaccine must be administered each year, whereas pneumococcal vaccine is not. Children at high risk for influenza-related complications may receive influenza vaccine at the same time they receive other routine vaccinations, including pertussis vaccine (DTP or DTaP). Because influenza vaccine can cause fever when administered to young children, DTaP may be preferable in those children  $\geq 15$  months of age who are receiving the fourth or fifth dose of pertussis vaccine. DTaP is not licensed for the initial three-dose series of pertussis vaccine.

## **TIMING OF INFLUENZA VACCINATION ACTIVITIES**

Beginning each September (when vaccine for the upcoming influenza season becomes available) persons at high risk who are seen by health-care providers for routine care or as a result of hospitalization should be offered influenza vaccine. Opportunities to vaccinate persons at high risk for complications of influenza should not be missed.

The optimal time for organized vaccination campaigns for persons in high-risk groups is usually the period from mid-October through mid-November. In the United States, influenza activity generally peaks between late December and early March. High levels of influenza activity infrequently occur in the contiguous 48 states before December. It is particularly important to avoid administering vaccine too far in advance of the influenza season in facilities such as nursing homes because antibody levels may begin to decline within a few months of vaccination. Vaccination programs can be undertaken as soon as current vaccine is available if regional influenza activity is expected to begin earlier than December.

Children <9 years of age who have not been vaccinated previously should receive two doses of vaccine at least 1 month apart to maximize the likelihood of a satisfactory antibody response to all three vaccine antigens. The second dose should be administered before December, if possible. Vaccine should be offered to both children and adults up to and even after influenza virus activity is documented in a community.

## **STRATEGIES FOR IMPLEMENTING INFLUENZA VACCINE RECOMMENDATIONS**

Although rates of influenza vaccination have increased in recent years, surveys indicate that less than half of the high-risk population receives influenza vaccine each year. More effective strategies are needed for delivering vaccine to persons at high risk and to their health-care providers and household contacts.

In general, successful vaccination programs have combined education for health-care workers, publicity and education targeted toward potential recipients, a plan for identifying (usually by medical-record review) persons at high risk, and efforts to remove administrative and financial barriers that prevent persons from receiving the vaccine. Persons for whom influenza vaccine is recommended can be identified and vaccinated in the settings described in the following paragraphs.

### **Outpatient Clinics and Physicians' Offices**

Staff in physicians' offices, clinics, health-maintenance organizations, and employee health clinics should be instructed to identify and label the medical records of patients who should receive vaccine. Vaccine should be offered during visits beginning in September and throughout the influenza season. The offer of vaccine and its receipt or refusal should be documented in the medical record. Patients among high-risk groups who do not have regularly scheduled visits during the fall should be reminded by mail or telephone of the need for vaccine. If possible, arrangements should be made to provide vaccine with minimal waiting time and at the lowest possible cost.

### **Facilities Providing Episodic or Acute Care**

Health-care providers in these settings (e.g., emergency rooms and walk-in clinics) should be familiar with influenza vaccine recommendations. They should offer vaccine to persons in high-risk groups or should provide written information on why, where, and how to obtain the vaccine. Written information should be available in language(s) appropriate for the population served by the facility.

### **Nursing Homes and Other Residential Long-Term-Care Facilities**

Vaccination should be routinely provided to all residents of chronic-care facilities with the concurrence of attending physicians rather than by obtaining individual vaccination orders for each patient. Consent for vaccination should be obtained from the resident or a family member at the time of admission to the facility, and all residents should be vaccinated at one time, immediately preceding the influenza season. Residents admitted during the winter months after completion of the vaccination program should be vaccinated when they are admitted.

### **Acute-Care Hospitals**

All persons  $\geq 65$  years of age and younger persons (including children) with high-risk conditions who are hospitalized from September through March should be offered and strongly encouraged to receive influenza vaccine before they are discharged. Household members and others with whom they will have contact should receive written information about why and where to obtain influenza vaccine.

### **Outpatient Facilities Providing Continuing Care to Patients at High Risk**

All patients should be offered vaccine before the beginning of the influenza season. Patients admitted to such programs (e.g., hemodialysis centers, hospital specialty-care clinics, outpatient rehabilitation programs) during the winter months after the earlier vaccination program has been conducted should be vaccinated at the time of admission. Household members should receive written information regarding the need for vaccination and the places to obtain influenza vaccine.

### **Visiting Nurses and Others Providing Home Care to Persons at High Risk**

Nursing-care plans should identify patients in high-risk groups, and vaccine should be provided in the home if necessary. Care givers and others in the household (including children) should be referred for vaccination.

### **Facilities Providing Services to Persons $\geq 65$ Years of Age**

In these facilities (e.g., retirement communities and recreation centers), all unvaccinated residents/attendees should be offered vaccine on site before the influenza season. Education/publicity programs should also be provided; these programs should emphasize the need for influenza vaccine and provide specific information on how, where, and when to obtain it.

### **Clinics and Others Providing Health Care for Travelers**

Indications for influenza vaccination should be reviewed before travel, and vaccine should be offered if appropriate (see Foreign Travelers).

## Health-Care Workers

Administrators of all health-care facilities should arrange for influenza vaccine to be offered to all personnel before the influenza season. Personnel should be provided with appropriate educational materials and strongly encouraged to receive vaccine. Particular emphasis should be placed on vaccination of persons who care for members of high-risk groups (e.g., staff of intensive-care units [including newborn intensive-care units], staff of medical/surgical units, and employees of nursing homes and chronic-care facilities). Using a mobile cart to take vaccine to hospital wards or other work sites and making vaccine available during night and weekend work shifts may enhance compliance, as may a follow-up campaign early in the course of community outbreak.

## SOURCES OF INFORMATION ON INFLUENZA-CONTROL PROGRAMS

Information regarding influenza surveillance is available through the CDC Voice Information System (influenza update), telephone (404) 332-4551, or through the CDC Information Service on the Public Health Network electronic bulletin board. From October through May, the information is updated at least every other week. In addition, periodic updates about influenza are published in *MMWR*. State and local health departments should also be consulted regarding availability of vaccine, access to vaccination programs, and information about state or local influenza activity.

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