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MMWR

Weekly

May 05, 1989 / 38(17);297-311

Recommendations of the Immunization Practices Advisory Committee (ACIP) Prevention and Control of Influenza: Part I, Vaccines

These recommendations update information on the vaccine available for controlling influenza during the 1989-90 influenza season (superseding MMWR 1988;37: 361-73). Changes include statements about 1) updating of the influenza strains in the trivalent vaccine for 1989-90, 2) revision of the high-priority groups for immunization, 3) increased emphasis on the need for vaccination of health-care workers and household contacts of high-risk persons, 4) vaccination for travelers, and 5) review of strategies for reaching high-risk groups with vaccine.

Antiviral agents also have an important role in the control of influenza. Recommendations for the use of antiviral agents will be published in the summer or fall of 1989 as Part II of these recommendations. INTRODUCTION

Influenza A viruses are classified into subtypes on the basis of two antigens: hemagglutinin (H) and neuraminidase (N). Three subtypes of hemagglutinin (H1, H2, H3) and two subtypes of neuraminidase (N1, N2) are recognized among influenza A viruses that have caused widespread human disease. Immunity to these antigens, especially the hemagglutinin, reduces the likelihood of infection and lessens the severity of disease if infection occurs. However, over time, there may be enough antigenic variation (antigenic drift) within the same subtype 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 current strains provide the basis for selecting virus strains included in each year's vaccine. Typical influenza illness is characterized by abrupt onset of fever, sore throat, and nonproductive cough. Unlike many other common respiratory infections, influenza can cause extreme malaise lasting several days. More severe illness can result if the influenza virus invades the lungs (primary viral pneumonia) or if secondary bacterial pneumonia occurs. High attack rates of acute illness during influenza epidemics usually result in dramatic increases in visits to physicians' offices, walk-in clinics, and emergency rooms by persons of all ages and in increases in hospitalizations for management of lower-respiratory-tract complications.

Elderly persons and persons with underlying health problems are at increased risk for complications of influenza infection. Such high-risk persons are more likely than the general population to require hospitalization if infected. One recent study showed that, during major epidemics, hospitalization

rates for high-risk adults increased twofold to fivefold, depending on 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 in high-risk groups.

An increase in mortality further indicates the impact of influenza epidemics. Increased mortality results from not only pneumonia but also cardiopulmonary or other chronic diseases that can be exacerbated by influenza infection. Ten thousand or more excess deaths have been documented in each of 19 different epidemics during 1957-1986; more than 40,000 excess deaths occurred in each of several recent epidemics. Approximately 80%-90% of the excess deaths attributed to pneumonia and influenza were among persons greater than or equal to 65 years of age. However, influenza-associated deaths also occur in children and previously healthy adults less than 65 years of age during major epidemics.

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 toll from influenza can be expected to increase unless control measures are used more vigorously. The number of younger persons at high risk for infection- related complications is also increasing for various reasons, such as the success of neonatal intensive-care units, better management of diseases such as cystic fibrosis, and better survival rates for organ-transplant recipients. OPTIONS FOR THE CONTROL OF INFLUENZA

Two measures are available in the United States to reduce the impact of influenza: immunoprophylaxis with inactivated (killed-virus) vaccine and chemoprophylaxis or therapy with an influenza-specific antiviral drug (e.g., amantadine). Vaccination of high-risk persons each year before the influenza season is the most important measure for reducing the impact of influenza. Vaccination can be highly cost-effective 1) when it is aimed at persons who are most likely to experience complications or who have a higher-than-average risk for exposure and 2) when it is administered to high-risk persons during a hospitalization or routine health-care visit before the influenza season, thus making special visits to physicians' offices or clinics unnecessary. Recent reports indicate that, when vaccine and epidemic strains of virus are well matched, achieving high vaccination rates in closed populations can reduce the risk of outbreaks by inducing herd immunity. When outbreaks of influenza A occur in closed populations, they can be interrupted by chemoprophylaxis for all residents. (Additional information on chemoprophylaxis will be published in the MMWR before the 1989-90 season.) Other indications for immunization include the strong desire of any person to avoid an influenza infection, reduce the severity of disease, or reduce the chances of transmitting influenza to high-risk persons with whom they have frequent contact. INACTIVATED VACCINE FOR INFLUENZA A AND B

Influenza vaccine is made from highly purified, egg-grown viruses that have been rendered noninfectious (inactivated). Influenza vaccine contains three virus strains (two type A and one type B) representing influenza viruses recently circulating worldwide and believed likely to circulate in the United States the following winter. The composition of the vaccine is such that it causes minimal systemic or febrile reactions. Whole-virus, subvirion, and purified surface antigen preparations are available. Only subvirion or purified surface antigen preparations should be used for children to minimize febrile reactions. Subvirion, purified surface antigen, or whole- virus vaccines may be used in adults. Most vaccinated children and young adults develop high postvaccination hemagglutination-inhibition antibody titers that are likely to protect them against infection by strains like those in the vaccine and often by related variants that may emerge. 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 upper-respiratory-tract infection. Nevertheless, influenza vaccine can still be effective in preventing lower- respiratory-tract involvement or other

complications, thereby reducing the risk of hospitalization and death. RECOMMENDATIONS FOR USE OF INACTIVATED INFLUENZA VACCINE

Influenza vaccine is strongly recommended for any person greater than or equal to 6 months of age who, by virtue of age or underlying medical condition, is at increased risk for complications of influenza. It is also strongly recommended for health-care workers and others (including household members) who may have close contact with high-risk persons. In addition, influenza vaccine may be given to any other person who wishes to reduce his/her chance of becoming infected with influenza, even if that person is not at increased risk for complications.

Vaccine composition and dosages for the 1989-90 season are given in Table 1. Guidelines for the use of vaccine among different groups are given below.

Although the current influenza vaccine often contains one or more antigens used in previous years, immunity declines in the year following vaccination. Therefore, annual vaccination using the current vaccine is required. Remaining 1988-89 vaccine should not be used to provide protection for the 1989-90 influenza season.

Two doses may be required for a satisfactory antibody response in previously unvaccinated children less than or equal to 12 years of age; however, clinical studies with vaccines similar to those in current use have shown only marginal or no improvement in antibody response when a second dose is given to adults during the same season.

During the past decade, data on influenza vaccine immunogenicity and side effects have generally been obtained when vaccine has been administered intramuscularly. Because there has been no adequate evaluation of recent influenza vaccines administered by other routes, the intramuscular route should be used. 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, both the persons at risk and their close contacts should be targeted for organized vaccination programs. Groups at Increased Risk for Influenza-Related Complications

1. Adults and children with chronic disorders of the pulmonary or cardiovascular systems, including children with asthma. 2.Residents of nursing homes and other chronic-care facilities housing patients of any age with chronic medical conditions. 3.Persons greater than or equal to 65 years of age. 4.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. 5.Children and teenagers (aged 6 months-18 years) who are receiving long-term aspirin therapy and therefore may be at risk of developing Reye syndrome after an influenza infection. Groups Potentially Capable of Transmitting Influenza to High-Risk Persons

Persons attending high-risk persons can transmit influenza infections to them while they themselves are undergoing subclinical infection or working despite the existence of symptoms. Some high-risk persons (e.g., the elderly, transplant recipients, or persons with acquired immunodeficiency syndrome (AIDS)) can have relatively low antibody responses to influenza vaccine. Efforts to protect them against influenza may be improved by reducing the chances that their care providers may expose them to influenza. Therefore, the following groups should be vaccinated:

1. Physicians, nurses, and other personnel in both hospital and outpatient-care settings who have

extensive contact with high-risk patients in all age groups, including infants. 2.Providers of home care to high-risk persons (e.g., visiting nurses, volunteer workers). 3.Household members (including children) of high-risk persons. VACCINATION OF OTHER GROUPS General Population

Physicians should administer influenza vaccine to any person who wishes to reduce his/her chances of acquiring influenza infection. Persons who provide essential community services and students or other persons in institutional settings (i.e., schools and colleges) may be considered for vaccination to minimize the disruption of routine activities during outbreaks. Pregnant Women

Influenza-associated excess mortality among pregnant women has not been documented, except in the largest pandemics of 1918-19 and 1957-58. However, pregnant women who have other medical conditions that increase their risk for complications from influenza should be vaccinated, as the vaccine is considered safe for pregnant women. Administering the vaccine after the first trimester is a reasonable precaution to minimize any concern over the theoretical risk of teratogenicity. However, it is undesirable to delay vaccination of pregnant women with high-risk conditions who will still be in the first trimester of pregnancy when the influenza season begins. Persons Infected with HIV Increases in infections and complications caused by various respiratory pathogens have been observed in persons infected with HIV. However, similar increases due to influenza have not been reported during recent epidemics. Nevertheless, because influenza may result in serious illness and complications in some HIV-infected persons, vaccination is a prudent precaution. Foreign Travelers

Increasingly, the elderly and persons with high-risk medical conditions are embarking on international travel. The risk of exposure to influenza during foreign travel varies, depending on, among other factors, season of travel and destination. Influenza can occur throughout the year in the tropics; the season of greatest influenza activity in the Southern Hemisphere is April-September. Because of the short incubation period for influenza, exposure to the virus during travel will often result in clinical illness that begins during travel, 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 vaccination histories. If not vaccinated the previous fall/winter, they should be considered for influenza vaccination before travel. Persons in the high-risk categories especially should be encouraged to receive the vaccine. The most current available vaccine should be used. High-risk persons given the previous season's vaccine before travel should be revaccinated in the fall/winter with current vaccine. PERSONS WHO SHOULD NOT BE VACCINATED

Inactivated influenza vaccine should not be given to persons known to have an anaphylactic hypersensitivity to eggs (see below: Side Effects and Adverse Reactions).

Persons with acute febrile illnesses usually should not be vaccinated until their symptoms have abated. SIDE EFFECTS AND ADVERSE REACTIONS

Because influenza vaccine contains only noninfectious viruses, it cannot cause influenza. Occasional cases of respiratory disease following vaccination represent coincidental illnesses unrelated to influenza vaccination. The most frequent side effect of vaccination is soreness around the vaccination site for up to 2 days; this occurs in less than one third of vaccinees.

In addition, the following two types of systemic reactions have occurred:

1. 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. 2.Immediate, presumably allergic, reactions (such as hives, angioedema, allergic asthma, or systemic anaphylaxis) occur extremely rarely after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component--most likely residual egg protein. Although current influ- enza vaccines contain only a small quantity of egg protein, this protein is presumed capable of inducing immediate hypersensitivity reactions in persons with severe egg allergy, and such persons should not be given influenza vaccine, including persons who develop hives, have swelling of the lips or tongue, or experience acute respiratory distress or collapse after eating eggs. Persons with a documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses from occupational exposure to egg protein, may also be at increased risk for reactions from influenza vaccine.

Unlike the 1976 swine influenza vaccine, subsequent vaccines prepared from other virus strains have not been associated with an increased frequency of Guillain-Barre syndrome. Although influenza vaccination can inhibit the clearance of warfarin and theophylline, clinical studies have consistently failed to show any adverse effects attributable to these drugs in patients receiving influenza vaccine. SIMULTANEOUS ADMINISTRATION OF OTHER VACCINES, INCLUDING CHILDHOOD VACCINES

The target groups for influenza and pneumococcal vaccination overlap considerably. Both vaccines can be given at the same time at different sites without increasing side effects. However, influenza vaccine must be given annually, and with few ex ceptions, pneumococcal vaccine should be given only once.

High-risk children usually see a health professional to receive routine pediatric vaccines. These visits provide a good opportunity to administer influenza vaccine simultaneously but in a different site. Although studies have not been conducted, simultaneous administration should not diminish immunogenicity or increase adverse reactions. TIMING OF INFLUENZA VACCINATION ACTIVITIES

Influenza vaccine may be offered to high-risk persons presenting for routine care or hospitalization beginning in September but not until new vaccine is available. Except in years of pandemic influenza (e.g., 1957 and 1968), high levels of influenza activity generally do not occur in the contiguous 48 states before December. Therefore, organized vaccination campaigns in which high-risk persons are routinely accessible are optimally undertaken in November. In facilities such as nursing homes, it is particularly important to avoid administering vaccine too far in advance of the influenza season because antibody level begins to decline within a few months. Such vaccination programs may be undertaken as soon as current vaccine is available in September or October if regional influenza activity is expected to begin earlier than usual.

Children less than or equal to 12 years of age who have not been vaccinated previously should receive two doses at least 1 month apart to maximize the chance of a satisfactory antibody response to all three vaccine antigens. The second dose should be given before December, if possible. Vaccine should continue to be offered to both children and adults up to and even after influenza virus activity is documented in a community, which may be as late as April in some years. STRATEGIES FOR IMPLEMENTING INFLUENZA VACCINE RECOMMENDATIONS

Despite the recognition that optimum medical care for both adults and children includes regular review of immunization records and administration of vaccines as appropriate, in recent years, an

average of less than 30% of persons in high-risk groups have received influenza vaccine each year. More effective strategies for delivering vaccine to high-risk persons, their health-care providers, and their household contacts are clearly needed. In general, successful vaccination programs have been those that have combined education for health-care workers, publicity and education targeted toward potential recipients, a routine for identifying (usually by medical record review) persons at 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 immunized in the following settings: Outpatient Clinics and Physicians' Offices

Staff in physicians' offices, clinics, health maintenance organizations, and employee health clinics should be instructed to identify and mark the medical records of patients who should receive vaccine. Vaccine should be offered during visits beginning in September and continuing through the influenza season. Offer of vaccine and its receipt or refusal should be documented in the medical record. Patients in 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, and 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 (e.g., emergency rooms, walk-in clinics)

Health-care providers in these settings should be familiar with influenza vaccine recommendations and 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 Spanish or other language(s) appropriate for the population served by the facility. Nursing Homes and Other Residential Long-Term Care Facilities

Immunization should be routinely provided to residents of chronic-care facilities, with concurrence of physicians, rather than by procuring orders for administration of vaccine for each patient. Consent for immunization should be obtained at the time of admission to the facility, and all residents immunized at one period of time immediately preceding the influenza season. Residents admitted after completion of the vaccination program should be immunized at the time of admission during the winter months. Acute-Care Hospitals

Patients of any age in medically high-risk groups and all persons greater than or equal to 65 years of age who are hospitalized from September through March should be offered and strongly encouraged to receive vaccine before discharge. Household members and others with whom they will have contact should receive written information about reasons they should also receive influenza vaccine and places to obtain the vaccine. Outpatient Facilities Providing Continuing Care to High-Risk Patients (e.g., hemodialysis centers, hospital specialty-care clinics, outpatient rehabilitation programs)

All patients should be offered vaccine at one period of time shortly before the beginning of the influenza season. Patients admitted during the winter months after the vaccination program should be immunized at the time of admission for care. Household members should receive written information regarding need for immunization and places to obtain the vaccine. Visiting Nurses and Others Providing Home Care to High-Risk Persons

Nursing-care plans should identify high-risk patients, and vaccine should be provided in the home if necessary. Caregivers and others in the household should be referred for immunization. Facilities Providing Services to Persons greater than or equal to 65 Years of Age (e.g., retirement communities,

recreation centers) If possible, all unimmunized residents/attendees should be offered vaccine on site at one time period before the influenza season; alternatively, education/publicity programs should emphasize need for vaccine and should provide specific information on how, where, and when to obtain it. Clinics and Others Providing Health Care for Travelers

Indications for influenza vaccine should be reviewed before travel and vaccine offered if appropriate (see previous section: Vaccination for Foreign Travelers). Health-Care Workers

Administrators of all of the above facilities and organizations 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, with particular emphasis on immunization of persons caring for highest-risk patients (i.e., staff of intensive-care units (including newborn intensive- care units) and chronic-care facilities). Use of a mobile cart to take vaccine to hospital wards or other worksites, and availability of vaccine during night and weekend workshifts may enhance compliance, as may a follow-up campaign if an outbreak threatens. SOURCES OF INFORMATION ON INFLUENZA-CONTROL PROGRAMS

Educational materials about influenza and its control are available from a variety of sources, including CDC. For information on sources of educational materials, contact Technical Information Services, Center for Prevention Services, Mailstop E-07, CDC, Atlanta, GA 30333. SELECTED BIBLIOGRAPHY GENERAL

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