INFLUENZA VIRUS VACCINE (Systemic)

Category

Immunizing agent (active).

Indications

Accepted

Influenza (prophylaxis)¾Influenza virus vaccine is indicated for any person ³ 6 months of age who, because of age or underlying medical condition, is at increased risk of complications of influenza 2, 8 , including:
· Targeted high-risk children 3, 20, 21, 22.

Yearly immunization is recommended for children 6 months of age and older with one or more specific risk factors 3.

Data are insufficient regarding the potential severity of influenza in several of these groups of children; however, based on available data and knowledge of the pathophysiology of these disorders, children with the following risk factors warrant immunization:
¾Those with asthma and other chronic pulmonary diseases 3.

Influenza vaccination can be given safely and effectively to children with asthma regardless of asthma symptoms or concurrent prednisone therapy 7.

Vaccination of all patients with moderate to severe asthma who visit clinics or emergency departments would improve the overall vaccination rate significantly 7.

¾Those with hemodynamically significant cardiac disease 3.

¾Those undergoing immunosuppressive therapy 3.

¾Those with sickle-cell anemia and other hemoglobinopathies 3.

¾Other high-risk children 3.

Children who are potentially at increased risk for complicated influenza illness and who may benefit from influenza immunization are those with one or more of the following conditions 3 :
¾Human immunodeficiency virus (HIV) infection 3.

¾Diabetes mellitus 3.

¾Chronic metabolic diseases 3.

¾Recipients of long-term aspirin therapy, such as children with rheumatoid arthritis or Kawasaki disease, who may have an increased risk of developing Reye''s syndrome 3.

¾Influenza virus vaccination also may be considered for children who are marginally immunocompromised as a result of any underlying condition, since even uncomplicated influenza can have adverse effects on the course of an underlying illness 3.

¾Adults at increased risk for influenza-related complications 20, 21, 22, 28 :
¾Persons ³50 years of age 28.

¾Residents of nursing homes and other long-term care facilities that house persons of any age with chronic medical conditions 2, 5.

¾Those with chronic disorders of the pulmonary or cardiovascular systems 2, 5.

¾Those 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) 2, 5.

¾Women who will be in the second or third trimester of pregnancy during the influenza season 5.

¾Persons who can transmit influenza to others who are at high risk 2, 3, 5, 20, 21, 22.

Persons who are clinically or subclinically infected with influenza and who care for or live with members of high-risk groups can transmit influenza virus to them 2, 5.

Some persons at high risk (e.g., the elderly, transplant recipients, and persons with AIDS) can have a low antibody response to influenza vaccine 2, 5.

Efforts to protect these members of high-risk groups against influenza may be improved by reducing the likelihood of influenza virus exposure from their caregivers 2, 5.

Immunization of adults who are in close contact with children at high risk may be an important means of protecting these children, especially for infants < 6 months of age for whom vaccination is not recommended 3.

Immunization of pregnant women may be beneficial to the neonates, as well, since transplacentally acquired antibody appears to protect neonates from infection with influenza A virus 3.

Therefore, the following groups should be immunized 2, 3, 5 :
¾Physicians, nurses, and other personnel in both hospital and outpatient settings 2, 3, 5, 28.

¾Employees of nursing homes and long-term care facilities who have contact with patients or residents 2, 5, 28.

¾Providers of home care to persons at high risk (e.g., visiting nurses and volunteer workers) 2, 5, 28.

¾Household contacts of persons at high risk 2, 3, 5 , including children 2, 5 , siblings, and primary caretakers of children at high risk 2, 5.

HIV-infected children who are members of households with adults at high risk also should be immunized 2, 5.

¾General population 2, 5, 20, 21, 22.

Physicians should administer influenza virus vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza 2, 5, 28.

Persons who provide essential community services should be considered for vaccination, to minimize disruption of essential activities during influenza outbreaks 2, 5, 28.

Vaccination should be considered for groups of individuals whose close contact with each other facilitates rapid transmission of the virus infection resulting in disruption of routine activities 2, 3, 5.

Examples are students in colleges, schools, and other institutions of learning, particularly those who reside in dormitories or who are members of athletic teams, and those living in residential institutions 2, 3, 5, 28.

¾Persons infected with HIV 2, 5, 20, 21, 22, 28.

Limited information exists regarding the frequency and severity of 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 2, 5.

Influenza vaccine has produced protective antibody titers against influenza in vaccinated HIV-infected persons who have minimal AIDS-related symptoms and high CD4+ T-lymphocyte cell counts 28.

In patients who have advanced HIV infection-related disease and low CD4+ T-lymphocyte cell counts, however, influenza virus vaccine may not induce protective antibody titers; furthermore, a second dose of vaccine does not improve the immune response for these persons 28.

Recent studies have examined the effect of influenza virus vaccination on replication of HIV type 1 (HIV-1) 2, 5.

Although some studies have demonstrated a transient (i.e., 2- to 4-week) increase in replication of HIV-1 in the plasma or peripheral blood mononuclear cells of HIV-1-infected persons after vaccine administration, other studies using similar laboratory techniques have not indicated any substantial increase in replication 28.

Decline in CD4+ T-lymphocyte cell counts and progression of clinical HIV infection-related disease have not been demonstrated among HIV-infected persons who receive influenza virus vaccine 28.

Since influenza can result in serious illness and complications, and because influenza virus vaccination may result in protective antibody titers, vaccination will benefit many HIV-infected patients 28.

¾International travelers 2, 3, 5, 20, 21, 22, 28.

The risk of exposure to influenza during foreign travel varies, depending on the season and destination 2, 5.

In the tropics, influenza outbreaks can occur throughout the year; in the southern hemisphere, most outbreaks occur between April and September 2, 5, 28.

Because of the short incubation period for influenza, exposure to the virus during travel can result in clinical illness that begins while traveling, which could be an inconvenience or a potential danger, especially for persons at increased risk for complications 2, 5.

Persons preparing to travel to the tropics at any time of the year or to the southern hemisphere from April through September should review their influenza vaccination histories 2, 5, 28.

If they were not vaccinated during the previous fall or winter, they should consider receiving influenza vaccination before travel 28.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Source¾Each year's influenza vaccine contains three virus strains (usually two type A strains and one type B strain) representing the influenza viruses that are likely to circulate in the U.S. in the upcoming winter 2, 5.

The vaccine is made from highly purified, egg-grown viruses that have been made noninfectious (inactivated) 2, 5.

Whole-virus, subvirion, and purified-surface-antigen preparations are available 2, 5.

In collaboration with the World Health Organization (WHO), its international network of collaborating laboratories, and state and local health departments, the Centers for Disease Control and Prevention (CDC) conducts surveillance to monitor influenza activity and detect antigenic changes in the circulating strains of influenza viruses 1, 10, 11, 13.

Mechanism of action/Effect:

Humoral defenses against influenza infection are mainly conferred by serum and local immune globulin G (IgG) and immune globulin A (IgA) antibodies to the surface glycoproteins, hemagglutinin (H) and neuraminidase (N) 17.

Anti-H antibodies inhibit the attachment of the influenza virus to target cell membrane receptors and thus neutralize viral infectivity 17.

Depending on their concentration, these antibodies can either provide complete protection from the acquisition of infection or prevent the development of serious illness 17.

Protection studies have indicated that an anti-H antibody titer of ³ 40 is the protection threshold beyond which serious illness is unlikely to develop 17.

Protective effect

Most vaccinated children and young adults develop high titers of postvaccination hemagglutinin-inhibition (HI) antibody 2.

These antibodies protect the individual against illness caused by strains similar to those in the vaccine 2.

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 2.

However, even if such persons develop influenza illness despite vaccination, the vaccine can be effective in preventing lower respiratory tract involvement or other complications, thereby reducing the risks of hospitalization and death 2.

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 2.

When there is a good match between the vaccine and circulating viruses, influenza virus vaccine has been shown to prevent illness in approximately 70% of healthy persons < 65 years of age 2.

In these circumstances, studies have also indicated that the effectiveness of influenza virus vaccine in preventing hospitalization for pneumonia and influenza among elderly persons living in settings other than nursing homes or similar long-term care facilities ranges from 30 to 70% 2.

Among elderly persons residing in nursing homes, influenza virus vaccine is very effective in preventing severe illness, secondary complications, and death 2.

Studies in this population have indicated that the vaccine can be 50 to 60% effective in preventing hospitalization and pneumonia, and 80% effective in preventing death, even though the vaccine's efficacy in preventing influenza illness may only be in the range of 30 to 40% among the frail elderly 2.

Achieving a high rate of vaccination among nursing home residents can reduce the spread of infection in a facility, thus preventing disease through herd immunity 2.

Duration of protective effect

Since the antigenic properties of influenza virus surface antigens frequently change, the vaccine-induced protective immunity is short-lived 17.

For this reason, health authorities recommend annual revaccination of persons at risk, using influenza virus vaccines containing the expected epidemic strains for the next season 17.

Precautions to Consider

Pregnancy/Reproduction

Pregnancy¾Influenza-associated excess mortality among pregnant women has not been documented except during the pandemics of 1918-19 and 1957-58 5.

However, because death-certificate data often do not indicate whether a woman was pregnant at the time of death, studies conducted during interpandemic periods may underestimate the impact of influenza in this population 5.

Case reports and limited studies suggest that pregnancy may increase the risk of serious medical complications of influenza, as a result of increases in heart rate, increases in stroke volume and oxygen consumption, decreases in lung capacity, and changes in immunologic functions 5.

A recent study of the impact of influenza during 17 interpandemic influenza seasons documented that the relative risk of hospitalization for selected cardiorespiratory conditions among pregnant women increased from 1.4 during weeks 14 to 20 of gestation to 4.7 during weeks 37 to 42, as compared with rates among women who were 1 to 6 months postpartum 5.

Women in their third trimesters of pregnancy were hospitalized at a rate comparable to that of nonpregnant women with high-risk medical conditions for whom influenza virus vaccine has traditionally been recommended 5.

Using data from this study, it was estimated that an average of 1 to 2 hospitalizations among pregnant women could be prevented for every 1000 pregnant women immunized 5.

On the basis of these and other data suggesting that influenza infection may cause increased morbidity in women during the second and third trimesters of pregnancy, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) recommends that women who will be beyond the first trimester of pregnancy (14 weeks of gestation) during the influenza season be vaccinated 5.

Pregnant women who have medical conditions that increase the risk of complications from influenza should be vaccinated before the influenza season, regardless of the stage of pregnancy 5.

Studies of influenza immunization of more than 2000 pregnant women have demonstrated no adverse fetal effects associated with influenza virus vaccine; however, more data are needed 5.

Because influenza virus vaccine is not a live virus vaccine and major systemic reactions are rare, many experts consider influenza vaccination safe during any stage of pregnancy 5.

However, because spontaneous abortion is common in the first trimester and unnecessary exposures have traditionally been avoided during this time, some experts prefer influenza vaccination during the second trimester to avoid coincidental association of the vaccine with early pregnancy loss 5.

Studies have not been done in animals 20, 21, 22.

FDA Pregnancy Category C [20], [21], [22].

Breast-feeding

Influenza vaccine does not affect the safety of breast-feeding for mothers or infants [5].

Breast-feeding does not adversely affect the immune response and is not a contraindication for vaccination [5].

Pediatrics

In immunosuppressed children receiving chemotherapy, influenza immunization with a new vaccine antigen results in a sufficient immune response in only a minority of children [3].

The optimal time to immunize children with malignancies who still must undergo chemotherapy is 3 to 4 weeks after chemotherapy has been discontinued and the peripheral granulocyte and lymphocyte counts are greater than 1000 per cubic millimeter [3].

Children who are no longer receiving chemotherapy generally have high rates of seroconversion [3].

The immune response and safety of influenza vaccine in children with hemodynamically unstable cardiac disease (another large group of children potentially at high risk for complications of influenza) are comparable to those in healthy children [3].

The effect of corticosteroid therapy on influenza vaccine immunogenicity is unknown [3].

Since a high dose of corticosteroids (i.e., a dose equivalent to either 2 mg per kg of body weight or a total of 20 mg per day of prednisone) may impair antibody responses, particularly in unvaccinated or previously uninfected persons, vaccination may be deferred temporarily during high-dose corticosteroid therapy, provided deferral does not compromise the likelihood of immunization before the start of the influenza season [3].

Corticosteroid therapy should not unnecessarily delay the administration of influenza vaccine, particularly in children with asthma who require intermittent or maintenance corticosteroid therapy [3].

Infants younger than 6 months of age with high-risk conditions, especially those with compromised cardiopulmonary function may have the same or greater risk from influenza complications as of older children [3].

However, no information is available about the reactivity, immunogenicity, or the efficacy of the influenza vaccine in infants during the first 6 months of life [3].

In addition, the effect of influenza antigens in an inactivated vaccine on the infant's future immune response to influenza is unknown [3].

Therefore, alternative methods of protection for young infants should be considered [3].

Children and young adults with cystic fibrosis (CF) will benefit from annual influenza vaccination [6].

In a 10-year observational study with a cohort design of 38 children and young adults with CF, serum hemagglutinin-inhibition (HI) antibody titers were determined at the time of vaccination, and 4 weeks later each year in the fall before the influenza epidemic 6.

While the prevaccination and postvaccination geometric mean serum HI antibody titers varied from year to year, no upward or downward trend was evident over the 10-year period 6.

In addition, the majority of vaccinees had a presumably protective postvaccination serum HI titer ³ 1:40 each year for all three vaccine strains 6.

In children with little previous experience with influenza, two doses of vaccine, administered 1 month apart, are necessary to produce a satisfactory antibody response 3.

Children previously primed with a related strain of influenza virus by infection or vaccination almost uniformly exhibit a brisk antibody response to one dose of the vaccine 3.

Only the subviron or purified surface-antigen vaccines, i.e., those termed "split-virus" vaccines, should be used for children younger than 12 years of age 23.

Geriatrics

Although influenza vaccine reportedly provides 65 to 85% protection against influenza illness in young, healthy adults, studies of its effectiveness in high-risk groups, such as the elderly, have yielded inconsistent results 13.

In observational studies of high-risk patients, respiratory illness during influenza epidemics occurred often, despite vaccination 13.

A review of studies of influenza vaccination in nursing homes disclosed that the median protective effect in 16 outbreaks of influenza A was 26%, and it was only 19% in seven studies of influenza B outbreaks 13.

Among noninstitutionalized elderly persons, the number of medical care visits for upper respiratory illnesses during two influenza outbreaks was the same for those who had received influenza vaccine and those who had not 13.

Despite the apparent ineffectiveness of influenza vaccination in preventing respiratory infection, other nonrandomized studies have shown that it reduces serious complications and mortality due to influenza in the elderly or chronically ill 13.

In nursing homes, for example, significant reductions in pneumonia and mortality among vaccinees were documented during influenza A outbreaks 13.

Among noninstitutionalized elderly persons, compelling evidence for the effectiveness of influenza vaccine comes from retrospective studies of more than 10,000 elderly members of a prepaid health plan during four influenza epidemics from 1968 to 1981 13.

Hospitalizations and deaths from influenza and pneumonia among elderly vaccinees with chronic illnesses were reduced by more than 70% during two of these outbreaks 13.

Healthy elderly persons who received the vaccine also had fewer hospitalizations and deaths than their unvaccinated counterparts, although the differences were not statistically significant 13.

During a third epidemic in which there was pronounced antigenic drift, a statistically insignificant trend toward protection against hospitalization and death among vaccine recipients was observed 13.

Antigenic shift to a subtype different from that in the vaccine occurred during the fourth epidemic studied, and no protection from vaccination was observed 13.

More recently, several case-control studies during the influenza seasons from 1989 to 1992 showed that influenza vaccination was 31 to 45% effective in preventing hospitalizations for pneumonia 13.