VIRGINIA
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Prevention and Control of Influenza

Recommendations of the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service*

These recommendations update information on the vaccine and antiviral agents available for controlling influenza during the 1992-1993 influenza season. The primary changes include statements about vaccination of persons with known hypersensitivity to eggs or other components of the influenza vaccine, the optimal timing of influenza vaccination, and the influenza strains in the trivalent vaccine for 1992-1993.

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, 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 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 strains currently circulating provide the basis for selecting virus strains to include in each year's vaccine.

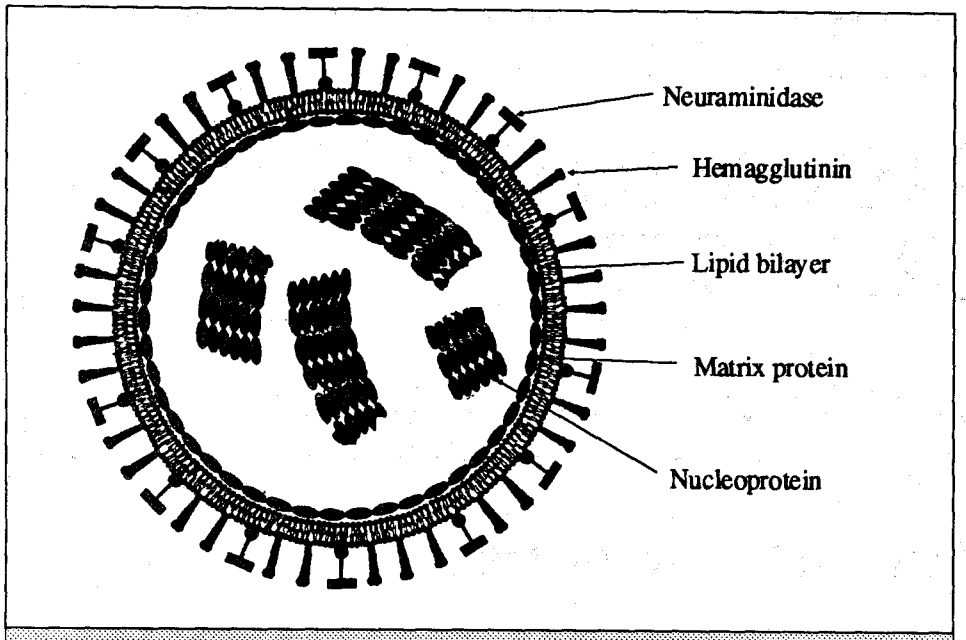
Typical influenza illness is characterized by abrupt onset of fever, myalgia, sore throat, and nonproductive cough. Unlike other common respiratory infections, influenza can cause severe malaise lasting several days. More severe illness can result if primary influenza pneumonia or secondary bacterial pneumonia occur. During influenza epidemics, high attack rates of acute illness result in 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 infection. If infected, such high-risk persons or groups (listed as "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 high-risk persons may increase 2- to 5-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 infection. It is estimated that more than 10,000 excess deaths occurred during each of seven different U.S. epidemics in the period 1977-1988, and more than 40,000 excess deaths occurred during each of two of these epidemics. Approximately 80%-90% of the deaths attributed to pneumonia and influenza occurred among persons ≥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 influ-

In This Issue:



Schematic diagram of an influenza virus (size ~150 nm).
Adapted from Choppin PW. Influenza: the agent. Hosp Pract 1977;(2):137-145.

enza illness, the toll from influenza can be expected to increase unless control measures are administered more vigorously. The number of younger persons at increased risk for influenza-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 acquired immunodeficiency syndrome (AIDS), and better survival rates for organ-transplant recipients.

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 (e.g., amantadine). Vaccination of high-risk persons 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 high-risk persons during hospitalization or a 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 among closed populations can reduce the risk of outbreaks by inducing herd immunity.

Other indications for vaccination include the strong desire of any person to avoid influenza infection, reduce the severity of disease, or reduce the chance of transmitting influenza to high-risk persons with whom the individual has frequent contact.

The antiviral agent available for use at this time (amantadine hydrochloride) is effective only against influenza A and, for maximum effectiveness as prophylaxis, must be administered throughout the period of risk. When administered as either prophylaxis or therapy, the potential effectiveness of amantadine must be balanced against potential side effects.

Chemoprophylaxis is not a substitute for vaccination. Recommendations for chemoprophylaxis are provided primarily to help health-care providers make decisions regarding persons who are at greatest risk of severe illness and complications if infected with an influenza A virus. Use of amantadine may be considered a) as a control measure when influenza A outbreaks occur in institutions housing high-risk persons, both for treatment of ill individuals and as prophylaxis for others; b) as short-term prophylaxis after late vaccination of high-risk persons (i.e., when influenza A infections are already occurring in the community) during the period when immunity is developing in response to vaccination; c) as seasonal prophylaxis for persons for whom vaccination is contraindicated; d) as seasonal prophylaxis for immunocompromised persons who may not produce protective levels of antibody in response to vaccination; and e) as prophylaxis for unvaccinated health-care workers and household contacts who care for high-risk persons either for the duration of influenza activity in the community or until immunity develops after vaccination.

Amantadine is also approved for use by any person who wishes to reduce his or her chances of becoming ill with influenza A.

Inactivated Vaccine for Influenza A and B

Influenza vaccine is made from highly purified, egg-grown viruses that have been rendered noninfectious (inactivated). Therefore, the vaccine cannot cause influenza. Each year's influenza vaccine contains three virus strains (usually two type A and one type B) representing influenza viruses believed likely to circulate in the United States in the upcoming winter. The composition of the vaccine is such that it 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 infection 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 upper-respiratory-tract infection. Nevertheless, even if such persons develop influenza illness, the vaccine has been shown to be effective in preventing lower-respiratory tract involvement or other complications, thereby reducing the risk of hospitalization and death.

Recommendations for Use of Influenza Vaccine

Influenza vaccine is strongly recommended for any person ≥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 high-risk persons 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 1992-1993 season will include A/Texas/36/91-like (H1N1), A/Beijing/353/89-like (H3N2), and B/Panama/45/90-like hemagglutinin antigens.

Table 1. Influenza vaccine* dosage, by age group, United States, 1992-93 season

Age group	Product	Dosage	No. doses	Route*
6-35 mos.	Split virus only	0.25 mL	1 or 2	IM
3-8 yrs.	Split virus only	0.50 mL	1 or 2	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 µg each of A/Texas/36/91-like (H1N1), A/Beijing/353/89-like (H3N2), and B/Panama/45/90-like hemagglutinin antigens in each 0.5 mL. Manufacturers include: Connaught Laboratories, Inc. (distributed by E.R. Squibb & Sons, Inc.) (Fluzone® whole or split); Evans Medical Ltd.-Lederle Laboratories (distributed by Lederle Laboratories) (Flu-Imune® purified surface antigen vaccine); Parke-Davis (Fluogen® split); and Wyeth-Ayerst Laboratories (Influenza Virus Vaccine, Trivalent® split). For further product information call Connaught, (800) 822-2463; Lederle, (800) 533-3753; Parke-Davis, (800) 223-0432; Wyeth-Ayerst, (800) 950-5099.*

†Because of the lower potential for causing febrile reactions, only split-virus vaccines should be used among 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.

§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.

¶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.

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 antigens administered in previous years, annual vaccination using the current vaccine is necessary because immunity for a person declines in the year following vaccination. Because the 1992-1993 vaccine differs from the 1991-1992 vaccine, supplies of 1991-1992 vaccine should not be administered to provide protection for the 1992-1993 influenza season.

Two doses administered at least 1 month apart may be required for a satisfactory antibody response 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 when vaccine has been administered intramuscularly. Because there has been no adequate evaluation of recent influenza vaccines administered by other routes, the intramuscular route is recommended for use. 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:

1. Persons ≥65 years of age.
2. Residents of nursing homes and other chronic-care facilities housing persons of any age with chronic medical conditions.
3. Adults and children with chronic disorders of the pulmonary or cardiovascular systems, including children with asthma.
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 (including immunosuppression caused by medications).
5. Children and teenagers (6 months-18 years of age) who are receiving long-term aspirin therapy, and therefore may be at risk of developing Reye syndrome after influenza.

Groups That Can Transmit Influenza to High-Risk Persons:

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

1. Physicians, nurses, and other personnel in both hospital and outpatient-care settings who have contact with high-risk persons among all age groups, including infants.
2. Employees of nursing homes and chronic-care facilities who have contact with patients or residents.
3. Providers of home care to high-risk persons (e.g., visiting nurses, volunteer workers).
4. 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 the chance of acquiring influenza infection. Persons who provide essential community services may be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Similarly, students or other persons in institutional settings such as those who reside in dormitories may be considered for vaccination 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 1918-1919 and 1957-1958. However, pregnant women who have other medical conditions that increase their risks 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 who have high-risk conditions and who will still be in the first trimester of pregnancy when the influenza season begins.

Persons Infected with HIV. Little information exists regarding the frequency and severity of influenza illness among human immunodeficiency virus (HIV)-infected persons, but recent reports suggest that symptoms may be prolonged and the risk of complications increased for HIV-infected persons. Because influenza may 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 has not improved the immune response for these individuals.

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 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 also 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 among the high-risk categories should be especially encouraged to receive the most currently available vaccine. High-risk persons administered 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). Amantadine hydrochloride 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 infections may benefit from vaccine after appropriate allergy evaluation and desensitization. Specific information about vaccine components can be found in warnings and contraindications in package inserts for each manufacturer.

It is usually preferable to delay vaccination of adults with acute febrile illnesses until their symptoms have abated. However, minor illnesses with or without fever should not contraindicate the use of influenza vaccine, particularly among children with a mild upper respiratory tract infection or allergic rhinitis (see American Academy of Pediatrics, *The Red Book*, 1991).

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 is soreness at the vaccination site that lasts for up to 2 days; this is reported for less than one-third of vaccinees. 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 (such as hives, angioedema, allergic asthma, or systemic anaphylaxis) occur rarely after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component; the majority 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 experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to assist in determining whether vaccination may proceed or should be deferred. Persons with documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses from 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 infection or its complications (See Murphy and Strunk, 1985).

Unlike the 1976 swine influenza vaccine, subsequent vaccines prepared from other virus strains have not been clearly associated with an increased frequency of Guillain-Barré syndrome. Although influenza vaccination can inhibit the clearance of warfarin and theophylline, studies have failed to show any adverse clinical effects attributable to these drugs among patients receiving influenza vaccine.

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

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 generally administered only once to all but those at highest risk of fatal pneumococcal disease (reference ACIP statement, MMWR 1989;38:64-8, 73-6).

Children at high risk for influenza-related complications may receive influenza vaccine at the same time as measles-mumps-rubella, Haemophilus b, pneumococcal, and oral polio vaccines. Vaccines should be administered at different sites on the body. Influenza vaccine should not be administered within 3 days of vaccination with pertussis vaccine.

Timing of Influenza Vaccination Activities

Beginning each September, when vaccine for the upcoming influenza season becomes available, high-risk persons 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 high-risk persons usually is the period between mid-October and mid-November. In the United States influenza activity generally peaks between late December and early March, and high levels of influenza activity infrequently occur in the contiguous 48 states before De-

cember. 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 previously been vaccinated should receive two doses of vaccine at least a month apart to maximize the chance 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, 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, <30% of persons among high-risk groups receive influenza vaccine each year. More effective strategies are needed for delivering vaccine to high-risk persons, their health-care providers, and their 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 below.

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 (e.g., emergency rooms, walk-in clinics). Health-care providers in these settings should be familiar with influenza vaccine recommendations. They should offer vaccine to persons among 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 ≥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 High-Risk Patients (e.g., hemodialysis centers, hospital specialty-care clinics, outpatient rehabilitation programs). All patients should be offered vaccine in one period shortly before the beginning of the influenza season. Patients admitted to such 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 High-Risk Persons. Nursing-care plans should identify high-risk patients, 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 ≥65 Years of Age (e.g., retirement communities, recreation centers). All unvaccinated residents/attendees should be offered vaccine on site at one time period before the influenza season; alternatively, education/publicity programs should emphasize the need for influenza 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 vaccination should be reviewed before travel and vaccine 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, with particular emphasis on vaccination of persons who care for high-risk persons (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 if an outbreak occurs in the community.

Antiviral Agents for Influenza A Viruses

The two antiviral agents with specific activity against influenza A viruses are amantadine hydrochloride and rimantadine hydrochloride. Only amantadine is licensed for use in the United States. These chemically related drugs interfere with the replication cycle of type A (but not type B) influenza viruses, although the specific mechanisms of their antiviral activity are not completely understood. When administered prophylactically to healthy young adults or children in advance of and throughout the epidemic period, amantadine is approximately 70%-90% effective in preventing illnesses caused by naturally occurring strains of type A influenza viruses. When administered to otherwise healthy young adults and children for symptomatic treatment within 48 hours after the onset of influenza illness, amantadine has been shown to reduce the duration of fever and other systemic symptoms and may permit a more rapid return to routine daily activities. Since antiviral agents taken prophylactically may prevent illness but not subclinical infection, some persons who take these drugs may still develop immune responses that will protect them

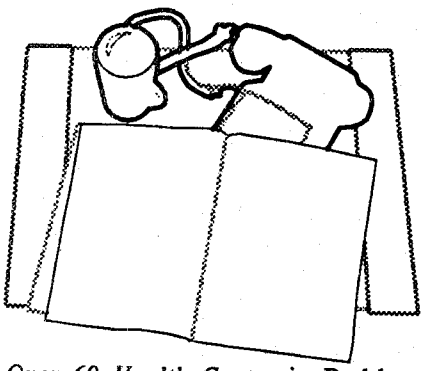
when exposed to antigenically related viruses in later years.

As with all drugs, symptoms may occur that are side effects of amantadine among a small proportion of persons. Such symptoms are rarely severe, but may be important for some categories of patients.

Staff Changes in Epidemiology

Amy Bloom, MD, has completed her two-year assignment by the Centers for Disease Control (CDC) to the VDH Office of Epidemiology. We wish her the best as she continues her training in a preventive medicine residency at CDC.

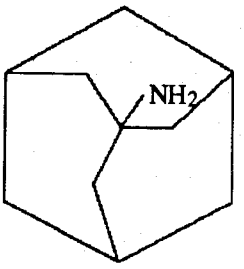
Taking her place is Elizabeth Barrett, DMD, MSPH. Dr. Barrett received her BA from Regis College and her DMD from Tufts University in 1981. From 1981 to 1982 she was a resident in general dental practice at the University of California at San Francisco. From 1982 to 1987 she was a dentist with the U.S. Public Health Service in Oakland and Galena. From 1987 to 1989 she was the dental director for the



Over 60 Health Center in Berkley, California. From 1989 to 1992 she was both a fellow in dental geriatrics at the Denver VA Medical Center and an Assistant Clinical professor at the University of Colorado School of Dentistry. Dr. Barrett has completed the Epidemic Intelligence Service course in Epidemiology at CDC and now joins the Office of Epidemiology where she will be working on investigations and surveillance projects during her two-year assignment. Please call her with any questions, concerns, or situations that might warrant her investigative attention. She can be reached at (804) 786-6261.

Recommendations for the Use of Amantadine

Outbreak Control in Institutions. When outbreaks of influenza A occur in institutions that house high-risk persons, chemoprophylaxis should begin as early as possible to reduce the spread of the infection. Contingency planning is needed to ensure rapid administration of amantadine to residents and employees. This should include preapproved medication orders or plans to obtain physicians' orders on short notice. When amantadine is used for outbreak control, it should be administered to all residents of the affected institution regardless of whether they received influenza vaccine the previous fall. The dose for each resident should be determined after consulting the dosage recommendations and precautions that follow in this document and those listed in the manufacturer's package insert. To reduce spread of virus and to minimize disruption of patient care, chemoprophylaxis should also be offered to unvaccinated staff who provide care to high-risk persons. To be fully effective as prophylaxis, the antiviral drug must be taken each day for the duration of influenza activity in the community.



Amantadine

Use as Prophylaxis

High-risk persons vaccinated after influenza A activity has begun. High-risk persons can still be vaccinated after an outbreak of influenza A has begun in a community. However, the development of antibodies in adults after vaccination usually takes 2 weeks, during which time amantadine should be administered. Children who receive influenza vaccine for the first time may require up to 6 weeks of prophylaxis, or until 2 weeks after the second dose of vaccine has been received. Amantadine does not interfere with the antibody response to the vaccine.

Persons providing care to high-risk persons. To reduce the spread of virus and to maintain care for high-risk persons in the home, hospital, or institutional setting, chemoprophylaxis should be considered for unvaccinated persons who have frequent contact with high-risk persons in the home setting (e.g., household members, visiting nurses, volunteer workers) and unvaccinated employees of hospitals, clinics, and chronic-care facilities. For employees who cannot be vaccinated, chemoprophylaxis should be continued for the entire period influenza A virus is circulating in the community; for those who are vaccinated at a time when influenza A is present in the community, chemoprophylaxis should be administered for 2 weeks after vaccination. Prophylaxis should be considered for all employees, regardless of their vaccination status, if the outbreak is caused by a variant strain of influenza A that is not covered by the vaccine.

Immunodeficient persons. Chemoprophylaxis may be indicated for high-risk persons who are expected to have a poor antibody response to influenza vaccine. This includes many persons with HIV infection, especially those with advanced disease. No data are available on possible interactions with other drugs used in the management of patients with HIV infection. Such patients must be monitored closely if amantadine is administered.

Persons for whom influenza vaccine is contraindicated. Chemoprophylaxis throughout the influenza season may be appropriate for high-risk persons for whom influenza vaccine is contraindicated because of anaphylactic hypersensitivity to egg protein or other vaccine components.

Other persons. Amantadine can also be administered prophylactically by anyone who wishes to avoid influenza A illness. This decision should be made by the physician and patient on an individual basis.

Use as Therapy

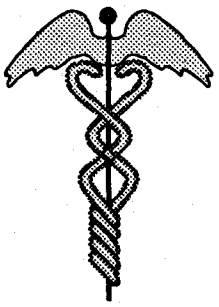
Amantadine can reduce the severity and shorten the duration of influenza A illness among healthy adults. However, there are no data on the efficacy of amantadine therapy in preventing complications of influenza A among high-risk persons. Therefore, no specific recommendations can be made regarding the therapeutic use of amantadine for these patients. This does not preclude physicians' using amantadine for high-risk patients who develop illness compatible with influenza during a period of known or suspected influenza A activity in the community. Whether amantadine is effective when treatment begins beyond the first 48 hours of illness is not known.

Other Considerations for the Selection of Amantadine for Prophylaxis or Treatment

Side Effects/Toxicity. When amantadine is administered to healthy young adults at a dose of 200 mg/day, minor central-nervous-system (CNS) side effects (nervousness, anxiety, insomnia, difficulty concentrating, and lightheadedness) or gastrointestinal side effects (anorexia and nausea) occur among approximately 5%-10% of patients. Side effects diminish or cease soon after discontinuing use of the drug. With prolonged use, side effects may also diminish or disappear after the first week of use. More serious but less frequent CNS-related side effects (seizures, confusion) associated with use of amantadine have usually affected only elderly persons, those with renal disease, and those with seizure disorders or other altered mental or behavioral conditions. Reducing the dosage to ≤100mg/day appears to reduce the frequency of these side effects among such persons without compromising the prophylactic effectiveness of amantadine.

The package insert should be reviewed before use of amantadine for any patient. The patient's age, weight, renal function, presence of other medical conditions, and indications for use of amantadine (prophylaxis or therapy) must be considered, and the dosage and duration of treatment adjusted appropriately. Modifications in dosage may be required for persons with impaired renal function, the elderly, children, persons who have neuropsychiatric disorders or who take psychotropic drugs, and persons with a history of seizures.

Development of Drug-Resistant Viruses. Amantadine-resistant influenza viruses can emerge when amantadine is administered for treatment. The frequency with which resistant isolates emerge and the extent of their transmission are unknown, but there is no evidence that amantadine-resistant viruses are more virulent or more transmissible than amantadine-sensitive viruses. Thus the use of amantadine remains an appropriate outbreak-control measure. In closed populations such as nursing homes, persons with influenza who are treated with amantadine should be separated, if possible, from asymptomatic persons who are administered amantadine as prophylaxis. Because of possible induction of amantadine resistance, it is advisable to discontinue amantadine treatment of persons who have influenza-like illness as soon as clinically warranted, generally within 3-5 days. Isolation of influenza viruses from persons who are receiving amantadine should be reported through state health departments to CDC and the isolates saved for antiviral sensitivity testing.



Sources of Information on Influenza-Control Programs

Educational materials about influenza and its control are available from several sources, including the CDC. Information can be obtained from Information Services, National Center for Prevention Services, Mailstop E06, CDC, Atlanta, GA 30333 Phone number: (404) 639-1819. State and local health departments should also be consulted regarding availability of vaccine and access to vaccination programs.

** Adapted from MMWR 1992;41:1-17.*

E. coli O157:H7 in Central Virginia

There has been an unusually high number of children in the Richmond area that have experienced severe gastroenteritis during the past month, June 15 - July 15, 1992. A number of children who became ill had *Escherichia coli* O157:H7 isolated from their stools. The ages have ranged from 22 months to 19 years and both males and females have been affected. Three of the suspected cases have resulted in hemolytic-uremic syndrome (HUS), a serious complication associated with *E. coli* O157:H7 infection.

The symptoms of infection with this pathogen include severe abdominal cramping and bloody or nonbloody diarrhea, with little or no fever. If vomiting occurs it is usually later in the course of the disease.

Transmission of this organism is primarily through food, although person-to-person contact and contaminated water have been implicated in some outbreaks. Foodborne outbreaks have been primarily associated with undercooked ground beef; poorly-cooked roast beef and dairy products have also been suspected.

Testing for this *E. coli* is not done in very many laboratories across the state so there are very likely to be more cases that are not being identified. In order to isolate the organism from stools, the sample should be obtained within 5-6 days of onset of illness and plated on sorbitol-MacConkey agar (regular MacConkey agar is not differential for this organism). *E. coli* O157:H7 ferments sorbitol slowly so colonies appear sorbitol-negative at 24 hours. Suspected sorbitol-negative colonies must be confirmed using commercial antiserum.

If your local laboratory isolates a sorbitol-negative *E. coli*, 5 to 6 colony isolates should be sent to the State Laboratory for confirmatory group typing. If the laboratory that you use is unable to screen for *E. coli* O157:H7, a stool sample from a patient with suspected infection can be sent, in Cary-Blair transport media, to the State Laboratory for culturing (if your lab does not have the necessary shipping containers and request forms, they should call the Enteric Bacteriology laboratory at 804/786-5147).

We would appreciate hearing about any suspected cases of *E. coli* O157:H7 infection, including secondary hemolytic uremic syndrome; this would assist us in our investigation of possible sources of exposure (contact Dr. Elizabeth Barrett, Assistant State Epidemiologist, at 804/786-6261).

Cases of Selected Notifiable Diseases, Virginia, July 1 through July 31, 1992.

Disease	Total Cases Reported This Month						Total Cases Reported to Date in Virginia		
		Regions							
	State	NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	70	8	18	6	15	23	395	416	275
Campylobacteriosis	85	13	16	9	28	19	352	307	321
Gonorrhea~	1542	-	-	-	-	-	10568	9915	9007
Hepatitis A	7	0	3	0	1	3	61	107	174
Hepatitis B	16	2	3	2	2	7	108	120	174
Hepatitis NANB	5	0	1	0	0	4	25	22	34
Influenza	0	0	0	0	0	0	122	689	1390
Kawasaki Syndrome	2	0	2	0	0	0	12	19	14
Legionellosis	0	0	0	0	0	0	10	7	6
Lyme Disease	36	7	11	11	0	7	60	58	32
Measles	3	0	3	0	0	0	14	28	53
Meningitis, Aseptic	28	4	8	3	3	10	115	153	101
Meningitis, Bacterial*	6	3	0	2	0	1	76	76	95
Meningococcal Infections	3	0	0	0	1	2	38	26	39
Mumps	5	0	3	0	0	2	38	43	71
Pertussis	2	1	1	0	0	0	6	16	19
Rabies in Animals	27	13	7	4	0	3	178	162	182
Reye Syndrome	0	0	0	0	0	0	0	2	1
Rocky Mountain Spotted Fever	4	0	2	0	1	1	5	6	7
Rubella	0	0	0	0	0	0	0	0	3
Salmonellosis	111	9	22	16	33	31	473	669	709
Shigellosis	26	17	5	1	3	0	111	232	189
Syphilis (1° & 2°)~	78	0	5	11	10	52	473	536	365
Tuberculosis	33	0	0	2	17	14	178	218	222

Localities Reporting Animal Rabies: Alexandria 1 raccoon; Augusta 1 raccoon; Clarke 1 raccoon; Fairfax 2 bats, 1 raccoon; Franklin 1 raccoon; Greene 1 skunk; King and Queen 1 cat; King William 1 raccoon; Loudoun 1 fox, 2 raccoons; Rappahannock 2 raccoons; Roanoke 1 goat; Roanoke City 1 cat, 1 raccoon; Rockbridge 1 bat; Rockingham 1 horse, 1 raccoon, 2 skunks; Shenandoah 1 raccoon; Spotsylvania 1 cat; Warren 1 fox; York 1 raccoon.

Occupational Illnesses: Asbestosis 12; Carpal Tunnel Syndrome 30; Coal Workers' Pneumoconiosis 6; Loss of Hearing 7.

~Total now includes military cases to make the data consistent with reports of the other diseases.

*Other than meningococcal

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