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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 the1990-1991 influenza season (superseding both the MMWR 1988;37:361-73 on antiviral agents and MMWR 1989;38:297-8, 303-11on the use of influenza vaccine). Changes include statements about a) the influenza strains in the trivalent vaccine for 1990-1991 and b) revised recommendations for the use of antiviral agents for controlling outbreaks of influenza.

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 are more likely than the general population to require hospitalization. During major epidemics, hospitalization rates for high-risk adults may increase two- to fivefold, 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

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diseases that can be exacerbated by influenza infection. At least 10,000 excess deaths have been documented in each of 19 different U.S. epidemics in the period 1957-1986; greater than 40,000 excess deaths occurred in each of three of these 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. 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 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

Two measures available in the United States that can reduce the impact of influenza are 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 used throughout the period of risk. When used 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 individuals (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 individuals for whom vaccination is contraindicated; d) as seasonal prophylaxis for immunocompromised individuals 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 individuals 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 that 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 greater than or equal to 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 given to any person who wishes to reduce the chance of becoming infected with influenza.

The trivalent influenza vaccine prepared for the 1990-1991 season will include A/Taiwan/1/86-like (H1N1), A/

Shanghai/16/89-like (H3N2), and B/Yamagata/16/88-like hemagglutinin antigens. Recommended doses are listed in Table 1.Guidelines for the use of vaccine in different groups follow.

Although the current influenza vaccine can contain one or more antigens used in previous years, annual vaccination using the current vaccine is necessary because immunity for an individual declines in the year following vaccination. Because the 1990-1991 vaccine differs from the 1989-1990 vaccine, supplies of 1989-1990 vaccine should not be used to provide protection for the 1990-1991 influenza season.

Two doses may be required for a satisfactory antibody response in previously unvaccinated children less than 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 given 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 the one 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 greater than or equal to 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 in 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 and students or other persons in institutional settings (e.g., 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 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

TABLE 1. Influenza vaccine* dosage, by patient age — United States, 1990-1991 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 yrs.	Whole or split virus	0.50 mL	1	IM

*Contains 15μg each of A/Taiwan/1/86-like (H1N1), A/Shanghai/16/89 (H3N2), and B/Yamagata/16/88-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 in children ("split virus" refers to viruses that have been chemically treated to reduce the level of potentially pyrogenic components). They may be labeled as "split," "subvirion," or "purified-surface-antigen" vaccine. Immunogenicity and side effects of split- and whole-virus vaccines are similar in adults when vaccines are used 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 are recommended for children <9 years of age who are receiving influenza vaccine for the first time.

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 in human immunodeficiency virus(HIV)-infected persons, but recent reports suggest that symptoms may be prolonged and the risk of complications increased for this high-risk group. 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/winter, they should consider influenza vaccination before travel. Persons in the high-risk categories should be especially encouraged to receive the most currently available vaccine. 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 anaphylactic hypersensitivity to eggs (see "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. 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: 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 rarely after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component--most likely residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein presumably induces immediate hypersensitivity reactions in 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 not be given the influenza vaccine. 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. 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 associated with an increased frequency of Guillain-Barre 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 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 each year; with few exceptions, pneumococcal vaccine should be given only once.

High-risk children may receive influenza vaccine at the same time as measles-mumps-rubella, Haemophilus b, pneumococcal, and oral polio vaccines. Vaccines should be given at different sites. Influenza vaccine should not be given 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 hospitalized or who are seen by health-care providers for routine care should be offered influenza vaccine. Except in years of pandemic influenza (e.g., 1957 and 1968), high levels of influenza activity rarely occur in the contiguous 48 states before December.

Therefore, November is the optimal time for organized vaccination campaigns for high-risk persons. In facilities such as nursing homes, it is particularly important to avoid administering vaccine too far in advance of the influenza season because antibody levels begin declining within a few months. Vaccination programs may be undertaken as soon as current vaccine is available if regional influenza activity is expected to begin earlier than December.

Children less than 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 given 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, less than 30% of persons in 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. 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. 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 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 greater than or equal to 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 greater than or equal to 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 patients (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

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 given 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 in a small proportion of persons. Such symptoms are rarely severe, but may be important for some categories of patients.

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 patients. To be fully effective as prophylaxis, the antiviral drug must be taken each day for the duration of influenza activity in the community.

Use as Prophylaxis

High-risk individuals vaccinated after influenza A activity has begun:

High-risk individuals 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 given. 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 given 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 patients 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 used.

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.

Other persons:

Amantadine can also be used 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

Although amantadine can reduce the severity and shorten the duration of influenza A illness in healthy adults, there are no data on the efficacy of amantadine therapy in preventing complications of influenza A in high-risk persons. Therefore, no specific recommendations can be made regarding the therapeutic use of amantadine for these patients. This does not preclude physicians from using amantadine in 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) and/or gastrointestinal side effects (anorexia and nausea) occur in 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/behavioral conditions. Reducing the dosage to less than or equal to 100 mg /day appears to reduce the frequency of these side effects in such persons without compromising the prophylactic effectiveness of amantadine.

The package insert should be consulted 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 used 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 given 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 CDC. Information can be obtained from Technical Information Services, 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.

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Cases of notifiable diseases, Virginia, for the period July 1 through July 31,1990.

DISEASE	Total Cases Reported This Month						Total Cases Reported to Date		
		REGIONS					THIS YEAR	LAST YEAR	5 YR AVG.
	STATE	N.W.	N.	S.W.	C.	E.	(STATE TOTALS)		
Acquired Immunodeficiency Syndrome	52	2	33	5	8	4	377	244	145
Campylobacter Infections	74	14	21	14	10	15	317	377	332
Gonorrhea	1371	--	--	--	--	--	9979	8851	9203
Hepatitis A	13	1	4	1	0	7	166	190	155
B	14	0	2	5	2	5	126	169	243
Non A-Non B	2	0	0	1	0	1	26	40	44
Influenza	0	0	0	0	0	0	764	1852	2070
Kawasaki Syndrome	0	0	0	0	0	0	13	8	15
Legionellosis	0	0	0	0	0	0	7	5	7
Lyme Disease	21	3	3	2	0	13	53	18	11
Measles	2	2	0	0	0	0	70	21	49
Meningitis - Aseptic	17	0	1	5	4	7	104	93	96
Bacterial*	5	3	0	2	0	0	84	113	124
Meningococcal Infections	3	0	0	2	1	0	36	40	44
Mumps	8	1	3	2	1	1	85	59	57
Pertussis	1	0	0	1	0	0	14	9	18
Rabies in Animals	18	4	5	1	8	0	122	163	168
Reye Syndrome	0	0	0	0	0	0	1	0	1
Rocky Mountain Spotted Fever	6	1	2	1	2	0	8	5	12
Rubella	0	0	0	0	0	0	1	0	3
Salmonellosis	121	10	22	16	39	34	633	714	756
Shigellosis	10	2	6	0	0	2	84	304	143
Syphilis (Primary & Secondary)	77	1	16	6	25	29	485	319	224
Tuberculosis	44	2	8	4	14	16	203	206	223

Localities Reporting Animal Rabies: Albemarle 1 raccoon; Colonial Heights 1 raccoon, 1 skunk; Craig 1 cat; Dinwiddie 1 raccoon; Fairfax 2 bats; Loudoun 1 bat, 1 raccoon; Lunenburg 1 raccoon, 2 skunks; Madison 1 bobcat; Nottoway 1 raccoon; Prince George 1 raccoon; Prince William 1 raccoon; Warren 1 cat, 1 raccoon.

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Occupational Illnesses: Asbestosis 10; Carpal Tunnel Syndrome 22; Coal Workers' Pneumoconiosis 47; De Quervain's Disease 1; Loss of Hearing 8; Occupational Asthma 2; Repetitive Motion Disorder 3.

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