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Robert B. Stroube, M.D., M.P.H., Health Commissioner
John S. Marr, M.D., M.P.H., State Epidemiologist
Elizabeth Barrett, D.M.D., M.S.P.H., Editor
Vickie L. O'Dell, Layout Editor

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Prophylactic Use of Potassium Iodide in Nuclear Power Plant Emergencies

Local Significance

In September 2002, the Virginia Department of Health (VDH), in cooperation with the Virginia Department of Emergency Management, began distribution of potassium iodide (KI) tablets to individuals who live or work within 10 miles of the North Anna Nuclear Power Plant in Louisa County and Surry Nuclear Power Plant in Surry County. Approximately 330,000 citizens live or work within 10 miles of these two plants.

The Nuclear Regulatory Commission provided an initial supply of two doses per person of KI (660,000 tablets) to Virginia. One dose is being made available free of charge to people who live or work within 10 miles of a power plant, to be used in the event of a nuclear reactor accident. If radioactive iodines are released, the State Health Commissioner will make recommendations as to who should take KI. VDH will stockpile the second dose and will make it available, if needed, at evacuation assembly centers.

Rationale

Although nuclear reactors are constructed under extremely stringent specifications and operate under rigorous safety control measures, there is a small possibility that an accident could occur releasing radioactive products into the environment. The potential radiation exposure of the nearby population would depend upon the nature and amounts of various radioactive materials released, weather conditions, and the effectiveness of any protective actions taken. Radioactive isotopes of iodine, including ^{131}I, ^{132}I, and ^{133}I, are likely to be the major components of a release from a severe nuclear power plant accident. Radioactive iodines can result in external exposure from skin contact and internal exposure from inhalation and ingestion.

In the event of a nuclear accident, taking potassium iodide may reduce the risk of damage to the thyroid gland, especially in young children.

The effectiveness of KI as a specific blocker of thyroid radioiodine is well established, as are the dosages neccessary for blocking intake. KI saturates the thyroid gland with iodine helping to prevent the absorption of radioactive iodine. During a nuclear accident, inhalation of contaminated air and ingestion of contaminated food and drink could lead to uptake of radioactive iodines by the thyroid gland. Acute effects from thyroid exposure to high doses of radioactive iodines include hypothyroidism and acute thyroiditis. Chronic or delayed effects from thyroid exposure are thyroid cancer and benign thyroid nodules, especially among exposed children aged 0-15 years.

KI provides protection only for the thyroid from radioactive iodines. It has no impact on the uptake by the body of other radioactive materials and provides no protection against external radiation of any kind. The use of KI should only be as an adjunct to evacuation, sheltering, and control of foodstuffs. KI should not be considered as an antidote for radiation in general or a substitute for evacuation in the event of a nuclear reactor accident.

Dosages

KI comes in tablets of 130 mg. The table (page 2) describes dosage for infants through adults. A one-time dose at the levels recommended is usually all that is required. However, if exposure to radioactive iodines continues for more than 24 hours, recommendations may be made to take additional doses every 24 hours. Taking a higher dose than recommended or taking KI more often than recommended can result in allergic reactions and other side effects.

For optimal protection against inhaled radioactive iodines, KI should be adminis-

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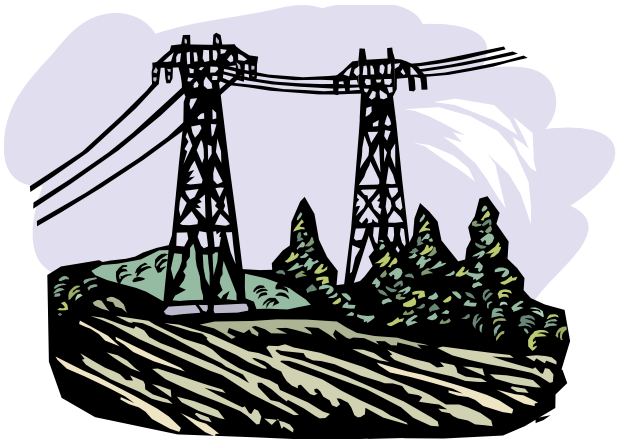


tered before or immediately coincident with passage of the radioactive plume. If taken about four hours after exposure, its effectiveness is diminished to about 50 percent. The protective action is substantially reduced about six hours after exposure.

Use in Children and Young Adults

Children are the most suceptible to the dangerous effects of radioactive iodine. The risk of acute and chronic effects of radioactive iodines can be minimized, especially in neonates and young children, by administration of KI in a timely manner and in appropriate dosages.

Young adults (18-40 years) have a lower risk than children of developing thyroid cancer or disease from exposure to radioactive iodine; however, the Food and Drug Administration (FDA) still recommends that people aged 18-40 take the recommended dose of KI.

Use During Pregnancy and Breast-Feeding

Pregnant women should be given KI for their own protection and for that of the fetus, since iodine (whether stable or radioactive) readily crosses the placenta. However, because of the risk of blocking fetal thyroid function with excess stable iodine, repeat dosing with KI of pregnant women should be avoided.

Lactating females should be administered KI for their own protection and potentially to reduce the radioactive iodine content of the breast milk, but not as a means to deliver KI to infants. Infants should get their dosage directly. Stable iodine in breast milk may also pose a risk of hypothyroidism in nursing neonates. Therefore, repeat dosing with KI should be avoided in the lactating mother, except during continuing severe contamination. If repeat dosing of the mother is necessary, the nursing neonate should be monitored for hypothyroidism.

Use in Adults >40 Years

The risk of radiation induced thyroid cancer in adults over 40 years is extremely low. However, the risk of side effects from KI administration may be higher in this group. Therefore, KI prophylaxis is not indicated in adults over 40 unless a large internal radiation dose to the thyroid is expected.

Side Effects and Contraindications

The risk of severe side effects from single doses of KI is minimal, less than one in 10 million in children and less than one in one million in adults. The risk may be higher after long term and repeated doses of KI. The adverse effects of KI administration include sialadenitis, gastrointestinal disturbances, allergic reactions, and minor rashes. Persons with known iodine sensitivity should not be administered KI, nor should individuals with dermatitis herpetiformis and hypocomplementemic vasculitis, extremely rare conditions associated with an increased risk of iodine hypersensitivity. Individuals with multinodular goiter, Graves' disease, and autoimmune thyroiditis should be treated with caution, especially if dosing extends beyond a few days. The vast majority of such individuals will be adults.

In neonates treated with KI, transient hypothyroidism has been observed in less than one percent of cases and without any reported sequelae to date. Certainly, the benefits of KI treatment to reduce the risk of thyroid cancer far outweigh the risks of side effects in neonates. Nevertheless, FDA recommends that neonates (within the first month of life) treated with KI be monitored for hypothyroidism by measurement of TSH (and FT4, if indicated) and that thyroid hormone therapy be instituted in cases in which hypothyroidism occurs.

Sources of Potassium Iodide

KI is a non-prescription medication and is available under the trade name Thyro-Block manufactured by MedPointe, Inc., and IOSAT manufactured by Anbex, Inc. MedPointe distributes Thyro-Block only to state, local, and federal agencies, as well as nuclear power plants and hospitals. Anbex, Inc. has made its product available to the general public.

Recommended Dosage for Potassium Iodide*

Age	Dosage
Infants birth - 1 month	16 mg (1/8 tablet)
Children >1month- 3 years	32 mg (1/4 tablet)
Children >3years-18 years	65 mg (1/2 tablet)
Adults >18 years - 40 years**	130 mg (1 tablet)
Adults >40 years***	130 mg (1 tablet)

**KI is available in tablets of 130 mg. A one-time dose is usually sufficient.*
***Adolescents approaching adult weight (~150 pounds) should receive the full adult does of 130 mg or 1 tablet.*
****KI is not recommended for adults >40 years, unless a very large dose of radioactive iodine is expected.*

Submitted by Khizar Wasti, Ph.D., Director, Division of Health Hazards Control and Elaine Perry, M.D., M.S., Director, Penninsula Health District. Adapted from FDA's "Guidance Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies," December 2001. The FDA's guidance is available on the internet at http://www.fda.gov/cder/guidance4825fnl.htm.

Prevention and Control of Influenza

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

This article summarizes the 2002 recommendations by the ACIP on the use of influenza vaccine and antiviral agents (MMWR 2002;51[No. RR03]:1-31). The complete report can be accessed on the CDC website at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5103a1.htm>.

What's New

The 2002 recommendations include four principal changes or updates, as follows:

1. The optimal time to receive influenza vaccine is during October and November. However, because of vaccine distribution delays during the past 2 years, ACIP recommends that vaccination efforts in October focus on persons at greatest risk for influenza-related complications and on health-care workers. Vaccination of other groups should begin in November.

2. Vaccination efforts for all groups should continue into December and later, for as long as vaccine is available.

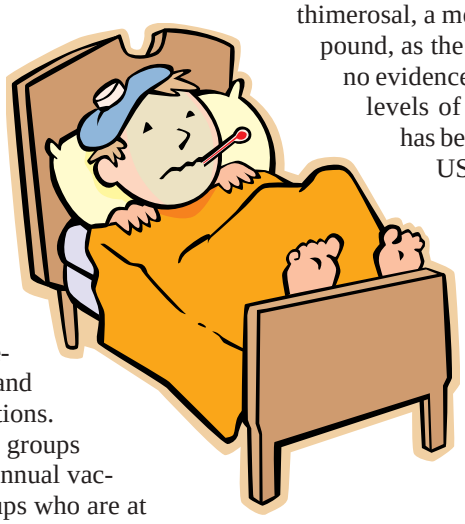
3. Because young, otherwise healthy children are at increased risk for influenza-related hospitalization, influenza vaccination of healthy children aged 6–23 months is encouraged when feasible. Vaccination of children aged ≥6 months who have certain medical conditions continues to be strongly recommended.

4. A limited amount of influenza vaccine with reduced thimerosal content will be available for the 2002–2003 influenza season.

Background

Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms such as fever, myalgia, headache, severe malaise, nonproductive cough, sore throat, and rhinitis. Illness typically resolves after several days, although cough and malaise can persist for ≥2 weeks. In some persons, influenza can exacerbate underlying medical conditions, lead to secondary bacterial pneumonia or primary influenza viral pneumonia, or occur as part of a coinfection with other viral or bacterial pathogens. Influenza infection has also been associated with encephalopathy, transverse myelitis, Reye syndrome, myositis, myocarditis, and pericarditis.

Influenza viruses are spread from person-to-person primarily through the coughing and sneezing of infected persons. Persons can be infectious starting the day before symptoms begin until approximately 5 days after illness onset; children can be infectious for a longer period.



Influenza vaccination is the primary method for preventing influenza and its severe complications. The primary target groups recommended for annual vaccination are 1) groups who are at increased risk for influenza-related complications (e.g., persons aged ≥65 years and persons of any age with certain chronic medical conditions); 2) persons aged 50-64 years, because this group has an elevated prevalence of certain chronic medical conditions; and 3) persons who live with or care for persons at high risk.

Although influenza vaccination remains the cornerstone for the control and treatment of influenza, information is also presented regarding antiviral medications, because these agents are an adjunct to vaccine.

Influenza Vaccine Composition

The trivalent influenza vaccine recommended for the 2002-2003 season includes A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Hong Kong/330/2001-like antigens. The vaccine is made from highly purified, egg-grown viruses that have been made non-infectious. Subvirion and purified surface-antigen preparations are available (Table 1). Because the vaccine viruses are initially grown in embryonated hens' eggs, the vaccine might contain small amounts of residual egg protein.

Manufacturers might use additional compounds to inactivate the influenza viruses and an antibiotic to prevent bacterial contamination. Package inserts should be consulted for additional information.

Influenza vaccine also might contain thimerosal, a mercury-containing compound, as the preservative. Although no evidence of harm caused by low levels of thimerosal in vaccines has been reported, in 1999, the US Public Health Service and other organizations recommended that efforts be made to reduce the thimerosal content in vaccines to decrease total mercury exposure, chiefly among infants and pregnant women. For the 2002-2003 influenza season, a limited number of individually packaged doses of reduced thimerosal-content influenza vaccine (<1mcg thimerosal /0.5 mL-dose) will be available. Thus far, reduced thimerosal-content vaccine is available from one manufacturer, Evans Vaccines. This manufacturer's vaccine is approved for use in persons aged ≥4 years.

Recommendations for Use of Influenza Vaccine

Influenza vaccine is strongly recommended for any person aged ≥6 months who, because of age or underlying medical condition, is at increased risk for complications of influenza.

Target Groups for Vaccination

Persons at Increased Risk for Complications

Vaccination is recommended for the following groups of persons who are at increased risk for complications from influenza:

- persons aged ≥65 years;
- residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions;

Table 1. Influenza vaccine* dosage, by age group, United States, 2002-2003 season

Age group	Dose	No. of doses	Route§
6-35 mos	0.25 mL	1 or 2¶	Intramuscular
3-8 years	0.50 mL	1 or 2¶	Intramuscular
≥9 yrs	0.50 mL	1	Intramuscular

**Manufacturers include Aventis Pasteur, Inc. (Fluzone® split); Evans Vaccines, Ltd. (Fluvirin™ purified surface antigen vaccine); and Wyeth Lederle Laboratories (Flushield™ split). Fluzone and Flushield are Food and Drug Administration approved for persons aged ≥6 months. Fluvirin is approved for use among persons aged ≥4 years. For further product information, call Aventis Pasteur, (800) 822-2463; Evans Vaccine, Ltd. (800) 200-4278; or Wyeth Lederle, (800) 358-7443.*
§For adults and older children, the recommended site of vaccination is the deltoid muscle. The preferred site for infants and young children is the anterolateral aspect of the thigh.
¶Two doses administered ≥1 month apart are recommended for children <9 years who are receiving influenza vaccine for the first time.

- adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma;
- adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression;
- children and adolescents (aged 6 months to 18 years) who are receiving long-term aspirin therapy and, therefore, might be at risk for developing Reye syndrome after influenza infection; and
- women who will be in the second or third trimester of pregnancy during the influenza season.

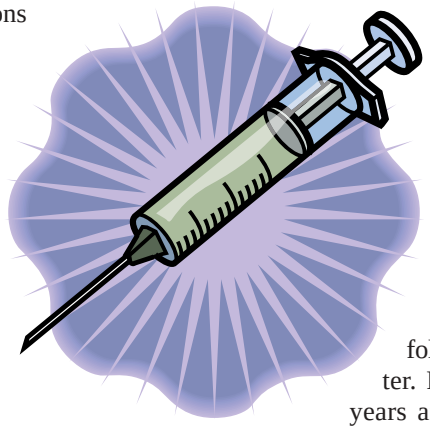
Persons Aged 50-64 Years

Vaccination is recommended for persons aged 50-64 years because approximately 25% of this group has ≥1 high-risk medical conditions.

Persons Who Can Transmit Influenza to Those at High Risk

Persons who are clinically or subclinically infected can transmit influenza virus to persons at high risk for complications from influenza. Vaccination of health-care workers is associated with decreased deaths among nursing home patients. The following groups should be vaccinated:

- physicians, nurses, and other personnel in both hospital and outpatient-care settings, including emergency response workers;
- employees of nursing homes and chronic-care facilities who have contact with patients or residents;
- employees of assisted living and other residences for persons in groups at high risk;
- persons who provide home care to persons in groups at high risk; and
- household members of persons in groups at high risk.



Additional Information Regarding Vaccination of Specific Populations

Pregnant Women

Women who will be beyond the first trimester of pregnancy during the influenza season should be vaccinated. Pregnant women who have medical conditions that increase their risk for complications from influenza should be vaccinated before the influenza season, regardless of the stage of pregnancy.

Because currently available influenza vaccine is an inactivated vaccine, experts consider influenza vaccine safe during any stage of pregnancy. However, some experts prefer to administer influenza vaccine during the second trimester to avoid a coincidental association with spontaneous abortion, which is common in the first trimester, and because exposures to vaccines traditionally have been avoided during the first trimester.

Persons Infected with HIV

Vaccinations will benefit HIV-infected patients, including HIV-infected pregnant women.

Breast-Feeding Mothers

Influenza vaccine does not affect the safety of mothers who are breast-feeding or their infants. Breast-feeding does not adversely affect the immune response and is not a contraindication for vaccination.

Travelers

Persons at high risk for complications of influenza who were not vaccinated with influenza vaccine during the preceding fall or winter should consider receiving influenza vaccine before travel if they plan to:

- travel to the tropics;
- travel with large, organized tourist groups at any time of year; or
- travel to the Southern Hemisphere during April-September.

No information is available regarding the benefits of revaccinating persons before summer travel who were already vaccinated in the preceding fall. Persons at high risk who received the previous season's vaccine before travel should be revaccinated with the current vaccine in the following fall or winter. Persons aged ≥50 years and others at high risk might wish to consult with their physicians before embarking on travel during the summer to discuss the symptoms and risks for influenza and the advisability of carrying antiviral medications for either prophylaxis or treatment of influenza.

General Population

In addition to the groups for which annual influenza vaccination is recommended, physicians should administer influenza vaccine to any person ≥6 months old who wishes to reduce the likelihood of becom-

ing ill with influenza, depending on vaccine availability. Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.

Healthy Young Children

Studies have shown that young children are at substantially increased risk for influenza-related hospitalizations. Their increased rate of hospitalization is comparable with rates for other groups considered at high risk for influenza-related complications. Therefore, influenza vaccination of all children aged 6-23 months is encouraged when feasible. Currently, influenza vaccine is not approved by the Food and Drug Administration (FDA) for use among children <6 months, the pediatric group ar greatest risk for influenza-related complications. Vaccinating their household contacts and out-of-home caretakers might decrease the probability of influenza among these children.

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). However, persons who have a history of anaphylactic hypersensitivity to vaccine components but who are also at high risk for complications from influenza can benefit from vaccine after appropriate allergy evaluation and desensitization.

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

Timing of Annual Vaccination

The optimal time to vaccinate is usually during October-November. However, because of substantial vaccine distribution delays during the past two influenza seasons and the possibility of similar situations in future years, ACIP recommends that vaccine providers focus their vaccination efforts in October on high risk persons and health-care workers. Vaccination of children aged <9 years who are receiving vaccine for the first time should also begin in October because they need a booster dose one month after the initial dose. Vaccination of all other groups should begin in November.

Health-care providers should continue to offer vaccination to unvaccinated persons after November and throughout the influenza season even after influenza activity has been documented in the community. In the United States, influenza activity has not reached peak levels in the majority of recent seasons until late December through early March. Therefore, vaccine administered after November is likely to be beneficial in most influenza seasons. Adults develop peak antibody protection against influenza infection 2 weeks after vaccination.

When educating patients about influenza vaccine, clinicians should emphasize that a) inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza; and b) coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination.

Persons planning substantial organized vaccination campaigns should consider scheduling these events after mid-November because the availability of vaccine cannot be ensured consistently in the early fall. Campaigns conducted before November should focus efforts on vaccination of persons at high risk, health-care workers, and household contacts of persons at high risk. In facilities housing elderly persons (e.g., nursing homes), vaccination before October generally should be avoided because antibody levels in such individuals can begin to decline within a short time after vaccination.

Dosage

Dosage recommendations vary according to age group (Table 1). Among previously unvaccinated children aged <9 years, two doses administered ≥1 month apart are recommended for satisfactory antibody responses. If possible, the second dose should be administered before December. Among adults, studies have indicated limited or no improvement in antibody response when a second dose is administered during the same season.

Route

The intramuscular route is recommended for influenza vaccine. Adults and older children should be vaccinated in the deltoid muscle. A needle length of ≥1 inches can be considered for these age groups because needles <1 inch might be of insufficient length to penetrate muscle tissue in certain adults and older children. Infants and young children should be vaccinated in the anterolateral aspect of the thigh.

Vaccine Use Among Young Children

Of the three influenza vaccines currently licensed in the United States, two influenza vaccines (Flushield®, from Wyeth Laboratories, Inc. and Fluzone® split-virus, from Aventis Pasteur, Inc.) are approved for use among persons aged ≥6 months. Fluvirin® (Evans Vaccines Ltd.) is labeled in the United States for use only among persons aged ≥4 years because its efficacy among younger persons has not been demonstrated (Table 1).

Side Effects and Adverse Reactions

Local Reactions

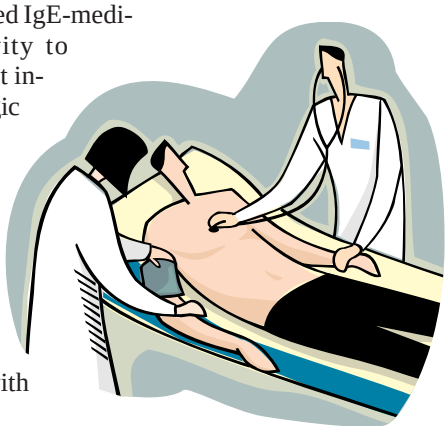
The most frequent side effect of vaccination is soreness at the vaccination site that lasts ≤2 days. These local reactions typically are mild and rarely interfere with the person's ability to conduct usual daily activities.

Systemic Reactions

Fever, malaise, myalgia, and other systemic symptoms can occur after vaccination and most often affect persons who have had no prior exposure to the influenza virus antigens in the vaccine. These reactions begin 6-12 hours after vaccination and can persist for 1-2 days.

Immediate and presumably allergic reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to certain vaccine components; most reactions likely are caused by residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who

have developed hives, have had swelling of the lips or tongue, or have experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons who have documented IgE-mediated hypersensitivity to eggs might also be at increased risk for allergic reactions to influenza vaccine, and consultation with a physician should be considered. Protocols have been published for safely administering influenza vaccine to persons with egg allergies.



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

Simultaneous Administration of Other Vaccines

For persons at high risk who have not previously been vaccinated with pneumococcal vaccine, health-care providers should strongly consider administering pneumococcal and influenza vaccines concurrently. Both vaccines can be administered at the same time at different sites without increasing side effects. However, influenza vaccine is administered each year, whereas pneumococcal vaccine is not. A patient's verbal history is acceptable for determining prior pneumococcal vaccination status. When indicated, pneumococcal vaccine should be administered to patients who are uncertain regarding their vaccination history. Children at high risk for influenza-related complications, can receive influenza vaccine at the same time they receive other routine vaccinations.

Recommendations for Using Antiviral Agents

Antiviral drugs for influenza are an adjunct to influenza vaccine for control and prevent of influenza. However, these agents are not a substitute for vaccination. Four licensed influenza antiviral agents are available in the United States: amantadine and rimantadine, chemically-related antivirals with activity against influenza A only; and zanamivir and oseltamivir, neuraminidase inhibitors with activity against both influenza A and B viruses.

An overview of the indications for use, administration, and known side effects of these medications is presented in the following sections. Package inserts should be consulted for additional information.

Indications for Use

Treatment

When administered within 2 days of illness onset to otherwise healthy adults, amantadine and rimantadine can reduce the duration of uncomplicated influenza A illness, and zanamivir and oseltamivir can reduce the duration of uncomplicated influenza A and B illness, by approximately 1 day. None of the four antiviral agents has been demonstrated to be effective in preventing serious influenza-related complications, such as bacterial or viral pneumonia or exacerbation of chronic diseases.

To reduce the emergence of antiviral drug-resistant viruses, amantadine or rimantadine therapy for persons with influenza A illness should be discontinued as soon as clinically warranted, generally after 3-5 days of treatment or within 24-48 hours after the disappearance of signs and symptoms. The recommended duration of treatment with either zanamivir or oseltamivir is 5 days.

Chemoprophylaxis

Both amantadine and rimantadine are approximately 70%-90% effective in preventing illness from influenza A infection. When used as prophylaxis, these antiviral agents can prevent illness while permitting subclinical infection and the development of protective antibody against circulating influenza viruses. Amantadine and rimantadine do not interfere with the antibody response to the vaccine. Both drugs have been studied extensively among nursing home populations as a component of influenza outbreak control programs.

Among the neuraminidase inhibitor antivirals, only oseltamivir has been approved for prophylaxis, but community studies of healthy adults indicate that both drugs are approximately 80% effective in preventing febrile, laboratory-confirmed influenza illness. Both antiviral agents also have been reported to prevent influenza illness among persons given chemoprophylaxis after a household member was diagnosed with influenza. Experience with prophylactic use of these agents in institutional settings or among patients with chronic medical conditions is limited. One 6-week study of oseltamivir prophylaxis among nursing home residents found a 92% reduction in influenza illness.

To be maximally effective as prophylaxis, an antiviral drug must be taken each day for the duration of influenza activity in the community. However, to be most cost-effective, one study of amantadine or rimantadine prophylaxis reported that the drugs should be taken only during the period of peak influenza activity in a community. Data are not available on the efficacy of any of the four antiviral agents in preventing influenza among severely immune compromised persons.

Control of Outbreaks in Institutions

Using antiviral drugs for treatment and prophylaxis of influenza is a key component of institutional outbreak control. In addition to using antiviral medications, other outbreak control measures include instituting droplet precautions and cohorting patients with confirmed or suspected influenza, vaccinating staff and patients who are unvaccinated, restricting staff movement between wards or buildings, and restricting contact between ill staff or visitors and patients.

When confirmed or suspected outbreaks of influenza occur in institutions that house persons at high risk, chemoprophylaxis should be started as early as possible to reduce the spread of the virus. In these situations, having preapproved orders from physicians or plans

to obtain orders for antiviral medications on short notice is extremely useful.

When institutional outbreaks occur, chemoprophylaxis should be administered to all residents, regardless of whether they received influenza vaccinations during the previous fall, and should continue for ≥2 weeks or until approximately 1 week after the end of the outbreak. The dosage for each resident should be determined individually. Chemoprophylaxis also can be offered to unvaccinated staff who provide care to persons at high risk. Prophylaxis should be considered for all employees, regardless of their vaccination status, if the outbreak is caused by a variant strain of influenza that is not well-matched by the vaccine.

In addition to nursing homes, chemoprophylaxis also can be considered for controlling influenza outbreaks in dormitories or other settings where persons live in close proximity.

To limit potential transmission of drug-resistant virus during institutional outbreaks, measures should be taken to reduce contact as much as possible between persons taking antiviral drugs for treatment and other persons, including those taking chemoprophylaxis.

Dosage

Dosage recommendations vary by age group and medical conditions (Table 2).

Table 2. Recommended daily dosage of influenza antiviral medications for treatment and prophylaxis

Antiviral agent	Age group (years)				
	1-6	7-9	10-12	13-64	≥65
Amantadine*					
Treatment, influenza A	5 mg/kg/day up to 150 mg in two divided doses†	5 mg/kg/day up to 150 mg in two divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Prophylaxis, influenza A	5 mg/kg/day up to 150 mg in two divided doses†	5 mg/kg/day up to 150 mg in two divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Rimantadine¶					
Treatment, influenza A	NA	NA	NA	100 mg twice daily§, **	100 mg/day††
Prophylaxis, influenza A	5 mg/kg/day up to 150 mg in two divided doses†	5 mg/kg/day up to 150 mg in two divided doses†	100 mg twice daily§	100 mg twice daily§	100 mg/day††
Zanamivir§§					
Treatment, influenza A and B	NA	10 mg twice daily	10 mg twice daily	10 mg twice daily	10 mg twice daily
Oseltamivir***					
Treatment, influenza A and B	Dose varies by child's weight†††	Dose varies by child's weight†††	Dose varies by child's weight†††	75 mg twice daily	75 mg twice daily
Prophylaxis, influenza A and B	NA	NA	NA	75 mg/day	75 mg/day

***NOTE**: Amantadine manufacturers include Endo Pharmaceuticals (Symmetrel®, tablet and syrup); Geneva Pharms Tech and Rosemont (Amantadine HCL, capsule); and Alpharma, Copley Pharmaceutical, HiTech Pharma, Mikart, Morton Grove, and Pharmaceutical Associates (Amantadine HCL, syrup). Rimantadine is manufactured by Forest Laboratories (Flumadine®, tablet and syrup) and Corepharma (Rimantadine HCL, tablet). Zanamivir is manufactured by GlaxoSmithKline (Relenza®, inhaled powder). Oseltamivir is manufactured by Hoffman-LaRoche, Inc. (Tamiflu®, tablet).*

**A reduction in dosage is recommended for patients with creatinine clearance ≤50 mL/min/1.73m^2. See the drug package insert for dosage recommendations.*

†5 mg/kg of amantadine or rimantadine syrup = 1 tsp/22 lbs.

§Children aged ≥10 years who weigh <40 kg should be administered amantadine or rimantadine at a dosage of 5 mg/kg/day.

¶A reduction in dosage to 100mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

***Rimandatine is approved by FDA for treatment of adults. However, certain specialists consider rimantadine appropriate treatment among children (see American Academy of Pediatrics. 2000 Red Book: Report of the Committee on Infectious Diseases).*

††Elderly nursing home residents should be administered only 100 mg/day of rimantadine. A reduction in dosage to 100 mg/day should be considered for all persons aged ≥65 years, if they experience side effects when taking 200 mg/day.

§§Zanamivir is administered via inhalation by using a plastic device included in the package with the medication. Patients will benefit from instruction and demonstration of correct use of the device. Zanamivir is not approved for prophylaxis.

****For persons with creatinine clearance <30mL/min, a reduction of the treatment dose of oseltamivir to 75mg/day and in the prophylaxis dose to 75mg every other day is recommended.*

†††The dose recommendation for children who weigh ≤15 kg is 30 mg twice a day; for children weighing >15-23 kg, the dose is 45 mg twice a day; for children weighing >23-40 kg, the dose is 60 mg twice a day; and for children weighing >40 kg, the dose is 75 mg twice a day.

Route

Amantadine, rimantadine, and oseltamivir are administered orally. Amantadine and rimantadine are available in tablet or syrup form, and oseltamivir is available in capsule or oral suspension form. Zanamivir is available as a dry powder that is self-administered via oral inhalation by using a plastic device included in the package with the medication. Patients should receive instruction and demonstration of correct use of this device.

Side Effects and Adverse Reactions

Amantadine and Rimantadine

Both amantadine and rimantadine can cause central nervous system (CNS) and gastrointestinal side effects when administered to young, healthy adults at equivalent dosages of 200 mg/day. However, incidence of CNS side effects (e.g., nervousness, anxiety, insomnia, difficulty concentrating, and lightheadedness) is higher among persons taking amantadine than among those taking rimantadine. A study of elderly persons also demonstrated fewer CNS side effects associated with rimantadine compared with amantadine. Gastrointestinal side effects (e.g., nausea and anorexia) occur in approximately 1%-3% of persons taking either drug, compared with 1% of persons receiving the placebo.

An increased incidence of seizures has been reported among patients with a history of seizure disorders who have received amantadine. Patients with seizure disorders should be observed closely for possible increased seizure activity when taking amantadine. Seizures (or seizure-like activity) also have been reported among persons with a history of seizures who were not receiving anticonvulsant medication while taking rimantadine.

Side effects associated with amantadine and rimantadine are usually mild and cease soon after discontinuing the drug. Side effects can diminish or disappear after the first week, despite continued drug ingestion. Serious side effects such as marked behavioral changes, delirium, hallucinations, agitation, and seizures have been associated with high plasma drug concentrations, most often among persons who have renal insufficiency, seizure disorders, or certain psychiatric disorders, and among elderly persons who have been taking amantadine as prophylaxis at a dosage of 200 mg/day. In acute overdosage of amantadine, CNS, renal, respiratory, and cardiac toxicity, including arrhythmias, have been reported.

Zanamivir

Zanamivir is generally not recommended for treatment for patients with underlying airway disease because of the risk for serious adverse events and because the efficacy has not been demonstrated in this population. If physicians decide to prescribe zanamivir to patients with underlying chronic respiratory disease, the drug should be used with caution under conditions of proper monitoring and supportive care. Patients with asthma or chronic obstructive pulmonary disease who use zanamivir are advised to a) have a fast-acting inhaled bronchodilator available when inhaling zanamivir and b) stop using zanamivir and contact their physician if they develop difficulty breathing. No clear evidence is available regarding the safety or efficacy of zanamivir for persons with underlying respiratory or cardiac disease or for persons with complications of acute influenza.

In clinical treatment studies of persons with uncomplicated influenza, the frequencies of adverse events were similar for persons receiving inhaled zanamivir and those receiving placebo. The most common adverse events reported by both groups were diarrhea; nausea; sinusitis; nasal signs and symptoms; bronchitis; cough; headache; dizziness; and ear, nose, and throat infections. Each of these symptoms was reported by <5% of persons in the clinical treatment studies combined.

Oseltamivir

Nausea and vomiting were reported more frequently among adults receiving oseltamivir for treatment than among persons receiving placebo. Among children treated with oseltamivir, 14.3% had vomiting, compared with 8.5% of placebo recipients. Similar types and rates of adverse events were found in studies of oseltamivir prophylaxis. Nausea and vomiting might be less severe if oseltamivir is taken with food.

Use During Pregnancy

No clinical studies have been conducted regarding the safety or efficacy of amantadine, rimantadine, zanamivir, or oseltamivir for pregnant women. However, both amantadine and rimantadine have been demonstrated in animal studies to be teratogenic and embryotoxic when administered at very high doses. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these four drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

Drug Interactions

Careful observation is advised when amantadine is administered concurrently with drugs that affect the CNS, especially CNS stimulants. Concomitant administration of antihistamines or anticholinergic drugs can increase the incidence of adverse CNS reactions. No clinically significant interactions between rimantadine and other drugs have been identified.

Clinical data are limited regarding drug interactions with zanamivir. However, no known drug interactions have been reported, and no clinically important drug interactions have been predicted on the basis of in vitro data and data from studies involving rats.

Limited clinical data are available regarding drug interactions with oseltamivir. Because oseltamivir and oseltamivir carboxylate are excreted in the urine by glomerular filtration and tubular secretion via the anionic pathway, a potential exists for interaction with other agents excreted by this pathway. For example, coadministration of oseltamivir and probenecid resulted in reduced clearance of oseltamivir carboxylate by approximately 50% and a corresponding approximate twofold increase in the plasma levels of oseltamivir carboxylate.

Cases of Selected Notifiable Diseases Reported in Virginia*

Disease	Total Cases Reported, July 2002: State	Regions: NW	N	SW	C	E	Total Cases Reported Statewide, January through July: This Year	Last Year	5 Yr Avg
AIDS	51	5	13	4	7	22	472	524	520
Campylobacteriosis	64	17	7	20	9	11	287	286	324
***E. coli* O157:H7**	6	1	3	0	1	1	27	28	35
Giardiasis	17	3	1	2	10	1	118	213	210
Gonorrhea	750	27	61	84	219	359	5,903	6,031	5,179
Hepatitis A	8	0	1	1	5	1	55	76	103
B, acute	17	2	0	3	7	5	122	88	74
C/NANB, acute	0	0	0	0	0	0	5	0	8
HIV Infection	107	7	21	7	26	46	577	544	487
Lead in Children†	94	9	11	16	35	23	379	336	317
Legionellosis	2	0	0	2	0	0	10	14	12
Lyme Disease	20	9	3	1	1	6	43	83	50
Measles	0	0	0	0	0	0	0	0	2
Meningococcal Infection	2	0	0	0	2	0	28	30	31
Mumps	0	0	0	0	0	0	3	2	5
Pertussis	4	3	0	0	1	0	92	13	20
Rabies in Animals	41	9	8	5	13	6	325	249	323
Rocky Mountain Spotted Fever	8	2	0	0	4	2	15	12	7
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	133	17	39	25	27	25	503	771	582
Shigellosis	100	2	7	2	28	61	557	121	157
Syphilis, Early§	12	2	5	0	2	3	93	154	237
Tuberculosis	24	0	15	0	3	6	145	141	168

Localities Reporting Animal Rabies This Month: Amelia 1 groundhog; Campbell 1 skunk; Caroline 1 fox; Chesterfield 1 cat; Clarke 1 raccoon; Culpeper 1 fox; Fairfax 1 cat, 1 fox, 4 raccoons; Gloucester 1 cat; Goochland 1 raccoon; Halifax 1 fox; Hampton 1 raccoon; Hanover 1 fox, 2 raccoons; Henrico 1 cat; Henry 1 raccoon; Loudoun 1 raccoon; Mecklenburg 1 fox; Nelson 1 skunk; Page 1 skunk; Patrick 1 raccoon; Petersburg 1 fox, 1 raccoon; Pittsylvania 1 skunk; Prince William 1 raccoon; Rockbridge 1 skunk; Rockingham 2 cats; Shenandoah 1 skunk; Suffolk 2 raccoons; Sussex 1 raccoon; Tazewell 1 raccoon; Virginia Beach 1 cat, 1 fox.

Toxic Substance-related Illnesses: Asbestosis 13; Lead Exposure 10; Pneumoconiosis 6.

*Data for 2002 are provisional. †Elevated blood lead levels ≥10µg/dL.

§Includes primary, secondary, and early latent.

West Nile Virus Update

Since mid-August 2002, the Centers for Disease Control and Prevention has received 29 reports of patients who developed West Nile virus (WNV) infections within one month of receiving blood components: 25 patients with West Nile meningoencephalitis and 4 with other WNV-associated illnesses. All of these patients resided in areas with high levels of WNV activity. Investigation of these cases indicates that WNV can be transmitted through blood transfusion.

We'd like to remind physicians to:

- Report to their local health department any cases of WNV infection in patients who have received blood transfusions within the 4 weeks preceding illness onset. Serum or tissue samples should be retained for later studies
- Ask patients with WNV infection whether they have donated blood within the 2 weeks prior to becoming ill.

Prompt reporting of these cases will facilitate withdrawal of potentially infectious blood components.

Laboratory Confirmed Cases of WNV, Virginia, 2002	
Humans	24*
Horses	41
Birds	858
Mosquito Pools	180
**Includes two deaths.*	

Cases of Selected Notifiable Diseases Reported in Virginia*

Disease	Total Cases Reported, August 2002: State	Regions: NW	N	SW	C	E	Total Cases Reported Statewide, January through August: This Year	Last Year	5 Yr Avg
AIDS	38	1	15	3	3	16	511	645	609
Campylobacteriosis	95	17	36	24	11	7	381	356	407
***E. coli* O157:H7**	5	0	1	2	1	1	32	38	48
Giardiasis	56	13	22	5	8	8	174	247	259
Gonorrhea	699	37	43	81	201	337	6,598	7,510	6,245
Hepatitis A	18	0	13	3	2	0	73	89	119
B, acute	18	3	3	2	6	4	140	101	84
C/NANB, acute	4	0	0	3	0	1	5	0	9
HIV Infection	69	3	25	3	12	26	645	663	572
Lead in Children†	100	12	8	28	33	19	483	434	405
Legionellosis	6	1	1	3	0	1	16	17	17
Lyme Disease	24	9	7	0	3	5	67	94	69
Measles	0	0	0	0	0	0	0	1	2
Meningococcal Infection	1	0	0	0	1	0	28	31	33
Mumps	0	0	0	0	0	0	3	6	7
Pertussis	13	1	4	2	3	3	107	27	26
Rabies in Animals	66	9	18	18	12	9	391	278	367
Rocky Mountain Spotted Fever	7	2	0	0	4	1	22	15	10
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	142	20	37	24	31	30	640	894	728
Shigellosis	61	1	9	4	21	26	614	185	206
Syphilis, Early§	21	2	2	1	9	7	115	174	269
Tuberculosis	40	2	32	1	1	4	184	172	198

Localities Reporting Animal Rabies This Month: Accomack 1 fox; Albemarle 1 raccoon; Arlington 1 raccoon; Augusta 2 skunks; Bedford 1 cat, 1 skunk; Bland 1 raccoon; Buckingham 1 skunk; Carrool 1 cat, 1 fox; Charlotte 1 skunk; Dinwiddie 2 raccoons; Fairfax 2 bats, 8 raccoons; Fauquier 1 raccoon; Floyd 1 skunk; Franklin 1 raccoon; Frederick 2 skunk; Galax 1 bovine, 1 skunk; Grayson 1 raccoon; Halifax 1 fox; Hanover 1 raccoon; Henrico 1 raccoon; Isle of Wight 1 skunk; James City 1 skunk; King William 1 skunk; Lancaster 1 raccoon; Loudoun 1 fox, 2 raccoons, 1 skunk; Lynchburg 1 skunk; Mecklenburg 2 raccoons; Norfolk 1 raccoon; Pittsylvania 1 raccoon; Powhatan 1 bat; Prince Edward 1 bat; Prince William 3 raccoons; Rockingham 1 cat; Smyth 1 skunk; Spotsylvania 2 foxes; Stafford 1 bat; Sussex 1 fox; Tazewell 1 cat; Virginia Beach 1 cat, 1 fox, 1 raccoon; Washington 3 foxes; Wythe 1 raccoon.

Toxic Substance-related Illnesses: Asbestosis 32; Lead Exposure 10; Pneumoconiosis 5.

*Data for 2002 are provisional. †Elevated blood lead levels ≥10µg/dL.

§Includes primary, secondary, and early latent.

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Telephone: (804) 786-6261

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