

## INFLUENZA NEWS 2005

EPIDEMICS OF INFLUENZA typically occur during the winter months in temperate regions and have been responsible for an average of approximately 36,000 deaths a year in the United States. Influenza viruses can also cause pandemics, during which rates of illness and death from influenza-related complications can increase dramatically worldwide. Influenza viruses cause disease among all age groups. The rates of infection are the highest among children, but rates of serious illness and death are highest among people 65 years of age and older, children less than 2 years of age and persons of any age who have medical conditions that place them at increased risk for complications from influenza.

According to the Advisory Committee on Immunization Practices (ACIP), vaccination is cost-effective and is associated with reductions in influenza-related respiratory illness and physician visits among all age groups, hospitalization and death among persons at high risk, otitis media among children and work absenteeism among adults. The ACIP recommends using strategies to improve vaccination rates, including standing orders, recall systems, and vaccination during routine health care visits or during hospitalization. Additional efforts need to be made to reduce racial and ethnic disparities in vaccine coverage.

Two control measures are available in the U.S. to reduce the impact of influenza:

- vaccination with either the inactivated (i.e., killed virus) or live attenuated influenza vaccine
- antiviral agents.

Vaccination of high-risk persons each year before the influenza season is currently the most effective measure for reducing the impact of influenza. The current vaccine prepared for the 2005-2006 season will include:

<b>A/New Caledonia/20/99 (H1N1)-like strain</b>	<b>A/California/7/2004 (H3N2)-like strain</b>	<b>B/Shanghai/361/2002-like strain</b>
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### CLINICAL MANIFESTATIONS OF INFLUENZA

**TRANSMISSION:** Person-to-person primarily through coughing and sneezing.

**INCUBATION:** 1 to 4 days, with an average of two days.

**PERIOD OF CONTAGION:** One day before symptoms begin and for approximately five days after illness onset. Children can be infectious for a longer period.

**SYMPTOMS:** Abrupt onset of fever, myalgia (muscle pain), headache, nonproductive cough, severe malaise (fatigue), sore throat and rhinitis. Among children, otitis media, nausea, and vomiting are also commonly reported. Influenza typically resolves after several days, although cough and malaise can persist for more than two weeks. In some persons, influenza can exacerbate underlying medical conditions (e.g., pulmonary or cardiac disease), lead to secondary bacterial pneumonia or primary influenza viral pneumonia, or occur as part of a co-infection with other viral or bacterial pathogens. Influenza infection has also been associated with encephalopathy, transverse myelitis, Reye syndrome, myositis, myocarditis, and pericarditis.

## VACCINATION WITH INACTIVATED (KILLED-VIRUS) VACCINE

Inactivated influenza vaccine is made from highly purified, egg-grown viruses that have been rendered noninfectious (inactivated).

### Vaccine Administration

Age Group	Area	Needle length	Route
Infants 6-12 months	Anterolateral aspect of thigh	7/8 – 1 inch	IM*
Children 12 months and up	As above or deltoid if has sufficient mass	1 ¼ inch	IM
Adults and older children	Deltoid muscle	Greater than 1 inch	IM

\* Intramuscular

### Dosage Considerations

Age Group	Product	Dosage	Number of Dosages
6-35 months	Split virus	0.25 ml	1 or 2*
3-8 years	Split virus	0.50 ml	1 or 2*
9 years and above	Split virus	0.50 ml	1

\*Two doses given one month apart are recommended for children under nine years of age who are receiving the influenza vaccine for the first time, to ensure satisfactory antibody response.

### Manufacturers

Sonofi Pasteur (Fluzone®) (six months and over) (800) 822-2463

Chiron (Fluvirin®) (four years and over) (800) 244-7668

*Product package inserts should be consulted for more information. A limited supply of thimerosal-free vaccine is available*

## WHO SHOULD BE IMMUNIZED?

### Groups at High Risk for Influenza-Related Complications

Vaccination with inactivated influenza vaccine is recommended for the following persons who are at increased risk for complications from influenza:

- persons aged  $\geq 65$  years;
- residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions;
- adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma (hypertension is not considered a high-risk condition);
- 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 or by human immunodeficiency virus [HIV]);
- adults and children who have any condition (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration;
- children and adolescents (aged six months to 18 years) who are receiving long-term aspirin therapy and, therefore, might be at risk for experiencing Reye syndrome after influenza infection;
- women who will be pregnant during the influenza season; and
- children aged six to 23 months.

### **Persons Aged 50 to 64 Years**

Influenza vaccination is recommended for this entire age group to raise the low vaccination rates among persons in this age group with high-risk conditions. Age-based strategies for vaccination are more successful than strategies based on medical conditions.

### **Persons Who Can Transmit Influenza to Those at High Risk**

- Physicians, nurses, and other personnel in both hospital and outpatient care settings, including emergency response workers
- Employees of nursing homes and chronic care facilities
- Employees of assisted living and other residences for persons in high-risk groups
- Providers of home care to high-risk persons
- Household contacts (including children) of high-risk persons, and out-of-home caregivers of children 0 to 23 months.

### **Health-Care Workers**

All health-care workers should be vaccinated against influenza annually. Facilities that employ health-care workers should be strongly encouraged to provide vaccine to workers by using approaches that maximize vaccination rates. This will protect health-care workers, their patients, and communities, and will improve prevention of influenza-associated disease and patient safety, and will reduce disease burden.

### ***Other Groups***

#### **Foreign Travelers**

The risk for exposure to influenza during travel depends on the time of year and destination. In the tropics, influenza can occur throughout the year. In the temperate regions of the Southern Hemisphere, the majority of influenza activity occurs from April through September. In temperate climate zones of the Northern and Southern Hemispheres, travelers also can be exposed to influenza during the summer when coming into contact with persons from areas of the world where influenza viruses are circulating.

Persons at high risk for complications of influenza are those preparing to travel:

- to the tropics at any time of year
- to the Southern Hemisphere from April through September
- with organized tourist groups at any time of year.

If not vaccinated the previous fall/winter, they should consider influenza vaccination before travel. They should be especially encouraged to receive the most current vaccine. If that is not available for summer travel, antiviral medications could be carried for either prophylaxis or treatment. High-risk persons given the previous season's vaccine before travel should be revaccinated in the fall/winter with current vaccine.

#### **Breastfeeding Mothers**

The influenza vaccine does not affect the safety of mothers who are breastfeeding or their infants. Breastfeeding does not adversely affect immune response and is not a contraindication for vaccination.

#### **General Population**

Any person who wishes to reduce his/her chances of acquiring influenza infection should be vaccinated if vaccine is available. Persons who provide essential community services, students and/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.

## **WHO SHOULD NOT BE VACCINATED?**

- Persons who have an anaphylactic hypersensitivity to eggs (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) should not be vaccinated with influenza vaccine.
- Persons with acute febrile illnesses (100.4°F or higher) normally should not be vaccinated until their fever has abated.

## WHEN SHOULD YOU VACCINATE?

This recommended schedule is proposed in view of the potential for delays in vaccine supply.

<b>September</b>	If vaccine is available, high-risk persons receiving routine health care visits or hospitalizations including previously unvaccinated children under nine years who will need a second dose.
<b>October</b>	-Persons 50 years and older -Adults and children at high risk for serious influenza illness -Health care workers -Household contacts of high-risk individuals (including contacts of infants under six months who are not eligible for influenza vaccine)
<b>November</b>	Other persons who wish to decrease their risk for influenza infection
<b>December through March</b>	Influenza vaccine can continue to be given.

It is recommended that mass immunization clinics not be scheduled until after mid-October to ensure vaccine availability. Influenza and pneumococcal vaccines can be given at the same time in different arms without increasing side effects.

### Side Effects and Adverse Reactions

Soreness around the vaccination site for up to two days may occur. This reaction is generally mild and rarely interferes with the person's ability to conduct usual daily activities.

Fever, malaise, myalgia, and other systemic symptoms occur infrequently and most often affect persons with no prior exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6 to 12 hours after vaccination and can persist for one or two 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 – most likely residual egg protein.

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.

## VACCINATION WITH LIVE ATTENUATED INFLUENZA VACCINE

### Vaccine Administration and Dosage

Live, attenuated influenza vaccine (LAIV) is administered via nasal spray and is approved for healthy persons 5 to 49 years, including health care workers and other persons in close contact with groups at high risk and those wanting to avoid influenza. This vaccine must be stored in a non-frost-free freezer to be maintained continuously at -15°C or below. LAIV must be thawed before administration. Prior to administration it may be thawed in a refrigerator and stored at 2°C to 8°C for no more than 60 hours prior to use. It may also be thawed just prior to use by holding the individual sprayer in the palm of the hand. LAIV should not be refrozen after thawing. It is supplied in a pre-filled, single-use sprayer containing 0.5ml of vaccine. Approximately 0.25ml is sprayed into the first nostril with the recipient in the upright position. An attached dose-divider clip is removed to administer the second half of the dose into the other nostril. If the recipient sneezes, the dose does not have to be repeated.

### Manufacturer

MedImmune, Inc. (FluMist®) **800-FLU-MIST**

## WHO SHOULD NOT BE VACCINATED?

- persons aged <5 years or those aged  $\geq 50$  years
- adults and children with asthma, reactive airways disease, or other chronic disorders of the pulmonary or cardiovascular systems
- adults and children with other underlying medical conditions, including chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus [HIV])
- children or adolescents receiving long-term aspirin therapy and, therefore, might be at risk for experiencing Reye syndrome after influenza infection
- persons with a history of Guillain-Barré Syndrome
- pregnant women
- persons who have an anaphylactic hypersensitivity to eggs (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis)

**A table of comparison of LAIV and inactivated influenza vaccine**

<b>Factor</b>	<b>LAIV</b>	<b>Inactivated influenza vaccine</b>
Route of administration	Intranasal spray	Intramuscular injection
Type of vaccine	Live virus	Killed virus
Number of included virus strains	3 (2 influenza A, 1 influenza B)	Same as LAIV
Grown in an egg based medium	Yes	Yes
Vaccine virus strains updated	Annually	Same as LAIV
Frequency of administration	Annually	Same as LAIV
Approved age and risk groups	Healthy Persons Aged 5 to 49 years	Persons $\geq$ six months
Can be administered to contacts (including healthcare workers) of immunosuppressed persons not requiring a protected environment	Yes	Yes
Can be administered to contacts of immunosuppressed persons requiring a protected environment	No	Yes
Can be simultaneously administered with other vaccines	Yes	Yes
If not simultaneously administered, can be administered in less than four weeks of another live vaccine	No, wait a total of four weeks	Yes
If not simultaneously administered, can be administered within four weeks of an inactivated vaccine	Yes	Yes
Can be given to pregnant women	No	Yes
Can be given to children or adolescents receiving aspirin therapy	No	Yes
For children under nine years receiving vaccine for the first time, timing of the two doses	6 to 10 weeks apart	four weeks apart

# ANTIVIRAL AGENTS FOR INFLUENZA

Antiviral drugs for influenza are an important adjunct to influenza vaccine for the control and prevention of influenza. However, they are not a substitute for vaccination.

## Influenza A Only

Agent	Approved for Treatment	Approved for Prophylaxis
Amantadine	One year and older	One year and older
Rimantadine	13 years and older	One year and older

## For Influenza A and B

Agent	Approved for Treatment	Approved for Prophylaxis
Oseltamivir	One year and older	13 years and older
Zanamivir	Seven years and older	N/A

### Treatment Recommendations

When administered within two days of illness onset to otherwise healthy adults, these medications can reduce the duration of uncomplicated influenza. These four drugs differ in terms of their pharmacokinetics, side effects, and costs. You should consult the package inserts for more information.

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

### Prophylaxis Recommendations

In order to be maximally effective, amantadine, rimantadine or oseltamivir must be taken each day for the duration of influenza activity in the community. However, cost, compliance, and potential side effects should always be considered. When outbreaks of influenza occur, or are suspected, in institutions housing persons at risk, chemoprophylaxis should be started as soon as possible to reduce the spread of virus. To be fully effective, the chosen drug should be administered daily to all residents of a contained facility, regardless of their influenza vaccination status, for at least two weeks or approximately one week after the end of the outbreak.

Chemoprophylaxis with one of these three drugs is also recommended in the following situations:

- Persons at high-risk, vaccinated after influenza activity has begun (for two weeks after vaccination)
- Unvaccinated persons providing care to those at high-risk
- Persons with an immune deficiency who may be expected to have an inadequate antibody response to influenza vaccine
- Persons for whom influenza vaccine is contraindicated – see “Side Effects and Adverse Reactions”
- Anyone else under the advice of their physician.

### Considerations

Both amantadine and rimantadine can cause central nervous system (CNS) and gastrointestinal side effects. These CNS side effects include nervousness, anxiety, impaired concentration, lightheadedness and dizziness. A study among healthy young adults in a controlled setting found the incidence of these side effects to be higher in participants receiving amantadine rather than rimantadine. The incidence of gastrointestinal side effects (nausea and anorexia) is approximately one percent. Side effects for both drugs are usually mild and cease soon after discontinuing the drug.

Modifications in dosage may be required for persons with impaired renal or liver function, the elderly, children, persons with neuropsychiatric disorders or those who take psychotropic drugs, and persons with a history of seizures.

Always consult the package insert before the use of any antiviral agent.

Influenza viruses resistant to amantadine and/or rimantadine can emerge in up to one-third of patients when either drug is used for treatment. Resistant strains can be transmitted between people, although data indicates that these resistant viruses are no more virulent or transmissible than amantadine-rimantadine-sensitive viruses.

Studies have shown that zanamivir can cause a decline in respiratory function among patients with underlying chronic respiratory disease so it is not recommended for these persons. If physicians decide to prescribe zanamivir to patients with asthma and COPD, the drug should be used with caution under conditions of proper monitoring and supportive care, including the availability of short acting bronchodilators. Patients should be advised to have a fast-acting inhaled bronchodilator handy and to stop using zanamivir and contact their physician if they have difficulty breathing.

Oseltamivir may cause nausea and vomiting. If severe, oseltamivir should be taken with food.

The manufacturers include:

<b>Medication</b>	<b>Manufacturer</b>
Amantadine	Endo Pharmaceuticals (Symmetrel®-tablet & syrup) <b>800-462-3636</b> Geneva Pharms Tech (Amandine HCL-capsule) USL Pharma (Amantadine HCL- capsule & tablet) <b>800-654-2299</b> Alpharma, Carolina Medical, Copley Pharmaceutical, HITech Pharma, Mikart, Morton Grove, and Pharmaceutical Associates (Amantadine HCL-syrup), and Sandoz
Rimantadine	Corepharma, Impax Labs (Rimantadine HCL- tablet ) <b>732-868-1090</b> Forest Laboratories (Flumadine®-tablet and syrup) <b>800-678-1605</b> Amide Pharmaceuticals (Rimantadine HCL-tablet) <b>215-289-2220</b>
Zanamivir	GlaxoSmithKline (Relenza®-inhaled powder) <b>800-334-0089</b>
Oseltamivir	Roche Pharmaceuticals (Tamiflu®-tablet) <b>800-526-6367</b>

## **Sources of Information**

Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR July 13, 2005/Vol 53;1-40

Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP) Revision MMWR July 29, 2005/Vol.54/No.RR-8

National Foundation for Infectious Diseases

Information regarding influenza surveillance, prevention, detection, and control is available at [www.cdc.gov/flu/weekly/fluactivity.htm](http://www.cdc.gov/flu/weekly/fluactivity.htm). Surveillance information is available through the CDC Voice Information System (influenza update) at 888-232-3228 or CDC Fax Information Service at 888-232-3299. During October through May, surveillance information is updated at least every other week. In addition, periodic updates regarding influenza are published in the MMWR. Additional information regarding influenza vaccine can be obtained by calling the CDC Immunization Hotline at 800-232-2522 (English) or 800-232-0233 (Spanish). State and local health departments should be consulted regarding availability of influenza vaccine, access to vaccination programs, information about state or local influenza activity, and for reporting influenza outbreaks and receiving advice concerning outbreak control.

**Influenza News 2005** was updated by the Connecticut Influenza and Pneumococcal Coalition, cosponsored by the American Lung Association of Connecticut.