



## *Influenza*

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**I**nfluenza is a respiratory illness caused by either influenza A or influenza B viruses. Sporadic cases or outbreaks of influenza can occur at any time during the year, but epidemic activity peaks during the winter months in temperate climates. Influenza is usually a self-limited illness; however, elderly persons and those with pre-existing chronic cardiac and pulmonary disease are at higher risk for developing severe complications from influenza. Vaccination is the most effective means of preventing influenza and its complications.

### **Prevalence and Distribution**

The timing of influenza activity differs by zone. The onset of influenza activity in temperate climates typically occurs in late fall, although the timing of individual influenza seasons can vary substantially from year to year. In the northern hemisphere, peak influenza activity typically occurs between December and March, while in the southern hemisphere influenza peak activity typically occurs between May and August. Outbreaks of influenza often occur in unvaccinated populations.

Rates of infection are highest in children, but elderly persons and persons with certain medical conditions which predispose them to complications from influenza have the highest rates of serious morbidity and mortality. Millions are infected with influenza each year in the United States and over 100,000 individuals on average are hospitalized annually for influenza or its complications. Influenza is estimated to cause an average of 36,000 deaths per year in the United States.

Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus:

the hemagglutinin and the neuraminidase. Minor changes in the hemagglutinin are referred to as “antigenic drift” and facilitate seasonal epidemics. Replacement of the hemagglutinin with a new hemagglutinin is known as “antigenic shift”. Such changes are associated with the development of influenza pandemics.

### **Mode of Transmission**

Influenza virus is primarily spread from person to person through coughing and sneezing of virus particles in respiratory secretions. On average the incubation period lasts two days, but can range from one to four days. The period of infectivity for adults begins about 1 day prior to the development of symptoms and typically lasts for 3 to 5 days after the onset of symptoms.

### **Symptoms and Diagnosis**

The classic symptoms of influenza include the abrupt onset of fever accompanied by chills, myalgias, headache, malaise, nonproductive cough and sore throat. Rhinitis may also be present. The

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*“The Sneeze”.*  
*Sneezing is a very efficient way to spread many airborne diseases, such as influenza. The virus is contained in the many small droplets shown by backlighting in this photograph.*  
*Photo courtesy of the CDC*

**Table 1: Drugs Used in Prevention and Treatment of Influenza**

Drug	Type of influenza	Effectiveness in prevention	Side effects
amantadine (Symmetrel™)	A	70-90%	CNS (dizziness, jitteriness, insomnia, anxiety), CHF, anticholinergic effects
rimantadine (Flumadine™)	A	70-90%	CNS (less than amantadine)
oseltamivir (Tamiflu™)	A and B	82%	Nausea, vomiting
zanamivir* (Relenza™)	A and B	84%	Bronchospasm

\*zanamivir is not approved for the prevention of influenza

symptoms of influenza are difficult to distinguish from many other viral upper respiratory infections that occur during the winter months and the predictive value of these symptoms for diagnostic purposes reflects the degree of co-circulation of other respiratory pathogens and influenza viruses. When influenza viruses are circulating, fever and cough are the most useful diagnostic symptoms, with reports of sensitivity ranging from 63-73% and reports of specificity ranging from 55-71%. A fever of 100°F/37.7°C (or 99°F/37.2°C in the elderly) and cough within 48 hours of symptom development in one study had a positive predictive value of 79%. The positive predictive value increases to greater than 80% if the fever increases to 100.4°F (38°C). Since influenza cases can occur year-round, health care providers must remain alert to the possibility of influenza throughout the year, especially when outbreaks of respiratory illness occur.

The physical examination is usually unrevealing in uncomplicated influenza infection. Confirmatory testing can be very helpful in making a diagnosis of influenza. The gold standard for laboratory testing is viral culture. Other diagnostic tests include rapid antigen testing, polymerase chain reaction and immunofluorescence. Serology requires the collection of an acute and convalescent serum sample. The sensitivity and specificity of these tests vary greatly depending on the lab performing the test, the type of test and the specimen type. Rapid antigen tests have become widely used in outpatient clinics because results can be obtained within 30 minutes or less. When interpreting the results of rapid tests, one should take into account the community prevalence of influenza and the pre-test probability of disease.

### Treatment and Complications

Influenza is usually a self-limited illness that resolves after several days, although cough and malaise may persist for 2 weeks or longer. The treatment of uncomplicated influenza is supportive, with analgesics to treat fever and myalgias, and antitussives for cough when needed. Aspirin should be avoided in children with fever. Fever can increase insensible losses, and fluids are necessary to prevent dehydration. Influenza can exacerbate pre-existing medical conditions such as asthma or chronic obstructive pulmonary disease (COPD), and these patients should be monitored closely for exacerbation of underlying conditions.

Antiviral medications can reduce the duration of illness by 1 day when started within 48 hours of illness onset (Table 1). They have not been shown to be effective at preventing serious influenza-related complications such as bacterial pneumonia. The adamantanes, amantadine and rimantadine, are older drugs that are effective only against influenza A. Side effects of the adamantanes include central nervous system disturbances such as jitteriness, insomnia, and anxiety. These side effects occur more frequently with amantadine and are more pronounced in the elderly. Neuraminidase inhibitors, oseltamivir (Tamiflu™) and zanamivir (Relenza™), are approved for the treatment of both influenza A and B, and have fewer side effects than amantadine or rimantadine.

Antivirals can be useful for prophylaxis of unvaccinated persons or those at high risk for influenza related complications, as well as for treatment of ill individuals.

Pneumonia is the most common secondary bacterial complication of influenza. Less often influenza may lead to primary viral pneumonia,

which is usually severe and should be suspected in a patient with progression of fever and respiratory symptoms beyond what would be expected from uncomplicated infection. Secondary bacterial pneumonia is more common and should be suspected when symptoms associated with pneumonia appear after initial improvement of influenza illness. One case series reported that *Streptococcus pneumoniae* and *Staphylococcus aureus* are the most common pathogens, occurring in 48% and 19% of secondary bacterial pneumonia cases, respectively.

Myositis and rhabdomyolysis are infrequent complications of influenza, occurring more often in children. Aspirin should not be used in treating children with suspected influenza because of the association with Reye syndrome, a rare illness marked by central nervous system disturbance and hepatic dysfunction. Central nervous system complications of influenza are uncommon, but influenza should be considered in the differential diagnosis of encephalitis/encephalopathy in children

### Prevention and Control

Vaccination is the best way to prevent influenza and is indicated for persons at increased risk of complications from influenza, as well as close contacts of those at increased risk (Table 2). The most widely used influenza vaccine is a trivalent inactivated vaccine and consists of two A viruses and one B virus. Vaccine effectiveness depends on the match between the vaccine and circulating virus, as well as the age and immune status of

the host. In years when the match between the vaccine and the circulating virus has been good, vaccination has prevented influenza in 70-90% of vaccinated, healthy adults under the age of 65, and 58% of vaccinated elderly persons. Vaccination is 30-70% effective in preventing hospitalization for pneumonia and influenza in persons aged 65 years. The vaccine is less effective in preventing primary influenza illness in nursing home residents, but can be 50-60% effective in preventing pneumonia and hospitalization, and 80% effective in preventing death in this high-risk population.

Recently, a live, attenuated trivalent influenza vaccine (LAIV) was approved by the Food and Drug Administration (FDA) for intranasal administration. Efficacy is similar to the inactivated influenza vaccine in healthy adults and children. Currently LAIV is approved only for healthy persons aged 5-49 years.

Influenza vaccine can be cost-effective in some circumstances. Savings in the elderly population are related to decreased hospitalization and death. In those younger than 65, savings are due to a decrease in direct medical costs, as well as indirect costs associated with a decrease in work absenteeism.

The ideal time to vaccinate in the northern hemisphere is October and November, as most influenza infections occur in late December through March. Peak antibody protection occurs two weeks after vaccination. Antibody levels begin to fall in the elderly within 4 months, but data are not available to support a second administration of the vaccine to boost immunity. A new vaccine, updated to cover

**Table 2: Indications for Influenza Vaccination**

#### Increased Risk of Complications

- ◆ Age ≥ 65
- ◆ Residents of nursing homes and chronic care facilities
- ◆ Chronic cardiovascular and pulmonary disease, including asthma
- ◆ Chronic metabolic diseases (diabetes), renal disease, hemoglobinopathies, or immunosuppression (chronic steroids, HIV)
- ◆ Children receiving long-term aspirin therapy
- ◆ Women who will be pregnant during influenza season
- ◆ All children aged 6 -23 months

#### Age 50-64 years

- ◆ Exposure to high risk persons
- ◆ Health care workers
- ◆ Employees of nursing homes and chronic care facilities
- ◆ Household contacts of high risk persons

newly circulating strains, must be given annually.

Individuals with hypersensitivity to eggs should not receive the vaccine without consultation with a physician. Vaccination generally should be deferred in patients with an acute febrile illness.

The most common side effect of influenza vaccination is soreness at the injection site, occurring in 10-64% of patients and lasting <2 days. Fever, malaise and myalgias may also occur after vaccination. These side effects usually begin within 6-12 hours of inoculation, persist for 1-2 days and are more common in first time recipients of the vaccine. Influenza vaccine cannot cause influenza.

Despite its effectiveness and safety, influenza vaccine remains underutilized. Only 64% of the elderly and 32% of those aged 50-64 were vaccinated in the 2000-2001 season. Vaccination rates are lower in African-Americans and Latinos than in Caucasians.

Antiviral agents are effective in the prevention of influenza, but vaccination remains the primary means for prevention. Amantadine and rimantadine are 70-90% effective in preventing influenza A infection. The newer antivirals, oseltamivir (Tamiflu™) and zanamivir (Relenza™) are 82% and 84% effective in preventing influenza, respectively. Chemoprophylaxis may be warranted in populations such as residents of chronic care facilities during outbreaks of influenza. In addition to vaccination and antiviral agents, hand washing is important for decreasing transmission rates of respiratory infections.

### Special Considerations for Homeless Populations

Influenza infection rates, morbidity, mortality, and vaccination coverage in homeless populations are unknown. The crowded living conditions and

poor ventilation in many shelters, as well as the high incidence of chronic medical conditions, may place homeless persons at increased risk for contracting influenza. Homeless shelters offer a unique opportunity to administer influenza vaccines to both residents and staff. Vaccination may be provided to all residents and staff who do not have specific contraindications. Since homeless populations are often mobile, a coordinated effort to vaccinate all staff and residents during the same day or week in a particular area may be attempted. This effort should include outreach efforts to vaccinate homeless populations not living in shelters to maximize coverage.

### Summary

Influenza is a contagious respiratory illness that occurs primarily during the winter months in temperate climates. The illness is usually self-limited, but the elderly and persons with chronic medical conditions are at increased risk for serious complications. Vaccination is the most effective way to prevent influenza and its complications. To prevent the spread of influenza, residents of shelters and homeless persons should consider receiving annual influenza vaccination. The optimal time for vaccination is in the fall, and vaccination of all homeless persons on the same day or within the same week may be an effective strategy. ■

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Influenza Medication List		
Generic	Brand Name	Cost
amantadine	Symmetrel	\$
oseltamivir	Tamiflu	\$\$\$
rimantadine	Flumadine	\$\$
zanamivir	Relenza	\$\$

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