Flu Season! 2011/2012

3.0 contact hours: $19

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Course Summary: Annual review of clinical features, epidemiology, and vaccine schedule and use for prevention and treatment of seasonal influenza.

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This course will be reviewed yearly. It will be updated or discontinued on October 1, 2012.

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Course Objectives

When you finish this course, you will be able to:

- Describe the origins of the flu.
- Explain the major features and behavior of influenza viruses.
- Outline the epidemiological features of influenza.
- List the methods and purpose of influenza surveillance.
- Identify the clinical features of influenza.
- Explain the process for laboratory diagnosis of influenza.
- Delineate the treatment of those with the flu, including basic prevention measures.
- Highlight those populations that are at high risk for infection.
- Outline the use of antiviral agents for influenza.
- Discuss the influenza vaccine, including its characteristics and efficacy and scheduling and use.

Bulletin as Flu Season Begins

August 30, 2011. *The New York Times* reports: "The Food and Agriculture Organization of the United Nations on Monday warned of 'a possible major resurgence' of the H5N1 highly pathogenic **avian influenza virus** in the coming months."

The *Los Angeles Times*: "Booster Shots" blog reports that "the United Nations' Food and Agriculture Organization (FAO) 'urged heightened readiness and surveillance against a possible major resurgence'" of avian flu, which is rising after a previous decline. This year, seven people in Cambodia have died of avian influenza. The FAO says the cause of the virus' reappearance is "birds' migrations, boosted by poultry farming practices," in conjunction with "a new mutant strain of the virus, resistant to vaccines and known as H5N1 2.3.2.1," which has been found in China and Vietnam.

The *Associated Press*: "FAO says bird migrations over the past two years have brought H5N1 to countries that had been virus-free for several years, including Israel, the Palestinian territories, Bulgaria, Romania, Nepal, and Mongolia." FAO's chief veterinary officer, Juan Lubroth, expressed worry that an H5N1 outbreak may occur in winter 2011.

Introduction

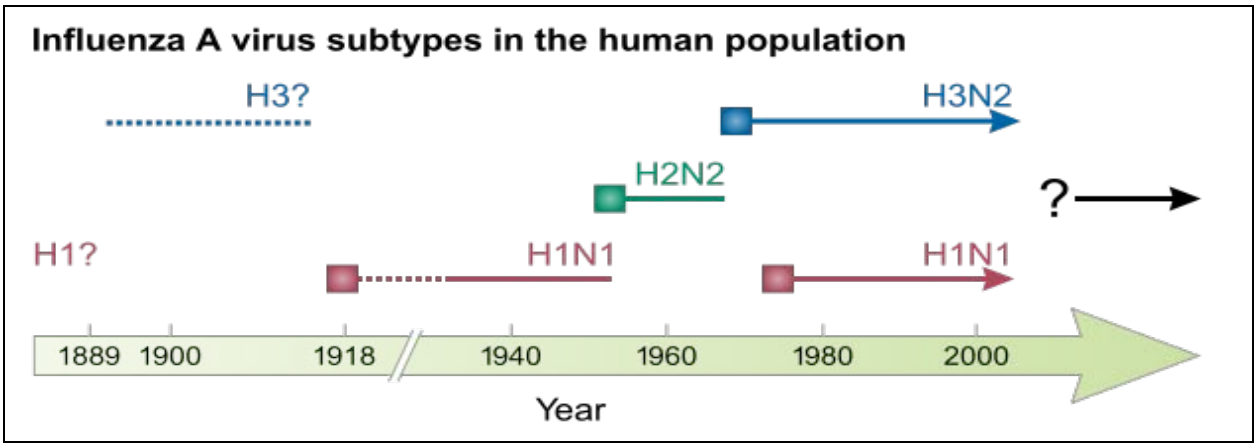
Influenza (the flu) is a contagious respiratory illness caused by influenza viruses. It can cause mild to severe illness, and at times can lead to death. Older adults, young children, and people with certain health conditions are at especially high risk for serious flu complications. The best way to prevent the flu is by vaccination each year (CDC, 2011).

In the spring of 2009 a new influenza A virus (H1N1) emerged to cause illness in humans. This virus was very different from regular influenza A, and it caused the first influenza pandemic in more than forty years. The 2009 H1N1 has now mostly replaced the H1N1 virus that was previously circulating in humans. The CDC expects the 2009 H1N1 virus, along with other influenza viruses, to cause illness again this year, and so the updated flu vaccine will protect against 2009 H1N1 plus two other influenza viruses (CDC, 2011a).

The name **influenza** most likely comes from the Italian word for influence and refers to the early belief that diseases were influenced by astrological or other forces. While modern doctors believe that outbreaks of influenza may be traced as far back as 412 B.C.E., the first **pandemic**, or worldwide epidemic, that clearly fits the description of influenza occurred in 1580. It began in Asia and spread to much of the rest of the world, affecting nearly all of Europe in just six weeks (Ghendon, 1994).

At least four pandemics of influenza occurred in the nineteenth century, and they were followed with three more in the twentieth century. The pandemic of "Spanish" influenza in 1918/1919 caused an estimated 21 million deaths worldwide (CDC, 2011 Pink Book).

Influenza A Virus Subtypes in the Human Population



The various strains of influenza that have infected the human population in the twentieth century. Source: Palese, 2004.

The influenza A virus was isolated in ferrets in 1933, and the influenza B virus was isolated in 1936. In that same year, it was discovered that influenza virus could be grown in embryonated hens' eggs. This led to the study of the characteristics of the virus and the development of inactivated vaccines. The protective efficacy of these inactivated vaccines was determined in the 1950s, and the first live attenuated influenza vaccine was licensed in 2003 (CDC, 2011PB).

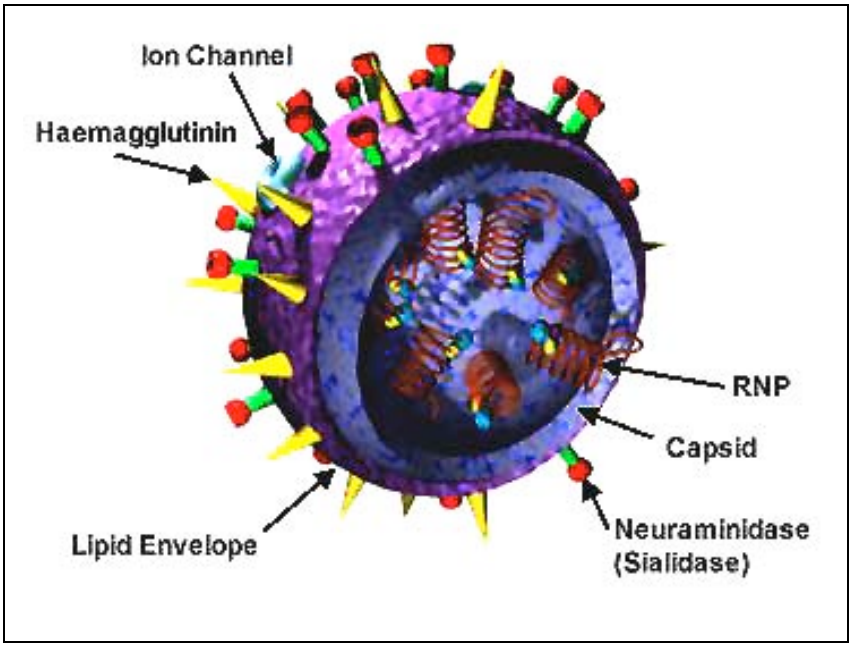
The Influenza Virus and Its Antigenic Changes

Influenza is a single-strand, helically shaped RNA virus of the orthomyxovirus family. There are three types of influenza viruses—A, B and C—which are determined by the nuclear material of the virus. Human influenza A and B viruses cause seasonal epidemics of disease almost every winter in the United States. Influenza type C infections cause a mild respiratory illness and are not thought to cause epidemics (CDC 2011a; CDC, 2011PB).

Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: hemagglutinin (H) and neuraminidase (N). There are sixteen hemagglutinin subtypes and nine neuraminidase subtypes. Three types of hemagglutinin in humans—H1, H2, and H3—have a role in the virus's attachment to cells. Two types of neuraminidase—N1 and N2—have a role in virus penetration into cells (CDC, 2011PB). These proteins are also referred to as **antigens**, substances that, when introduced into the body, stimulate the production of an antibody.

Influenza A viruses can be further broken down into a number of strains. Current subtypes of influenza A viruses found in people are influenza A (H1N1) and influenza A (H3N2) viruses (CDC, 2011a; CDC, 2011PB).

Structure and Cross Section of the Influenza Virus



Structure of the influenza virus. The hemagglutinin and neuraminidase proteins are shown on the surface of the particle. The viral RNAs that make up the genome are shown as red coils inside the particle and bound to ribonuclear proteins (RNPs). From: NIH, public domain.

Influenza A causes moderate to severe illness and affects all age groups. The virus infects both humans and other animals. Influenza A viruses are perpetuated in nature by wild birds, predominantly waterfowl. Most of these viruses are not pathogenic to their natural hosts and do not change or evolve (CDC, 2011PB).

Influenza B generally causes milder disease than type A and primarily affects children. Influenza B is more stable than influenza A, with less **antigenic drift** (change over time) and consequent immunologic stability. It affects only humans (CDC, 2011PB).

Influenza C is rarely reported as a cause of human illness, probably because most cases are subclinical. It has not been associated with epidemic disease (CDC, 20011PB).

Influenza Virus

- Single-stranded RNA virus
- Orthomyxoviridae family
- 3 types: A, B, C
- Subtypes of type A determined by hemagglutinin and neuraminidase

Source: NLM, 2004a.

Strains of Influenza Virus

- Type A
  - moderate to severe illness
  - all age groups
  - humans and other animals
- Type B
  - milder disease
  - primarily affects children
  - humans only
- Type C
  - rarely reported in humans
  - no epidemics

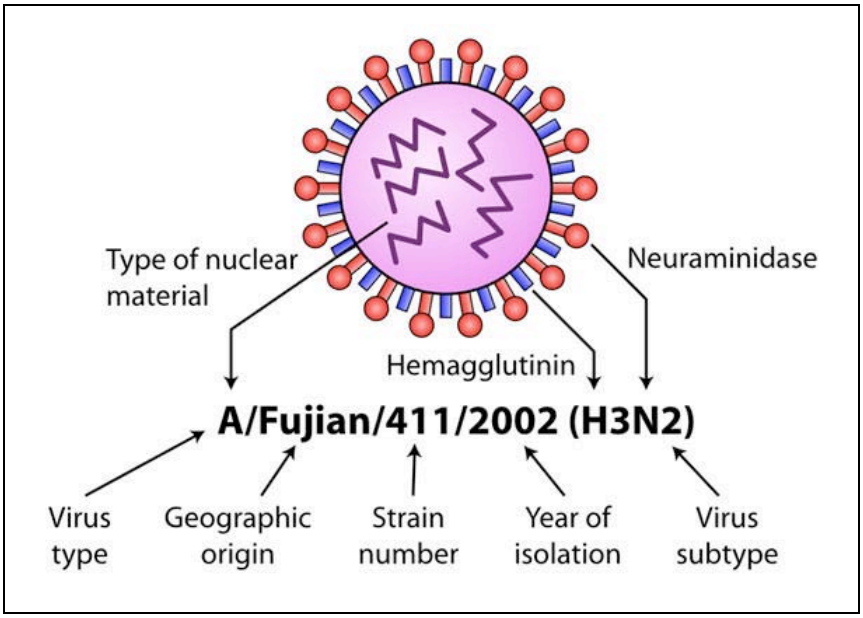
Source: CDC Pink Book p.151.

The nomenclature used to describe the type of influenza virus is expressed in this order:

1. Virus type,
2. Geographic site where it was first isolated,
3. Strain number,
4. Year of isolation, and
5. Virus subtype.

The following illustration shows the influenza nomenclature.

Influenza Virus Nomanclature



Source: CDC Pink Book, p. 151.

Hemagglutinin and neuraminidase periodically change, apparently evolving in response to antibodies arising in immune or partly immune populations. Thus infection is followed by the production of antibodies, which trigger mutations that allow the virus to survive. At irregular intervals of 10 to 40 years, viruses appear that show major antigenic differences from prevalent subtypes and, because the population does not have protective antibodies against these new antigens, they cause pandemic disease in all age groups (CDC, 2011PB).

Influenza viruses can change in two ways. One type of change is called **antigenic drift**. These are small changes in the virus's surface antigens that happen continually over time. Antigenic drift produces new virus strains that may not be recognized by the body's immune system. This process works as follows: a person infected with a particular flu virus strain develops antibodies against that virus. As newer virus strains appear, the antibodies against the older strains do not recognize the newer virus, and reinfection can occur (CDC, 2011b; CDC, 2011PB).

This is why people can get the flu more than once. In most years, one or two of the three virus strains in the influenza vaccine are updated to keep up with the changes in the circulating flu viruses; thus, people who want to be protected from flu need to get a flu shot every year. Antigenic drift may result in an epidemic because the protection that remains from past exposures to similar viruses is incomplete. Drift occurs in all three types of influenza virus (A, B, C) (CDC, 2011b; CDC, 2011PB).

The other type of change is called **antigenic shift**—a major abrupt change in influenza A viruses in one or both surface antigens (H or N) that occurs at varying intervals. Antigenic shifts are probably due to genetic recombination (an exchange of a gene segment), also called reassortment, between influenza A viruses, usually those that affect humans and birds. Shift results in a new influenza A subtype or a virus with a hemagglutinin or a hemagglutinin and neuraminidase combination that has emerged from an animal population that is so different from the same subtype in humans that most people do not have immunity to the new virus (CDC, 2011b; CDC, 2011PB).

An antigenic shift may result in a worldwide pandemic if the virus is efficiently transmitted from person to person. Since the late nineteenth century, four occurrences of antigenic shifts have led to major pandemics. Such a shift occurred in the spring of 2009, when a new H1N1 virus with a new combination of genes emerged to infect people and quickly spread, causing a pandemic. When shift happens, most people have little or no protection against the new virus (CDC, 2011b; CDC, 2011PB).

While influenza viruses are changing by antigenic drift all the time, antigenic shift happens only occasionally. Type A viruses undergo both kinds of changes; influenza type B viruses change only by the more gradual process of antigenic drift (CDC, 2011b; CDC, 2011PB).

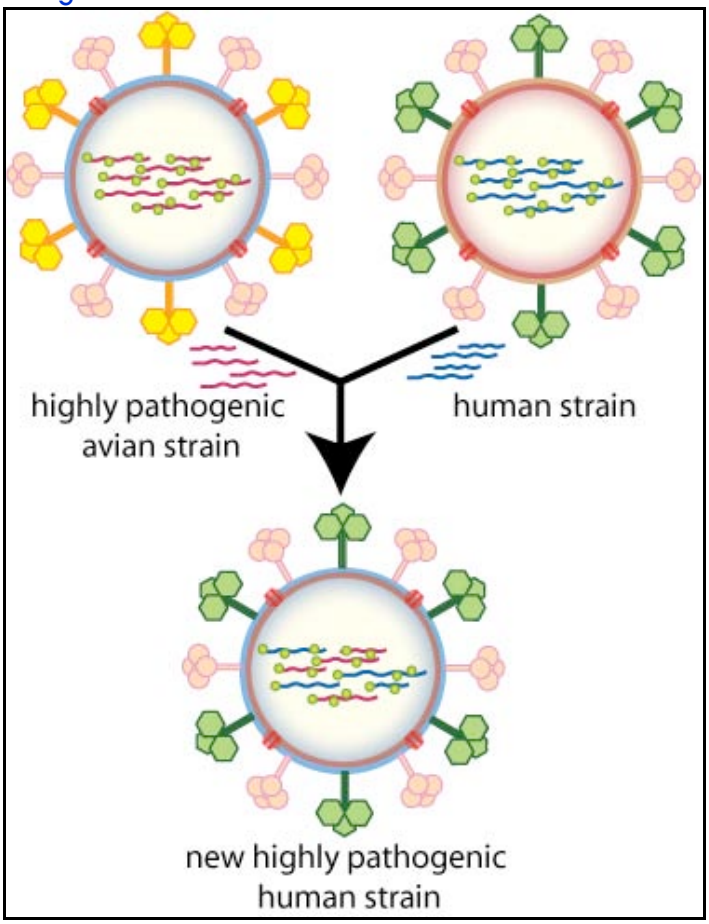
Influenza Antigenic Changes

- Antigenic Shift
  - major change, new subtype
  - caused by exchange of gene segments
  - may result in pandemic

- Antigenic Drift
  - minor change, same subtype
  - caused by point mutations in gene
  - may result in epidemic

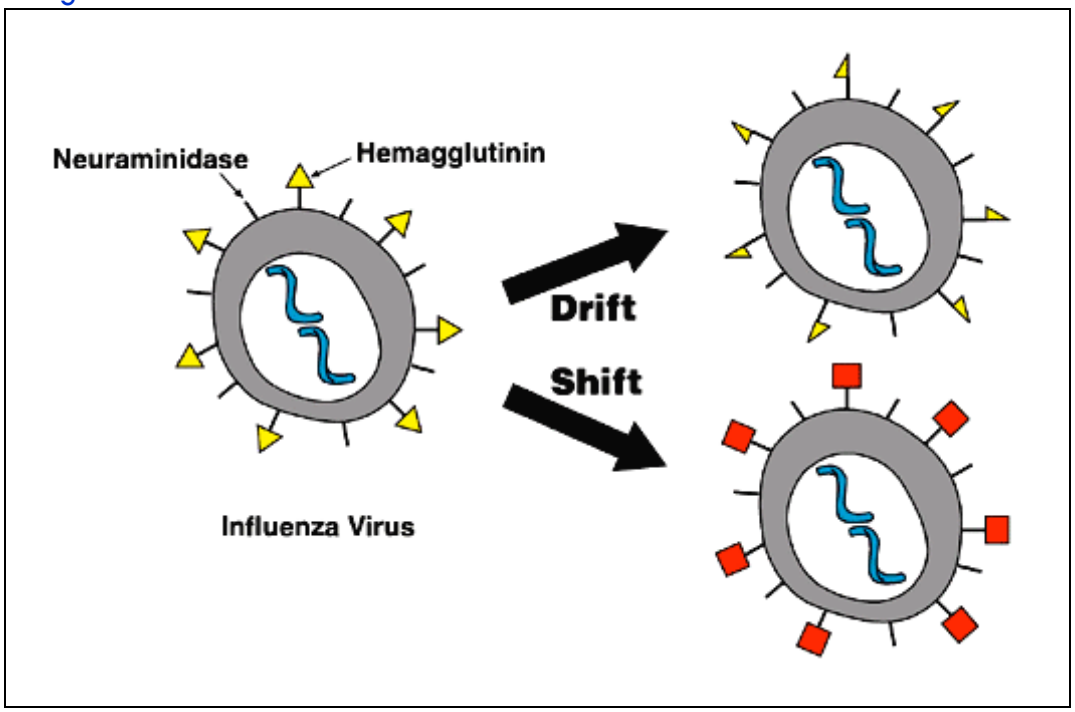
Source: Adapted from CDC Pink Book, p. 152.

Antigenic Shift of Influenza Strains



Antigenic shift. Source: Wikipedia Commons.

Antigenic Shift and Drift of Influenza Strains



Antigenic shift vs. drift. Antigenic drift creates influenza viruses with slightly modified antigens, while antigenic shift generates viruses with entirely new antigens. Source: Wikipedia Commons and USDA.

Epidemiology

Influenza occurs throughout the world. Humans are the only known reservoir of influenza types B and C. Influenza A may infect both humans and animals, and influenza A viruses are found in many different animals, including ducks, chickens, pigs, whales, horses, and seals.

Influenza in Animals

Wild birds are the primary natural reservoir for all subtypes of influenza A viruses and are thought to be the source of influenza A viruses in all other animals. Most influenza viruses cause asymptomatic or mild infection in birds; however, the range of symptoms in birds varies greatly depending on the viral strain. Infection with certain avian influenza A viruses (eg, some strains of H5 and H7 viruses) can cause widespread disease and death among some species of wild—and especially domestic—birds such as chickens and turkeys (CDC, 2011c).

Pigs can be infected with both human and avian influenza in addition to swine influenza viruses. Infected pigs get symptoms similar to humans, such as cough, fever, and runny nose. Because pigs are susceptible to avian, human, and swine influenza viruses, they potentially may be infected with influenza viruses from different species (eg, ducks and humans) at the same time. If this happens, it is possible for the genes of these viruses to mix and create a new virus (CDC, 2011c).

For example, if a pig were infected with a human influenza virus and an avian influenza virus at the same time, the viruses could mix (**reassort**) and produce a new virus that had most of the genes from the human virus, but a hemagglutinin and/or neuraminidase from the avian virus. The resulting new virus would likely be able to infect humans and spread from person to person, but it would have surface proteins (hemagglutinin and/or neuraminidase) not previously seen in influenza viruses that infect humans. This type of major change in the influenza A viruses is an example of antigenic shift (CDC, 2011c).

While it is unusual for people to get influenza infections directly from animals, sporadic human infections and outbreaks caused by certain avian influenza A viruses have been reported (CDC, 2011c).

2009 influenza A (H1N1) was a new flu virus of swine origin that first caused illness in Mexico and the United States in March and April, 2009. This virus was originally referred to as "swine flu" because laboratory testing showed that many of the genes in this new virus were very similar to influenza viruses that normally occur in pigs (swine) in North America.

Further study, however, has shown that this new virus is very different from the one that has formerly circulated in North American pigs. It has two genes from flu viruses that have circulated in pigs in Europe and Asia, plus bird (avian) genes and human genes. Scientists call this a "quadruple reassortant" virus (CDC, 2011c).

Influenza in Humans

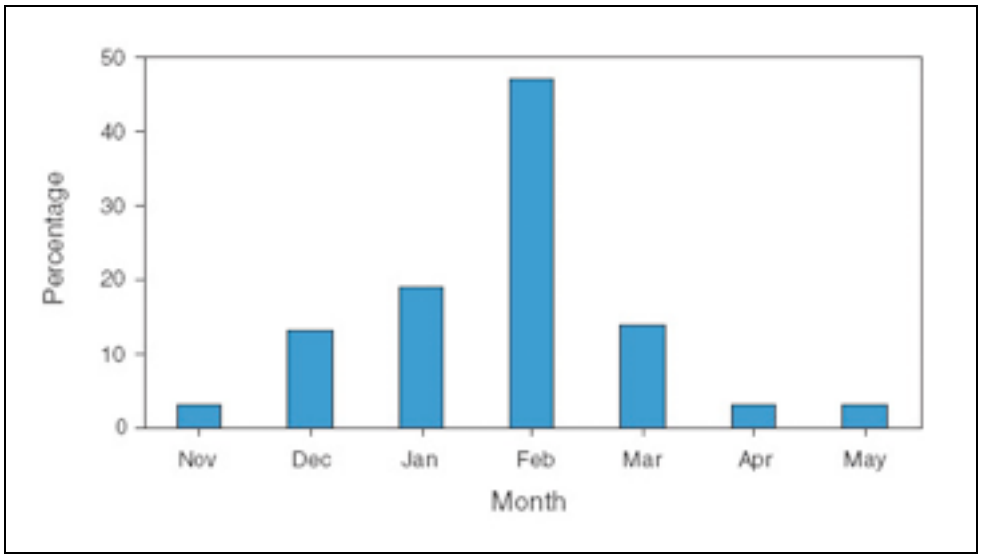
In humans, influenza is primarily transmitted from person to person via large virus-laden droplets (particles more than 5 microns in diameter) that are generated when infected individuals cough or sneeze. These large droplets can then settle on the mucosal surfaces of the upper respiratory tracts of susceptible people who are nearby (within 3 feet).

Cone-Shaped Dispersion of Sneeze Particles

This photograph captures a sneeze in progress, revealing the plume of salivary droplets as they are expelled in a large cone-shaped array from this man's open mouth, thereby dramatically illustrating the reason for covering your mouth when coughing or sneezing, in order to protect others from germ exposure. Source: CDC, 2009.

Transmission may also occur through direct contact or indirect contact with respiratory secretions, such as when touching surfaces contaminated with influenza virus and then touching the eyes, nose, or mouth. Adults can transmit influenza from the day before symptom onset to approximately 5 days after symptoms begin. Children can transmit influenza to others for 10 or more days (CDC, 2011PB).

Peak Month of Influenza Activity from 1976 through 2009



The figure above shows peak influenza activity for the United States by month for the 1976/1977 through 2008/2009 influenza seasons. The month with the highest percentage of cases (nearly 50%) was February, followed by January with 20% and March and December, with approximately 15% of all cases (CDC, 2011d).

Disease Trends in the United States

An association between influenza and increased morbidity in high-risk adult populations has been documented. Hospitalization for adults with high-risk medical conditions increases two- to fivefold during major epidemics (CDC, 2011PB).

The impact of influenza in the United States is quantified by measuring pneumonia and influenza (P and I) deaths. Death certificate data are collected from 122 U.S. cities with populations of more than 100,000 (total of approximately 70 million). Pneumonia and influenza deaths include all deaths for which pneumonia is listed as a primary or underlying cause or for which influenza is listed on the death certificate (CDC, 2011PB).

An expected ratio of deaths due to P and I compared with all deaths for a given period of time is determined. The epidemic threshold for influenza seasons is generally estimated at 1.645 standard deviations above observed P and I deaths for the previous 5-year period excluding periods during influenza outbreaks. Influenza epidemic activity is signaled when the ratio of deaths due to P and I exceeds the threshold ratio for 2 consecutive weeks (CDC, 2011PB).

Impact of Influenza

An increase in mortality typically accompanies an influenza epidemic. Increased mortality results not only from influenza and pneumonia but also from cardiopulmonary and other chronic diseases that can be exacerbated by influenza (CDC, 2011PB). That said, the major impact is in morbidity, with high attack rates and rates of hospitalization, especially for adults with respiratory disease. Absenteeism from work and school is high, and visits to healthcare providers increase (CDC, 2011PB).

In the Northern Hemisphere, epidemics usually occur in late fall and continue through early spring. In the Southern Hemisphere, epidemics occur six months before or after those in the Northern Hemisphere, in accordance with the fall/winter season there. Activity generally peaks from December to March in temperate climates, but it may occur earlier or later.

In the period from 1976 to 2008, peak influenza activity in the United States occurred most frequently in January (19%) and February (47%); however, peak influenza activity occurred in March, April, or May in 19% of occurrences. Influenza occurs throughout the year in tropical areas. Sporadic outbreaks can occasionally be localized to families, schools, and isolated communities (CDC, 2011PB).

The risk for complications and hospitalizations from influenza are higher among adults 65 years of age and older, young children, and people of any age with certain underlying medical conditions. An average of more than 200,000 hospitalizations per year are related to influenza, more than 57% of which are among people younger than 65 years. A greater number of hospitalizations occur during years that influenza A (H3N2) is predominant. In nursing homes, attack rates may be as high as 60%, with fatality rates as high as 30% (CDC, 2011PB).

Among children 0 to 4 years of age, hospitalization rates have varied from 100 per 100,000 healthy children to as high as 500 per 100,000 for children with underlying medical conditions. Hospitalization rates for children 24 months of age and younger are comparable to rates for individuals 65 and older. Children 24 to 59 months of age are at less risk of hospitalization from influenza than are younger children, but are at increased risk for influenza-associated clinic and emergency department visits (CDC, 2011PB).

Healthy children 5 through 18 years of age are not at increased risk of complications of influenza. However, children typically have the highest attack rates during community outbreaks. They also serve as a major source of transmission within communities. Influenza has a substantial impact among school-aged children and their contacts. These impacts include school absenteeism, medical care visits, and parental work loss. Studies have documented 5 to 7 influenza-related outpatient visits per 100 children annually, and these children frequently receive antibiotics (CDC, 2011PB).

In April 2009 the novel influenza A-H1N1 virus appeared and quickly spread across North America. By May 2009 the virus had spread to many areas around the world. Influenza morbidity caused by the 2009 H1N1 virus remained above seasonal baselines throughout spring and summer 2009 and was the cause of the first influenza pandemic since 1968 (CDC, 2011PB).

In the United States, the pandemic was characterized by a substantial increase in influenza activity that was well beyond historical norms. Influenza activity peaked in late October 2009 and returned to the seasonal baseline by January 2010. During that time, more than 99% of viruses identified were the 2009 pandemic influenza A-H1N1 virus (CDC, 2011PB).

CDC estimates that pandemic H1N1 influenza virus caused more than 60 million Americans to become ill, and led to more than 270,000 hospitalizations and 12,500 deaths. Ninety percent of hospitalizations and deaths occurred in individuals younger than 65 years of age. With typical seasonal influenza, approximately 90% of deaths occur in individuals older than 65 years (CDC, 2011PB).

In response to the pandemic, a monovalent influenza vaccine was produced and deployed in a nationwide vaccination campaign (CDC, 2011PB).

The U.S. Public Health Emergency for 2009 H1N1 Influenza expired on June 23, 2010. On August 10, 2010, the World Health Organization (WHO) declared an end to the 2009 H1N1 pandemic globally. Internationally, 2009 H1N1 viruses and seasonal influenza viruses are co-circulating in many parts of the world. It is likely that the 2009 H1N1 virus will continue to spread for years to come, like a regular seasonal influenza virus (CDC, 2010).

Emergence of a human influenza virus with pandemic potential presents a formidable response challenge. The pandemic of "Spanish" influenza in 1918/1919 caused an estimated 21 million deaths worldwide (CDC, 2011 PB). The Health and Human Services Pandemic Influenza Plan presented a blueprint for pandemic influenza preparation and response. It provides guidance to national, state, and local policy makers and health departments. The federal pandemic plan is available on the Department of Health and Human Services website (HHS, 2005).

Influenza Surveillance

The Centers for Disease Control (CDC) collects, compiles, and analyzes information on influenza activity year round in the United States and produces a weekly report from October through mid-May. The U.S. influenza surveillance system is a collaborative effort between CDC and its many partners in state and local health departments, public health and clinical laboratories, vital statistics offices, physicians, clinics, and emergency departments (CDC, 2011d). Information in five categories is collected from eight different data sources that allow CDC to:

- Find out when and where influenza activity is occurring
- Track influenza-related illness
- Determine what influenza viruses are circulating
- Detect changes in influenza viruses
- Measure the impact influenza is having on deaths in the United States (CDC, 2011d).

For more information about flu surveillance or to access the CDC monthly reports, visit Seasonal Influenza (Flu) (CDC, 2011e).

Clinical Features

Following respiratory transmission, the virus attaches to and penetrates respiratory epithelial cells in the trachea and bronchi. Viral replication occurs, which results in the destruction of the host cell. Viremia (entry of virus into the bloodstream) has rarely been documented. Virus is shed in respiratory secretions for 5 to 10 days (CDC, 2011PB).

Symptoms and Communicability

In general, only about 50% of infected individuals will develop the classic clinical symptoms of influenza. **Classic influenza** is characterized by the abrupt onset of fever, myalgia, sore throat, nonproductive cough, and headache. Fever is usually 101°F to 102°F and accompanied by prostration (CDC, 2011PB). The onset of fever is often so abrupt that the exact hour is recalled by the patient; however, it is also important to note that not everyone who has the flu will have a fever (CDC, 2011PB).

Myalgias mainly affect the back muscles. Cough is believed to be a result of tracheal epithelial destruction. Additional symptoms may include rhinorrhea (runny nose), headache, substernal chest burning, and ocular symptoms (eye pain, sensitivity to light) (CDC, 2011PB). Some people may have vomiting and diarrhea, though this is more common in children than adults. It is important to note that **not everyone with the flu will have fever** (CDC, 2011f).

Systemic symptoms and fever usually last from 2 to 3 days, rarely more than 5 days. They may be decreased by such medications as aspirin or acetaminophen. Aspirin should not be used for infants, children, or teenagers because they may be at risk for contracting Reye syndrome. Recovery is usually rapid, but some patients may have lingering depression and asthenia (lack of strength or energy) for several weeks (CDC, 2011PB).

Symptoms of the Flu

People who have the flu often feel some or all of these symptoms:

- Fever* or feeling feverish, chills
- Cough
- Sore throat
- Runny or stuffy nose
- Muscle or body aches
- Headaches
- Fatigue (very tired)
- Some people may have vomiting and diarrhea, though this is more common in children than adults.

* It's important to note that not everyone with flu will have a fever.
Source: CDC, 2011f.

Most experts believe that flu viruses spread mainly by droplets made when people with flu cough, sneeze, or talk (see earlier photo). These droplets can land in the mouths or noses of people who are nearby. Less often, people might get flu by touching a surface or object that has flu virus on it and then touching their own mouth, eyes, or nose (CDC, 2011f).

Infected individuals may be able to pass the flu to someone else both before knowing they are sick and after symptoms develop. Most healthy adults may be able to infect others beginning 1 day before symptoms develop and up to 5 to 7 days after becoming sick. Some people, especially young children and people with weakened immune systems, might be able to infect others for an even longer time (CDC, 2011f).

Severity

Flu is unpredictable, and its severity can vary widely from one season to the next, depending on many things:

- What flu viruses are spreading

- How much flu vaccine is available
- When vaccine is available
- How many people get vaccinated
- How well the flu vaccine is matched to flu viruses that are causing illness (CDC, 2011f)

Certain people are at greater risk for serious complications if they get the flu. This includes older people, young children, pregnant women, and people with certain health conditions (eg, asthma, diabetes, heart disease), and individuals who live in facilities like nursing homes (CDC, 2011f).

Over a period of thirty years, between 1976 and 2006, estimates of flu-associated deaths in the United States range from a low of about 3,000 to a high of about 49,000 people (CDC, 2011f). Case reports and limited studies suggest that pregnant women may be at increased risk for serious medical complications of influenza as a result of increases in heart rate, stroke volume, and oxygen consumption; decreases in lung capacity; and changes in immunologic function. A recent study found that the risk of hospitalization for influenza-related complications was more than 4 times higher for women in the second or third trimester of pregnancy than for nonpregnant women. The risk of complications for these pregnant women was comparable to that for nonpregnant women with high-risk medical conditions, for whom influenza vaccine has been traditionally recommended (CDC, 2011PB).

During the 2009 H1N1 pandemic, the United States experienced its first wave of influenza activity in the spring of 2009, followed by a second, larger wave of 2009 H1N1 activity in the fall and winter, during typical "flu season." Activity peaked in October and then declined quickly to below baseline levels by January. While activity was low and continuing to decline, 2009 H1N1 viruses were still reported in small numbers through the spring and summer of 2010 (CDC, 2011g).

2009 H1N1 activity was relatively more severe among people younger than 65 years of age compared with non-pandemic influenza seasons. Influenza activity was associated with significantly higher pediatric mortality, and higher rates of hospitalizations in children and young adults than previous seasons (CDC, 2011g).

Complications

Most people who get influenza will recover in a few days to less than 2 weeks, but some people will develop complications (eg, pneumonia) as a result of the flu, some of which can be life-threatening and result in death (CDC, 2011h). As stated earlier, certain people are at greater risk for serious complications if they get the flu. This includes older people, young children, pregnant women, and people with certain health conditions (eg, asthma, diabetes, heart disease) (CDC, 2011h).

Who Is at Higher Risk for Developing Flu-Related Complications?

- Children younger than 5, but especially children younger than 2 years old
- Adults 65 years of age and older
- Pregnant women
- People who have medical conditions including:
  - Asthma (even if it's controlled or mild)
  - Neurologic and neurodevelopmental conditions [including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or spinal cord injury].
  - Chronic lung disease (eg, chronic obstructive pulmonary disease [COPD] and cystic fibrosis)
  - Heart disease (eg, congenital heart disease, congestive heart failure, coronary artery disease)
  - Blood disorders (eg, sickle cell disease)
  - Endocrine disorders (eg, diabetes mellitus)
  - Kidney disorders
  - Liver disorders
  - Metabolic disorders (eg, inherited metabolic disorders, mitochondrial disorders)
  - Weakened immune system due to disease or medication (people with HIV or AIDS, or cancer, or those on chronic steroids)
  - People younger than 19 years of age who are receiving long-term aspirin therapy
  - People with chronic obstructive pulmonary disease (COPD)
  - People who are morbidly obese (body mass index [BMI] of 30 or greater)
- Also, American Indians and Alaskan Natives seemed to be at higher risk of flu complications.

Source: CDC, 2011h.

The most frequent complication of influenza is pneumonia, especially secondary bacterial pneumonia (eg, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*). Primary influenza viral pneumonia is an uncommon complication with a high fatality rate. Reye syndrome is a complication that occurs almost exclusively in children taking aspirin, primarily in association with influenza B (or varicella zoster), and presents with severe vomiting and confusion, which may progress to coma due to swelling of the brain (CDC, 2011PB).

Other complications can include myocarditis (inflammation of the heart), ear infections, sinus infections, and worsening of chronic bronchitis and other chronic pulmonary diseases. People with congestive heart failure may have a worsening of the condition triggered by the flu (CDC, 2011h). Death is reported in 0.5 to 1.0 per 1,000 cases. The majority of deaths occur among individuals 65 years of age and older (CDC, 2011PB).

Laboratory Diagnosis

The diagnosis of influenza is usually suspected on the basis of characteristic clinical findings, particularly if influenza has been reported in the community (CDC, 2011PB).

Virus can be isolated from throat and nasopharyngeal swabs obtained within 3 days of onset of illness. Culture is performed by inoculation of the amniotic or allantoic sac of chick embryos or certain cell cultures that support viral replication. A minimum of 48 hours is required to demonstrate virus, and 1 to 2 additional days to identify the virus type. As a result, **culture is helpful in defining the etiology of local epidemics, but not in individual case management** (CDC, 2011PB).

Serologic confirmation of influenza requires demonstration of a significant rise in influenza IgG. The acute-phase specimen should be taken less than 5 days from onset, and a convalescent specimen taken 10 to 21 days (preferably 21 days) following onset. Complement fixation (CF) and hemagglutination inhibition (HI) are the serologic tests most commonly used.

The key test is HI, which depends on the ability of the virus to agglutinate human or chicken erythrocytes and inhibition of this process by specific antibody. Diagnosis requires at least a fourfold rise in antibody titer. Rapid diagnostic testing for influenza antigen permits those in office and clinic settings to assess the need for antiviral use in a more timely manner (CDC, 2011PB).

Details about the laboratory diagnosis of influenza are available on the CDC influenza website (CDC, 2011PB).

Treatment and Prevention

A person with flu-like symptoms should stay home and avoid contact with other people except to get medical care. This means, if at all possible, not going to work or school, traveling, shopping, or attending social events or public gatherings. If sick people must leave home, they should wear a facemask or cover coughs and sneezes with a tissue, and wash hands often to keep from spreading flu to others. The CDC recommends a person stay home for at least 24 hours after the fever is gone, and fever should be gone without the use of a fever-reducing medicine (CDC, 2010a).

Home Treatment

[The following information is from CDC, 2010b.]

The five steps in home treatment are:

1. Stay at home and rest.
2. Avoid close contact with well people in the house so they are not made sick.
3. Drink plenty of water and other clear liquids to prevent fluid loss (dehydration).
4. Treat fever and cough with medicines that can be purchased OTC.
5. If the patient gets very sick, is pregnant, or has a medical condition that puts them at higher risk of flu complications, call a doctor. They may need antiviral medicine to treat flu.

If possible, isolate a sick room and follow sick-room rules and cleaning procedures. Try to give the sick person a room alone, but several sick people can share the room if necessary. If possible, the sick should use a separate bathroom from those who are well. Each sick person should have their own drinking glass, washcloth, and towel. Ideally the sick room can be outfitted with these additional supplies: tissues, trash can with lid and lined with a plastic trash bag, alcohol-based hand rub, cooler or pitcher with ice and drinks, cup with straw or squeeze bottle to help with drinking, thermometer, humidifier, and facemasks.

Sick people should wear a facemask if available when they leave the sick room or are around other people. The caregiver should write down the dosage and timing for any medications and be sure all medicines are stored out of the reach of children.

Observe the following sick room rules when caring for a person with influenza:

1. Avoid having other people enter the sick room. The sick person should not have visitors other than the caregiver. If visitors must enter, they should stay at least 6 feet away from the sick person.
2. Cover coughs and sneezes. Ask sick individuals to cover the nose and mouth with a tissue when they cough and sneeze. Ask them to throw used tissues in the trash.
3. Choose one caregiver, if you can, to take care of sick family members. Ask someone else to be the caregiver if you are pregnant or have certain chronic health problems. If you get the flu, it could be much more serious for you.
4. Keep the air clean. Open a window in the sick room, if possible, or use a fan to keep fresh air flowing.

The sick room should be cleaned each day following these tips:

- Cleaning hard surfaces
  - Clean hard surfaces that may have flu germs on them. These may include doorknobs, bedside tables, bathroom sinks, toilets, counters, phones, and toys.
  - Clean these hard surfaces by using water and dish soap, or use common household cleaners that kill germs.
- Cleaning bed linens and laundry
  - Wash bed sheets and towels with normal laundry soap and tumble dry on a hot dryer setting. Hold all dirty laundry away from your face and body. Wash your hands right after touching dirty laundry.
  - It's OK to wash the sick person's bedding or clothes with other people's laundry.
- Cleaning dishes
  - Wash the sick person's dishes with normal dish soap or place in the dishwasher.

Preventing Fluid Loss

Sick people with the flu need to drink extra fluids to keep from getting dehydrated and should begin taking plenty of liquids at the first sign of illness. Mild fluid loss can most often be treated at home. **Severe dehydration is very serious and must be treated in the hospital** (CDC, 2010b).

Tips to prevent dehydration:

- If the sick person is not eating well, encourage drinking liquids. Avoid alcohol or drinks with caffeine in them such as colas, tea, and coffee.
- Older adults and people with kidney problems should check with their doctor about safe amounts of liquid to drink when sick.
- Offer clear fluids such as water, broth, or sports drinks.
- Use a squeeze bottle or a straw for people too weak to drink from a cup, or offer ice chips or frozen ice pops.
- Continue to nurse or bottle feed a baby. Babies get all the fluid they need from breastfeeding or formula (CDC, 2010b).

If a baby refuses to breastfeed or take formula from the bottle, the caregiver should call the doctor, who may recommend giving the child a special drink like Pedialyte, which is meant to prevent dehydration.

Check for fluid loss by doing the following:

- Make sure babies have wet diapers. Check that wet diapers are as frequent and heavy as normal.
- Look for tears when the baby or toddler is crying.
- Check to see how wet the child's mouth is. The inside of the mouth should be wet. Wash your hands after you do this.
- Check to see that children, teens, and adults are making frequent trips to the bathroom to urinate.
- Check the urine color. Clear or light yellow-colored urine means the person is getting enough fluid. Dark yellow urine signals the person is dehydrated. (CDC, 2010b)

While anyone can become dehydrated, infants, children, and older adults are at greatest risk of getting dehydrated. Also, pregnant women will want to make sure they are getting enough fluids.

It is important to know when to call the doctor to ask for advice. Call right away if the sick person has any of the following symptoms of dehydration.

In infants and toddlers

- Sunken soft spot on top of infant's head
- Diarrhea or vomiting in infants 2 months or younger
- Less than normal amount of urine (fewer wet diapers or diapers that weigh less than normal)
- Much less active or more irritable than normal
- Fewer tears when crying, or not making tears

In children and adults

- Not making tears
- Less than normal amount of urine
- Skin that is dry and takes long to go back to position when pinched
- Dry mouth or dry eyes
- Fast-beating heart
- Blood in the stool or blood in vomit
- A child who has had a fever for 12 or more hours and also is not able to drink fluids, is throwing up, or has diarrhea
- A child may be cranky or irritable, hard to wake up, have little energy, appear doll weak (CDC, 2010b)

Treatable Symptoms

Fever, dry cough, and other symptoms can usually be successfully treated at home. Bringing down a fever will make the person feel better and help patients rest. To treat a fever without medicine place a cool, damp washcloth on the forehead, wash the arms and body with a cool cloth, or give the person a slightly warm bath. To treat a high fever with medicine, look for medicines containing acetaminophen or ibuprofen. These medicines may take 30 to 45 minutes to start working and they may not bring fevers down to normal temperature (CDC, 2010b).

In rare cases, a fever can bring on a seizure. These are called **febrile seizures** and are more common in young children. If a fever causes a seizure, call the doctor or get medical help. Note: **Any child younger than 3 months who has a fever should see a doctor** (CDC, 2010b).

Coughing can help clear out mucous and congestion from the lungs, yet dry coughs when there is no mucous can cause pain in the airways, throat, or chest. Treating a dry cough can stop this sore feeling and also help the person rest. An appropriate cough medicine, a humidifier, and cough drops or hard candy (for adults) all may help to lessen this symptom. If necessary, consult with a pharmacist to choose the best cough medicine and **do not give cough or cold medicines children younger than 4 years of age** (CDC, 2010b).

Acetaminophen or ibuprofen can be used to relieve the pain caused by a sore throat, body aches, or congestion. Some find that gargling with warm salt water helps relieve a sore throat, while ice chips or fruit pops can be effective for both relieving a sore throat and helping the sick person increase fluid intake. A humidifier and/or decongestants may help with head and chest congestion (ask a pharmacist for help in choosing an appropriate formulation of any medicine) (CDC, 2010b).

People with the flu may have stomach pain. They may even throw up or have loose stools (diarrhea). The sick person may be helped by eating plain foods that are easy on the stomach, drinking clear liquids, or using a medicine meant to treat loose stools (adults only). Anyone with severe stomach pain should call the doctor (CDC, 2010b).

Medication Safety

Whenever medicine is used to relieve the flu and its symptoms, the following cautions should be observed:

- Take the right amount of medicine, observing both individual and daily dosage limits.
- Avoid alcohol when taking medicine.
- Pregnant women should talk to their doctor **before** taking any medicines.
- Store all medicines out of the reach of children.
- Don't give cough or cold medicines to children younger than 4 years of age.
- For older children, be sure to buy child-appropriate formulations and observe dosage requirements. Consult a pharmacist or the doctor with any questions.
- Never give aspirin to children age 18 or under if they have the flu. Check all medicine labels to make sure they do not contain aspirin, or salicylate (CDC, 2010b).

Recognizing Severe Illness

Most people with the flu have mild illness and do not need medical care or antiviral drugs. However, some people are more likely to get flu complications (eg, young children, people 65 and older, people with asthma or diabetes, pregnant women) and they should talk to a healthcare provider about whether they need to be examined if they get flu symptoms.

It is possible for healthy people to develop severe illness from the flu, so anyone concerned about their illness should consult a healthcare provider. There are emergency warning signs, and anyone who manifests the following should obtain medical care right away (CDC, 2010b).

In children

- Fast breathing or trouble breathing
- Bluish skin color
- Not drinking enough fluids
- Not waking up or not interacting
- Being so irritable that the child does not want to be held
- Flu-like symptoms improve but then return with fever and worse cough
- Fever with a rash

In adults

- Difficulty breathing or shortness of breath
- Pain or pressure in the chest or abdomen
- Sudden dizziness
- Confusion
- Severe or persistent vomiting
- Flu-like symptoms that improve but then return with fever and worse cough (CDC, 2010b)

Antiviral Agents for Influenza

In the United States, four antiviral agents are approved for preventing or treating influenza: amantadine, rimantadine, zanamivir, and oseltamivir (CDC, 2011PB).

Testing of influenza A isolates from the United States and Canada has demonstrated that many of these viruses are resistant to amantadine and rimantadine. The CDC's Advisory Committee on Immunization Practices (ACIP) recommends that neither amantadine nor rimantadine be used for the treatment or prophylaxis of influenza A in the United States until susceptibility to these antiviral drugs has been re-established (CDC, 2011PB).

Zanamivir and oseltamivir are members of a new class of drugs called neuraminidase inhibitors and are active against both influenza type A and type B. Zanamivir is provided as a dry powder that is administered by inhalation. It is approved for treatment of uncomplicated acute influenza A or B in individuals 7 years of age and older who have been symptomatic for no more than 48 hours.

Oseltamivir is provided as an oral capsule. It is approved for the treatment of uncomplicated influenza A or B in individuals 1 year of age and older who have been symptomatic for no more than 48 hours. Oseltamivir is also approved for prophylaxis of influenza infection among individuals 1 year of age and older. Zanamivir is approved for prophylaxis of influenza in individuals 5 years and older (CDC, 2011PB).

In 2007/2008, a significant increase in the prevalence of oseltamivir resistance was reported among influenza A (H1N1) viruses worldwide; during that influenza season, 10.9% of H1N1 viruses tested in the United States were resistant to oseltamivir. During 2008 more than 90% of H1N1 viruses were resistant to oseltamivir. For the 2008/2009 influenza season CDC thus recommended that individuals who tested positive for influenza A should receive only zanamivir if treatment were indicated. Oseltamivir was to be used alone only if recent local surveillance data indicated that circulating viruses were likely to be influenza A (H3N2) or influenza B viruses, which had not been found to be resistant to oseltamivir. Additional information about influenza antiviral treatment is available on the CDC influenza website (CDC, 2011PB).

Antiviral agents for influenza are an adjunct to—and not a substitute for—vaccine. Vaccination remains the principal means for preventing influenza-related morbidity and mortality. Additional information on the use of influenza antiviral drugs can be found in the current ACIP statement on influenza vaccine and on the CDC influenza website at http://www.cdc.gov/flu (CDC, 2011PB).

Nosocomial Influenza Control

Many patients in general hospitals, and especially in referral centers, are likely to be at high risk for complications of influenza. Hospitalized susceptible patients may acquire influenza from patients, hospital employees, or visitors. The preferred method of control is to administer inactivated influenza vaccine to high-risk patients and medical personnel prior to the outbreak (CDC, 2011PB).

During community influenza A activity, the use of antiviral prophylaxis may be considered for high-risk patients who were not immunized or were immunized too recently to have protective antibody levels. Antiviral agents may also be considered for non-immunized hospital personnel. Other measures include restricting visitors with respiratory illness, cohorting patients with influenza for 5 days following onset of illness, and postponing elective admission of patients with uncomplicated illness (CDC, 2011PB).

Prevention

According to the CDC, the most effective preventive measure for dealing with the flu is annual vaccination. In addition to vaccination, the CDC recommends the following everyday preventive actions to stop the spread of germs: (CDC, 2011i):

- Cover your nose and mouth with a tissue when you cough or sneeze. Throw the tissue in the trash after you use it.
- Wash your hands often with soap and water. If soap and water are not available, use an alcohol-based hand rub.
- Avoid touching your eyes, nose and mouth. Germs spread this way.
- Try to avoid close contact with sick people.
- If you are sick with a flu–like illness, stay home for at least 24 hours after your fever is gone except to get medical care or for other necessities. (The fever should be gone without the use of a fever-reducing medicine.)
- While sick, limit contact with others as much as possible to keep from infecting them.

The CDC website provides extensive resources on handwashing technique and cough/sneeze etiquette, as well as printable materials for use in various institutional settings. These materials are available from: Centers for Disease Control and Prevention (CDC) at http://cdc.gov/flu/protect/stopgerms.htm (CDC, 2010c).

Influenza Vaccine

Prior to 2010, annual vaccination was already recommended for an estimated 85% of the U.S. population. The only group not included was healthy non-pregnant adults aged 18 to 49 years who did not have an occupational risk for infection and were not close contacts of individuals at higher risk for influenza-related complications (CDC, 2010MMWR).

On February 24, 2010, vaccine experts declared that everyone in the United States who is 6 months and older should get a flu vaccine each year starting with the 2010/2011 influenza season. The CDC stated that early vaccination is the single best way to protect against the flu (CDC, 2011 PB).

One of the reasons for expansion of annual vaccination recommendations to include all adults was based on concerns that 2009 viruses would continue to circulate during upcoming influenza seasons and that a substantial proportion of young adults might remain susceptible to infection from them. Data from epidemiologic studies conducted during the 2009 pandemic indicate that the risk for influenza complications among adults aged 19 to 49 years is greater than typical for seasonal influenza (CDC, 2010MMWR).

The United States Food and Drug Administration (FDA) chose the three influenza viruses for inclusion in the 2011/2012 seasonal flu vaccine based on recommendations from the World Health Organization (WHO). Each year, experts from FDA, WHO, CDC and other institutions study virus samples collected from around the world to identify the influenza viruses that are the most likely to cause illness during the upcoming flu season. This information is used to create a vaccine (CDC, 2011j).

WHO recommended that the Northern and Southern Hemisphere's 2011/2012 seasonal influenza vaccine contain the following three vaccine viruses:

- An A/California/7/2009 (H1N1)-like virus
- An A/Perth/16/2009 (H3N2)-like virus, and
- A B/Brisbane/60/2008-like virus (CDC, 2011j)

While the goal is for everyone to get a flu vaccine each flu season, it is especially important that the following groups get vaccinated, either because they are at high risk of having serious complications or because they live with or care for people at high risk (CDC, 2011k):

1. Pregnant women
2. Children younger than 5, but especially children younger than 2 years old
3. Adults 50 years of age and older.
4. People of any age with certain chronic medical conditions
5. People who live in nursing homes and other long-term care facilities
6. People who live with or care for those at high risk for complications from flu, including:
    - Healthcare workers
    - Household contacts of individuals at high risk for complications from the flu
    - Household contacts and out-of-home caregivers of children less than 6 months of age (these children are too young to be vaccinated) (CDC, 2011k)

There are some people who should consult with a physician before getting the flu vaccine. Talk with a doctor before getting a flu shot if you:

1. Have ever had a severe allergic reaction to eggs or to a previous flu shot, or
2. You have a history of Guillain–Barré syndrome that occurred after receiving influenza vaccine

If you have a fever when you go to get your flu shot, talk to the doctor or nurse about getting your shot at a later date. However, you can get a flu shot at the same time you have a respiratory illness without fever or if you have another mild illness (CDC, 2011k).

Characteristics

A **vaccine** is made from a virus or bacteria (referred to as an antigen) that causes the human body's immune system to develop antibodies. Substances may be added to a vaccine to help generate a stronger immune response so that less vaccine is needed for the body to recognize and fight the antigen.

When a new strain is isolated and identified as a novel influenza virus, work begins to prepare a **virus reference strain**—where a clinical sample of the virus is mixed with another influenza virus that grows in eggs—to develop a new virus that has some of the properties of the novel virus plus the ability to grow in eggs. Once a virus reference strain is ready, it is made available to influenza vaccine manufacturers so they can create a **master virus seed**, which is used to inoculate eggs to initiate the production of bulk vaccine batches (WHO, 2009).

Two types of influenza vaccine are available in the United States: trivalent inactivated influenza virus and live attenuated influenza virus. **Trivalent inactivated influenza vaccine** (**TIV**) has been available since the 1940s. TIV is administered intramuscularly (IM) and currently contains three inactivated viruses: type A (H1N1), type A (H3N2), and type B. Only split-virus and subunit inactivated vaccines are available in the United States. Vaccine viruses are grown in chicken eggs, and the final product contains residual egg protein. The vaccine is available in both pediatric (0.25-mL dose) and adult (0.5-mL dose) formulations. TIV is available with thimerosal as a preservative (in multidose vials), as well as in reduced and preservative-free formulations (CDC, 2011PB).

Giving an Influenza Vaccination

Source: United States Navy. Public domain.

Live attenuated influenza vaccine (**LAIV**) was approved for use in the United States in 2003. It contains the same three influenza viruses as TIV. The viruses are cold-adapted and replicate effectively in the mucosa of the nasopharynx. The vaccine viruses are grown in chicken eggs and the final product contains residual egg protein. The vaccine is provided in a single-dose sprayer unit; half of the dose is sprayed into each nostril. LAIV does not contain thimerosal or any other preservative. LAIV is approved for use only in healthy, nonpregnant individuals 2 through 49 years of age (CDC, 2011PB).

Vaccinated children can shed vaccine viruses in nasopharyngeal secretions for up to 3 weeks. One instance of transmission of vaccine virus to a contact has been documented. The transmitted virus retained its attenuated, cold-adapted, temperature-sensitive characteristics. The frequency of shedding of vaccine strains by individuals 5 to 49 years of age has not been determined (CDC, 2011PB).

Influenza Vaccines

Inactivated subunit (TIV)

- intramuscular
- trivalent

Live attenuated vaccine (LAIV)

- intranasal
- trivalent

FDA-Approved Vaccines for the 2011/2012 Season

Each year the FDA determines the formulation of vaccines that will be used in the United States based on recommendations from the World Health Organization (WHO). The vaccine formulation protects against the three virus strains that surveillance indicates will be most common during the upcoming season. In July 2011 the FDA approved the 2011/2012 influenza vaccine formulation for all six manufacturers licensed to produce and distribute influenza vaccine for use in the United States (FDA, 2011).

The brand names and manufacturers of the vaccines for the 2011/2012 season are:

1. Afluria*, CSL Limited
2. Fluarix, GlaxoSmithKline Biologicals
3. FluLaval, ID Biomedical Corporation
4. FluMist, MedImmune Vaccines Inc.
5. Fluvirin, Novartis Vaccines and Diagnostics Limited
6. Fluzone, Fluzone High-Dose,** and Fluzone Intradermal,*** Sanofi Pasteur Inc.

*Afluria (CSL Biotherapies) is approved by the FDA for use in individuals aged 6 months and older in the United States. However, the Advisory Committee on Immunization Practices (ACIP) recommends that Afluria not be administered to children aged 6 months through 8 years because of an increased frequency of febrile seizures reported among young children (mostly among children aged < 5 years) in Australia in 2010. Therefore, another age-appropriate, licensed seasonal influenza vaccine formulation should be used for prevention of influenza in

children aged 6 months through 8 years. If no other age-appropriate, licensed seasonal influenza vaccine is available for a child aged 5 years through 8 years who has a medical condition that increases the risk for influenza complications, providers should discuss the benefits and risks of influenza vaccination with the parents or caregivers before administering Afluria (CDC, 2011m).

**Fluzone High-Dose was approved for use in people 65 years of age and older during the 2010/2011 flu season. Human immune defenses become weaker with age, which places older people at greater risk of severe illness from influenza. Also, aging decreases the body's ability to have a good immune response after getting influenza vaccine. A higher dose of antigen in the vaccine is supposed to give older people a better immune response and therefore better protection against flu. Fluzone High-Dose vaccines contain 4 times the amount contained in regular flu shots. The additional antigen is intended to create a stronger immune response (more antibodies) in the person getting the vaccine. Whether the improved immune response leads to greater protection against flu after vaccination is not yet known. An ongoing study designed to determine the effectiveness of Fluzone High-Dose in preventing illness from influenza compared to Fluzone is expected to be completed in 2014/2015 (CDC, 2011l).

***Fluzone Intradermal was licensed by the FDA for use in the United States for the 2011/2012 flu season. The intradermal flu vaccine is given into the skin instead of a muscle. A much smaller needle is used and it requires 40% less antigen to be as effective as the regular flu shot (CDC, 2011o).

The intradermal flu vaccine has a similar safety profile to the regular Fluzone shot. Like all flu vaccines, the intradermal vaccine is made to protect against the three flu viruses that research suggests will be most common for the season (CDC, 2011o).

The intradermal vaccine has been approved by FDA for use in adults 18 through 64 years of age and is now another vaccination option for people in this age group. The regular flu shot continues to be an option for people 6 months and older, and the nasal spray vaccine is available for non-pregnant, healthy people ages 2 to 49 (CDC, 2011o).

The intradermal vaccine will be in a single-dose, preservative-free (without thimerosal), prefilled syringe. In adults 18-64 years of age, the intradermal vaccine was shown to provide an immune response similar to the regular intramuscular flu shot (CDC, 2011o).

Additional information is available at http://cdc.gov/flu/protect/vaccine/ (CDC, 2011n).

Vaccine Efficacy

TIV

For practical purposes, immunity following inactivated influenza vaccination is less than 1 year because of waning of vaccine-induced antibodies and antigenic drift of circulating influenza viruses. Influenza vaccine efficacy varies by the similarity of the vaccine strain(s) to the circulating strain and the age and health status of the recipient. Vaccines are effective in protecting from illness up to 90% of healthy vaccinees younger than 65 years of age when the vaccine strain is similar to the circulating strain. However, the vaccine is only 30% to 40% effective in preventing illness among individuals 65 years of age and older (CDC, 2011PB).

Although the vaccine is not highly effective in preventing clinical illness among elders, it is effective in preventing complications and death. Among older adults, the vaccine is 50% to 60% effective in preventing hospitalization and 80% effective in preventing death. During a 1982/1983 influenza outbreak in Genesee County, Michigan, unvaccinated nursing home residents were 4 times more likely to die than were vaccinated residents (CDC, 2011PB).

LAIV

LAIV has been tested in groups of both healthy children and healthy adults. A randomized double-blind, placebo-controlled trial among healthy children 60 to 84 months of age assessed the efficacy of the trivalent LAIV against culture-confirmed influenza during two influenza seasons (CDC, 2011PB).

In year 1, when vaccine and circulating virus strains were well matched, efficacy was 87% against culture-confirmed influenza. In year 2, when the type A component was not well matched between vaccine and circulating virus strains, efficacy was also 87%. Other results from this trial included a 27% reduction in febrile otitis media and a 28% reduction in otitis media with concomitant antibiotic use. Receipt of LAIV also resulted in decreased fever and otitis media in vaccine recipients who developed influenza (CDC, 2011PB).

A randomized double-blind, placebo-controlled trial among 3,920 healthy working adults aged 18 to 49 years assessed several endpoints and documented reductions in illness, absenteeism, healthcare visits, and medication use during influenza outbreak periods. This study was conducted during the 1997/1998 influenza season, when the vaccine and circulating type A strains were not well matched. This study did not include laboratory virus testing of cases. Three studies among children have demonstrated greater efficacy for LAIV compared to TIV. There is no evidence in adults that efficacy of LAIV is greater than that of TIV (CDC, 2011PB).

LAIV Efficacy in Healthy Children

- 87% effective against culture-confirmed influenza in children 5–7 years old
- 27% reduction in febrile otitis media (OM)
- 28% reduction in OM with accompanying antibiotic use
- Decreased fever and OM in vaccine recipients who developed influenza

Source: CDC Pink Book, p. 159.

LAIV Efficacy in Healthy Adults

- 20% fewer severe febrile illness episodes
- 24% fewer febrile upper respiratory illness episodes
- 27% fewer lost work days due to febrile upper respiratory illness
- 18%–37% fewer days of healthcare provider visits due to febrile illness
- 41%–45% fewer days of antibiotic use

Source: CDC Pink Book, p. 159.

Vaccination Schedule and Use

TIV

Manufacturers began shipping flu vaccines for the 2011/2012 season during the summer and distribution will continue through the fall. While some vaccine will be available in August, ample supplies should be available in September and October. Influenza activity usually lasts from October to May in the U.S. and CDC recommends that ***everyone 6 months of age and older get their yearly flu vaccine as soon as vaccines become available in their community*** (CDC, 2011p).

Vaccination before December is best since this timing ensures that protective antibodies are in place before flu activity is typically at its highest. CDC continues to encourage people to get vaccinated throughout the flu season, which can begin as early as October and last as late as May. Over the course of the flu season, many different influenza viruses can circulate at different times and in different places. As long as flu viruses are still spreading in the community, vaccination can provide protective benefit. One dose of TIV may be administered annually for individuals 9 years of age or older (CDC, 2011q).

In addition, there are other people who may benefit from seasonal flu vaccination as late as April or May, even if influenza viruses are no longer circulating in the United States. This includes:

1. Individuals likely to be traveling to the Southern Hemisphere where influenza may be circulating, and
2. Children younger than 9 being vaccinated for the first time who still have not received their second recommended dose of vaccine. Studies have shown that two doses are needed in children younger than 9 the first year they are vaccinated in order to maximize the protective benefit from vaccination (CDC, 2011q).

Inactivated Influenza Vaccine Dosage by Age Group, United States			
Age group	Dosage	Number of doses	Route
6–35 months	0.25 mL	1* or 2	IM
3–8 years	0.50 mL	1* or 2	IM
>=9 years	0.50 mL	1	IM

* Only one dose is needed if the child received 2 doses of influenza vaccine during the previous season. Source: CDC Pink Book, 2011.

Inactivated influenza vaccine should be given by the intramuscular (IM) route. Other methods, such as intradermal, subcutaneous, topical, or mucosal should not be used unless approved by the Food and Drug Administration or recommended by ACIP (CDC, 2011PB).

Beginning in the 2010/2011 influenza season, the ACIP recommended annual influenza vaccination for all individuals 6 months of age and older. Protection of individuals at higher risk for influenza-related complications should continue to be a focus of vaccination efforts as providers and programs transition to routine vaccination of all individuals aged 6 months and older (CDC, 2011PB).

When vaccine supply is limited, vaccination efforts should focus on delivering vaccination to the following groups of individuals (CDC, 2011PB):

- Children 6 months–4 years (59 months) of age
- Individuals 50 years and older
- Individuals with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)
- Individuals who are immunosuppressed (including immunosuppression caused by medications or by human immunodeficiency virus)
- Women who are or will be pregnant during the influenza season
- Children 6 months through 18 years of age and receiving long-term aspirin therapy and who therefore might be at risk for experiencing Reye syndrome after influenza virus infection
- Residents of nursing homes and other chronic-care facilities
- American Indians/Alaska Natives
- Individuals who are morbidly obese (body-mass index is 40 or greater)
- Healthcare personnel
- Household contacts and caregivers of children younger than 5 years of age and adults 50 years of age and older, with particular emphasis on vaccinating contacts of children aged younger than 6 months
- Household contacts and caregivers of individuals with medical conditions that put them at higher risk for severe complications from influenza

ACIP recommends vaccination of women who will be pregnant during influenza season. Case reports and limited studies suggest that pregnant women may be at increased risk for serious medical complications of influenza as a result of increases in heart rate, stroke volume and oxygen consumption; decreases in lung capacity; and changes in immunologic function. A study found that the risk of hospitalization for influenza-related complications was more than 4 times higher for women in the second or third trimester of pregnancy than for nonpregnant women. The risk of complications for these pregnant women was comparable to that for nonpregnant women with high-risk medical conditions. Vaccination can occur during any trimester and **only TIV should be administered to pregnant women** (CDC, 2011PB).

Available data suggest that individuals with HIV infection may have prolonged influenza illnesses and are at increased risk of complications of influenza. Many individuals with HIV infection will develop protective antibody titers following inactivated influenza vaccine. In individuals who have advanced HIV disease and low CD4+ T-lymphocyte cell counts, TIV vaccine may not induce protective antibody titers. A second dose of vaccine does not improve the immune response in these individuals (CDC, 2011PB).

Some studies have demonstrated a transient increase in viral titer in the blood of vaccinated individuals infected with HIV. There is no evidence of deterioration in CD4 counts or progression of clinical HIV disease. Because influenza can result in serious illness and complications and because influenza vaccination may result in protective antibody titers, ACIP believes that influenza vaccination will benefit many individuals with HIV infection. **LAIV should not be administered to individuals with HIV infection** (CDC, 2011PB).

Individuals who have contact with high-risk individuals should receive TIV. These include healthcare workers, employees of long-term care facilities, and household contacts of high-risk individuals. These individuals may be younger and healthier and more likely to be protected from illness than elders (CDC, 2011PB).

All healthcare providers should receive annual inactivated influenza vaccine. Groups to be targeted include physicians, nurses, and other personnel in hospitals and outpatient settings who have contact with high-risk patients in all age groups, and providers of home care to high-risk individuals (eg, visiting nurses, volunteers) (CDC, 2011PB).

LAIV may be administered to healthy healthcare workers 49 years of age or younger, except those who have contact with severely immunosuppressed individuals who require hospitalization and care in a protective environment (ie, in isolation because of severe immunosuppression) (CDC, 2011PB).

LAIV

LAIV is approved for healthy, nonpregnant individuals 2 through 49 years of age. The vaccine can be administered to those eligible as soon as it becomes available in the late summer or fall. Vaccination can continue throughout influenza season. One dose of LAIV may be administered by the intranasal route to individuals 9 through 49 years of age. Children 2 through 8 years of age receiving influenza vaccine for the first time should receive two doses administered at least 4 weeks apart (CDC, 2011PB).

Live Attenuated Influenza Vaccine Dosage by Age Group, United States

Age group	Number of doses	Route
2–8 years, no previous influenza vaccine	2 (separated by 4 weeks)	Intranasal
5–8 years, previous influenza vaccine*	1** or 2	Intranasal
9–49 years	1	Intranasal

*LAIV or inactivated vaccine

**Only one dose is needed if the child received two doses of influenza vaccine during a previous influenza season.

Source: CDC Pinkbook, 2011.

Close contacts of people at high risk for complications from influenza should receive influenza vaccine. Contacts of people at high risk of complications of influenza may receive LAIV if they are otherwise eligible (ie, 2 through 49 years of age, healthy and not pregnant). **Individuals in close contact with severely immunosuppressed individuals who are hospitalized and receiving care in a protected environment should not receive LAIV** (CDC, 2011PB).

Inactivated vaccines do not interfere with the immune response to live vaccines. Inactivated vaccines, such as tetanus and diphtheria toxoids, can be administered either simultaneously or at any time before or after LAIV. Other live vaccines can be administered on the same day as LAIV. Live vaccines not administered on the same day should be administered at least 4 weeks apart when possible (CDC, 2011PB).

Contraindications and Precautions to Vaccination

TIV

Individuals who have had a severe allergic reaction (anaphylaxis) to a vaccine component or following a prior dose of inactivated influenza vaccine should not receive TIV. People with a moderate or severe acute illness normally should not be vaccinated until their symptoms have decreased. A history of Guillain Barré syndrome (GBS) within 6 weeks following a previous dose of influenza vaccine is a precaution for TIV. Pregnancy, breastfeeding, and immunosuppression are not contraindications to inactivated influenza vaccination (CDC, 2011PB).

LAIV

People who should not receive LAIV include children younger than 2 years of age; those 50 years of age and older; those who have chronic medical conditions, including asthma, a recent wheezing episode, reactive airways disease, or other chronic pulmonary or cardiovascular conditions; metabolic disease such as diabetes, renal disease, or hemoglobinopathy, such as sickle cell disease; and children or adolescents receiving long-term therapy with aspirin or other salicylates, because of the association of Reye syndrome with wild-type influenza infection. These groups should receive inactivated influenza vaccine (CDC, 2011PB).

As with other live-virus vaccines, LAIV should not be given to individuals who are immunosuppressed because of disease, including HIV, or who are receiving immunosuppressive therapy. Pregnant women should not receive LAIV. Immunosuppressed individuals and pregnant women should receive inactivated influenza vaccine (CDC, 2011PB).

Since LAIV contains residual egg protein, it should not be administered to those who have a history of severe allergy to egg or any other vaccine component. A history of Guillain Barré syndrome (GBS) within 6 weeks following a previous dose of influenza vaccine is a precaution for LAIV (CDC, 2011PB).

As with all vaccines, LAIV should be deferred for individuals with a moderate to severe acute illness. If clinical judgment indicates that nasal congestion might impede delivery of the vaccine to the nasopharyngeal mucosa, deferral of administration should be considered until the condition has improved (CDC, 2011PB).

The effect on safety and efficacy of LAIV co-administration with influenza antiviral medications has not been studied. However, because influenza antiviral agents reduce replication of influenza viruses, LAIV should not be administered until 48 hours after cessation of influenza antiviral therapy, and influenza antiviral medications should not be administered for 2 weeks after receipt of LAIV (CDC, 2011PB).

Adverse Reactions Following Vaccination

TIV

Local reactions are the most common of adverse reactions following vaccination with TIV. Local reactions include soreness, erythema, and induration at the site of injection. These reactions are transient, generally lasting 1 to 2 days. Local reactions are reported in 15% to 20% of vaccinees (CDC, 2011PB).

Nonspecific systemic symptoms, including fever, chills, malaise, and myalgia, are reported in fewer than 1% of TIV recipients. These symptoms usually occur in those with no previous exposure to the viral antigens in the vaccine. They usually occur within 6 to 12 hours of TIV vaccination and last 1 to 2 days. Recent reports indicate that these systemic symptoms are no more common than in people given a placebo injection (CDC, 2011PB).

Rarely, immediate hypersensitivity—presumably allergic—reactions (eg, hives, angioedema, allergic asthma, systemic anaphylaxis) occur after vaccination with TIV. These reactions probably result from hypersensitivity to a vaccine component. The majority are most likely related to residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein may induce immediate allergic reactions in those with severe egg allergy. Individuals who have developed hives, 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 assist in determining whether influenza vaccination may proceed or should be deferred (CDC, 2011PB).

People 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 vaccines, and similar consultation should be considered. Protocols are available for influenza vaccination of patients who have egg allergies and medical conditions that place them at increased risk for influenza infection or its complications (CDC, 2011PB).

LAIV

Among children the most common adverse reactions are runny nose and headaches. However, there have been no significant differences between LAIV and placebo recipients in the proportion with these symptoms. In a clinical trial, children 6 to 23 months of age had an increased risk of wheezing. An increased risk of wheezing was not reported in older children (CDC, 2011PB).

Among healthy adults, a significantly increased rate of cough, runny nose, nasal congestion, sore throat, and chills was reported among vaccine recipients. These symptoms were reported in 10% to 40% of vaccine recipients, a rate 3% to 10% higher than reported for placebo recipients. There was no increase in the occurrence of fever among vaccine recipients. No serious adverse reactions have been identified in LAIV recipients, either children or adults (CDC, 2011PB).

No instances of Guillain-Barré syndrome have been reported among LAIV recipients. However the number of individuals vaccinated to date is too small to identify such a rare vaccine adverse reaction (CDC, 2011PB).

Vaccine Storage and Handling

TIV

Inactivated influenza vaccine is generally shipped in an insulated container with coolant packs. Although some brands of TIV vaccine can tolerate room temperature for a few days, CDC recommends that the vaccine be stored at refrigerator temperature (35°–46°F, or 2°–8°C). Inactivated influenza vaccine must not be frozen. Opened multidose vials may be used until the expiration date printed on the package if no visible contamination is present (CDC, 2011PB).

LAIV

LAIV should be stored at refrigerator temperature (35°–46° F, or 2°–8°C). LAIV inadvertently exposed to a freezing temperature should be placed at refrigerator temperature and used as soon as possible (CDC, 2011PB).

LAIV is intended for intranasal administration only and should never be administered by injection. LAIV is supplied in a prefilled single-use sprayer containing 0.2 mL of vaccine. Approximately 0.1 mL (ie, half of the total sprayer contents) is sprayed into the first nostril while the recipient is in the upright position. An attached dose-divider clip is removed from the sprayer to administer the second half of the dose into the other nostril. If the vaccine recipient sneezes after administration, the dose should not be repeated (CDC, 2011PB).

Conclusion

Seasonal influenza epidemics have been with us for a long time. Periodically these have been especially severe outbreaks and occasionally even influenza pandemics. The World Health Organization (WHO) has this to say about pandemic influenza:

> A disease epidemic occurs when there are more cases of that disease than normal. A pandemic is a worldwide epidemic of a disease. An influenza pandemic may occur when a new influenza virus appears against which the human population has no immunity. . . . Pandemics can be either mild or severe in the illness and death they cause, and the severity of a pandemic can change over the course of that pandemic. (WHO, 2011)

For the first time in forty years, on June 11, 2009, WHO declared the novel H1N1 flu virus to be pandemic. WHO declared the pandemic officially over on August 10, 2010, although the U.S. Public Health Emergency expired on June 23, 2010. In the year from April 2009 to April 2010 the CDC estimates that in the United States there were 43 million to 89 million cases of H1N1 influenza and between 8,870 and 18,300 H1N1-related deaths.

One of the most important things people did to protect themselves was to be vaccinated, but during 2009 they had to be given two vaccines—one for seasonal flu and one for H1N1. In 2010, H1N1 was one of the three strains included in the seasonal flu vaccine, so only one vaccine was needed to provide the best available protection.

Vaccines remain the best protection against influenza for virtually everyone. The influenza (flu) viruses selected for inclusion in the seasonal flu vaccines are updated each year based on information about which influenza viruses are being found, how they are spreading, and how well the previous season's vaccine viruses might protect against any that are being newly identified. The 2011/2012 influenza vaccine recommended for the Northern and Southern Hemispheres by WHO contains the same viral strains as the 2010/2011 vaccine (CDC, 2011j).

In past years, the CDC's goals emphasized the importance of increasing vaccination percentages among high-risk target groups. However, in 2010 the Advisory Committee on Immunization Practices (ACIP) voted for "universal" flu vaccination in the United States to expand protection against the flu to more people, saying that "All individuals aged 6 months or older should be vaccinated annually." This universal vaccination guideline continues into the 2011/2012 influenza season and reflects lessons learned from the 2009 pandemic (CDC, 2011PB).

The vaccines for the 2011/2012 influenza season will be available beginning in August and will be widely available by September and October. CDC recommends that people get the seasonal flu vaccine as soon as it becomes available in their community. Vaccination before December is best, since this timing ensures that protective antibodies are in place before flu activity is typically at its highest. CDC continues to encourage people to get vaccinated throughout the flu season, which can begin as early as October and last as late as May. It remains to be seen how these new recommendations will affect vaccination rates and what strategies will be employed to help meet them.

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(Post test begins on next page)

Post Test

Use the Answer Sheet following the test to record your answers. There are 23 questions.

1. Influenza A, B, and C viruses:
   a. Cause seasonal outbreaks of influenza every 3 to 4 years.
   b. Are all equally severe in humans.
   c. Are differentiated by the nuclear material of the virus.
   d. Affect domestic and wild animals predominantly.

2. Influenza A viruses:
   a. Cause severe illness only in older adults.
   b. Cause mild disease affecting children primarily.
   c. Rarely cause disease in humans.
   d. Cause moderate to severe illness in all age groups.

3. Influenza B viruses:
   a. Cause the most severe disease of the three influenza types.
   b. Primarily affect children.
   c. Are unstable because of antigenic drift.
   d. Affect both humans and animals.

4. Influenza C is rarely reported as a cause of human illness and has never been associated with epidemic disease.
   a. True
   b. False

5. **Antigenic drift** in one or more surface antigens of the influenza A virus:
   a. Causes such gradual change in the virus that it is unrelated to major outbreaks of influenza.
   b. Occurs because of the overuse of antibiotics, resulting in antibiotic-resistant strains of the virus.
   c. Happens because of mutations in a gene segment.
   d. May result in an epidemic because protection from past exposures is incomplete.

6. **Antigenic shift,** a major abrupt change in influenza A viruses:
   a. Is probably due to genetic recombination, an exchange of a gene segment.
   b. Occurs regularly, making it relatively easy to adjust vaccines.
   c. Occurs every few centuries and has caused pandemics every time it has happened.
   d. Has not been identified in the past hundred years.

7. Both antigenic drift and antigenic shift have the potential for epidemic.
   a. True
   b. False

8. Influenza in animals:
   a. Is never seen as a mixture of influenza strains.
   b. Has no crossover effect in humans.
   c. Can cause pigs to get cough, fever, and the sniffles.
   d. Rarely afflicts wild and domestic birds.

9. Transmission of influenza in humans:
   a. Occurs from chronic carriers of the disease who do not know they are infected.
   b. Is primarily through the blood of an infected person.
   c. Can be through contact with fecal material of individuals who have symptomatic diarrhea.
   d. Occurs primarily person to person via large virus-laden droplets generated by cough or sneeze.

10. The number of deaths attributed to influenza are:
    a. Remarkably consistent from year to year.
    b. Usually highest in children aged 0 to 4 and adults 65 years and older.
    c. Highest in children aged 5 to 18 years.
    d. Usually higher in an epidemic than in a pandemic.

11. The "classic" clinical symptoms of influenza:
    a. Include abrupt onset of fever, myalgia, sore throat, cough, and headache.
    b. Should be treated with aspirin in infants, children, and teenagers.
    c. Occur in all infected individuals.
    d. Typically last for at least 1 to 2 weeks.

12. Certain groups of people are at greater risk of complications if they get the flu. This includes:
    a. Healthy older adults living at home.
    b. People who live in nursing homes.
    c. Women of child-bearing age.
    d. Middle-aged adults.

13. The most common influenza complication is:
    a. Meningitis that may occur up to 2 weeks after initial symptoms.
    b. Secondary bacterial pneumonia.
    c. Reye syndrome.
    d. Myocarditis.

14. When caring for a person at home who has influenza:
    a. Restrict fluids to small amounts of slightly salty water.
    b. Treat as soon as possible with a broad-spectrum antibiotic.
    c. Give cough or cold medicines to all children under 4 years of age.
    d. Avoid having other people enter the sick room.

15. Common signs that an adult with influenza has severe illness requiring immediate medical care include:
    a. Fever with a rash and pain or pressure in the chest.
    b. Difficulty breathing, sudden dizziness, pain or pressure in the chest.
    c. Bluish skin color and pain or pressure in the chest.
    d. Fast breathing, bluish skin color, confusion.

16. The influenza antiviral agents amantadine and rimantadine:
    a. May be used instead of antibiotics for treatment of influenza.
    b. Are no longer recommended for use against influenza in the United States.
    c. Are approved for prophylaxis of influenza in individuals 5 years and older.
    d. Are approved for prophylaxis of influenza in individuals 65 years and older.

17. Antiviral agents for influenza:
    a. Are an adjunct to vaccine and are not a substitute for vaccine.
    b. May be used freely, as there are no problems with resistant viral strains.
    c. Are quickly replacing vaccines as the primary means to combat influenza.
    d. Were first used against the 2009 H1N1 influenza.

18. In 2010 the Advisory Committee on Immunization Practices (ACIP) issued a recommendation that calls for influenza vaccination of:
    a. All people aged 6 years and older.
    b. Everyone without exception.
    c. All people aged 6 months and older.
    d. All people under age 6 and over age 65.

19. Administration of the LAIV influenza vaccine:
    a. Must be followed up with two more vaccinations over two months.
    b. Must be given only intramuscularly or subcutaneously.
    c. Is approved for administration to healthy, pregnant women.
    d. Is approved for use only in healthy, non-pregnant persons 2 to 49 years of age.

20. Immunity following inactivated influenza vaccination lasts:
    a. Only for the winter months.
    b. Less than 1 year.
    c. More than 1 year.
    d. Up to 5 years in some people.

21. TIV (trivalent inactivated vaccine) is recommended:
    a. Before December to ensure protective antibodies are in place before the height of flu season.
    b. For individuals receiving chronic aspirin therapy due to the risk of Reye syndrome.
    c. To be given via intradermal, subcutaneous, mucosal, or topical routes.
    d. Not to be administered to pregnant women.

22. LAIV (live attenuated influenza vaccine):
    a. May be given IM to children younger than 2 years and adults over 50 years of age.
    b. Is recommended for pregnant women.
    c. Is recommended for those who have diabetes.
    d. Should not be given to people who are immunosuppressed.

23. Immediate hypersensitivity reactions to the influenza vaccine may occur:
    a. In individuals who have severe egg allergies.
    b. In those with no previous exposure to the viral antigens in the vaccine.
    c. If the person has had prior localized reactions to flu vaccine at the injection site.
    d. In 15% to 20 % of vaccine recipients.

(Answer sheet follows on next page)

Answer Sheet

Flu Season 2011/2012

Name (Please print your name): _____
Date: _____

Passing score is 80%

1. _____
2. _____
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21. _____
22. _____
23. _____

(Course evaluation follows on next page)

Course Evaluation

Please use this scale for your course evaluation. Items with asterisks (*) are required.

5 = Strongly agree

4 = Agree

3 = Neutral

2 = Disagree

1 = Strongly disagree

*1. Upon completion of the course, I was able to:

a. Describe the origins of the flu.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

b. Explain the major features and behavior of influenza viruses.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

c. Outline the epidemiological features of influenza.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

d. List the methods and purpose of influenza surveillance.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

e. Identify the clinical features of influenza.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

f. Explain the process for laboratory diagnosis of influenza.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

g. Delineate the treatment of those with the flu, including basic prevention measures.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

h. Highlight those populations that are at high risk for infection.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

i. Outline the use of antiviral agents for influenza.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

j. Discuss the influenza vaccine, including its characteristics, efficacy, scheduling, and use.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

*2. The course was written in a way that facilitated my learning.
❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

*3. This course was free from commercial bias.

❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

*4. The course met my continuing education needs.

❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

*5. The material presented was supported by evidence.

❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

*6. The author avoided the use of anecdotal information as the main source of material.

❑ 5 ❑ 4 ❑ 3 ❑ 2 ❑ 1

*7. The course was free of product promotion.

❑ Yes ❑ No**

** If you answered no, please answer #8.

8. Was product promotion the sole purpose of the presentation?

❑ Yes ❑ No**

*9. It took me 60 minutes per contact hour to complete the course, test, and evaluation.

❑ Yes ❑ No**

** If your answer was no, how long did it take?

_____

10. My professional educational level is (check one):

Nursing

❑ Nurse Aide ❑ LVN/LPN ❑ RN (diploma) ❑ RN (AD)

❑ BSN ❑ MSN ❑ Nurse Practitioner/Advanced Practice Nurse

❑ PhD/DNSc

Therapy

❑ OT Aide ❑ COTA ❑ OT ❑ MOT ❑ OTD

❑ PT Aide ❑ PTA ❑ PT ❑ MPT ❑ MSPT ❑ DPT ❑ PhD

Other (please specify): _____

11. I heard about ATrain Education from:

- ❑ Search engine
- ❑ Advertisement
- ❑ Government or Board website
- ❑ Returning customer
- ❑ Friend
- ❑ Publication (Magazine, etc.)
- ❑ Other _____

12. I found the ATrainCEU.com website easy to use:

❑ Yes ❑ No

13. Comments or suggestions (optional): _____

_____

_____

(Registration on next page)

Registration Information

Please answer all of the following questions (*required).

* Name: _____

* Address: _____

* City: _____ State: _____ Zip: _____

* Phone: _____

* Professional Designation: _____

* License Number and State: _____

Please email my certificate: ❑ Yes ❑ No
Email (required if you want your certificate sent by email): _____
(If you request an email certificate we will **not** send a copy of the certificate by US Mail.)

Payment Options
You may pay by credit card or by check.
Fill out this section only if you are **paying by credit card**.
3.0 contact hours: $19

Credit card information:
Name _____

Address (if different from above): _____

City: _____State: _____ Zip: _____

Card type: ❑ Visa ❑ MC ❑ American Express ❑ Discover

Card number _____ CVS # _____

Expiration date _____

Test Completion and Mailing Instructions

1. Complete all forms:
   - ❑ Answer Sheet
   - ❑ Evaluation Learning Activity
   - ❑ Registration Form (this page)
2. If you are **paying by check**, prepare a check for $19 made out to ATrain Education, Inc.
3. Mail the completed forms and your payment to:

   ATrain Education, Inc
   5171 Ridgewood Rd
   Willits, CA 95490

When we receive your forms and payment, we will mail (or email, if you request it) your certificate of completion. If you have any questions or concerns, please call or contact us at Sharon@ATrainCEU.com. And thanks for taking the ATrain!