LEARNING OUTCOME AND OBJECTIVES: Upon completion of this course, you will be able to demonstrate knowledge of the symptoms, treatment, and prevention of seasonal influenza for 2019–20. Specific learning objectives to address potential knowledge gaps include:

- Discuss key concepts related to the transmission, symptoms, diagnosis, and treatment of influenza (flu).
- Explain the rationale for vaccination and other preventative measures against seasonal flu, based on the chain of infection.

INTRODUCTION

Influenza (flu) is a highly contagious respiratory illness that has sickened and killed millions of people in local epidemics and global pandemics. Caused by different types of influenza viruses, it can bring about mild to severe illness, sometimes leading to hospitalization or death. Those at high risk for serious complications include older adults, very young children, pregnant women, and people with certain chronic medical conditions. An annual vaccination is the best way to prevent the flu. The composition of flu vaccines in the United States is reviewed and updated annually to protect against the types of flu virus that researchers believe will be most common that year (CDC, 2018a; Grohskopf et al., 2019).

The first documented pandemic that clearly fits the description of influenza was in 1580. The most lethal pandemic of record began in 1918, just after World War I, when an estimated 21 million people died from what was called the Spanish flu (CDC, 2018a).

Smith, Andrewes, and Laidlaw isolated influenza A virus in ferrets in 1933, and Francis isolated influenza B virus in 1936. In 1936, Burnet showed that the virus lost virulence when it was cultured in fertilized 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 (CDC, 2018a).

Since then, vaccination has limited the infection’s spread but has not prevented pandemics of the
disease (CDC, 2018j). In 1957, the Asian flu swept around the world, killing 1 to 1.5 million
people; and in 1968, a pandemic called Hong Kong flu killed nearly a million more. In April
2009, a novel influenza A (H1N1) evolved and spread throughout North America, and eventually
the world, becoming a pandemic. In the Unites States, the CDC reported that this H1N1
pandemic caused illness in more than 60 million people, led to more than 270,000
hospitalizations, and resulted in 12,500 deaths (CDC, 2018a).

INFLUENZA VIRUSES

All influenza viruses belong to the Orthomyxoviridae family of RNA viruses, including types A,
B, C, Isa virus, thogotovirus, and others.

Types of Influenza Viruses

The human influenza virus types A and B cause the seasonal epidemics of disease almost every
winter in the United States. When a new and very different influenza A virus emerges, it can
cause an influenza pandemic (CDC, 2017a).

Type A viruses are the most virulent of influenza types and produce the most severe symptoms.
There are multiple subtypes of influenza A viruses. Only two subtypes (H1N1 and H3N2) are, at
this time, in general circulation among people. The type A H1N1 virus that emerged in 2009 was
very different from the type A H1N1 viruses that had previously been circulating in humans, and
this new virus caused the first influenza pandemic in more than 40 years (see above) (CDC,
2017b).

Type B viruses infect only humans and generally cause milder disease than type A. Type B
viruses do not cause pandemics (WebMD, 2017).

Type C viruses have one serotype. Primarily a human pathogen, type C infection has also been
observed in pigs, dogs, horses, and cattle. Influenza type C is rarely reported as a cause of human
illness, probably because most cases are mild and present no obvious symptoms. It has not been
associated with epidemic disease (CDC, 2017a; Lambert et al., 2016).

Type D influenza viruses affect cattle primarily and are not known to infect or cause illness in
people (CDC, 2017a).

Immune Response

When viruses laden with antigens infect a human or an animal, the body recognizes them as
foreign substances and reacts in what is called an immune response. This response creates
antibodies against the foreign substance and is referred to as active immunity. After recovery
from the infection, the human or animal is usually immune to getting the same viral disease for years (perhaps a lifetime). Influenza vaccines help develop immunity over a few to several weeks by imitating an infection and causing the immune response that protects against the same virus in the future (CDC, 2017b).

Passive immunity occurs when a person is given antibodies to a disease rather than producing them through the immune system. Passive immunity can be obtained by receiving antibody-containing blood products such as immune globulin when immediate protection is required. Such protection lasts only for a few weeks or months (CDC, 2017b).

Antigen Drift and Shift

Influenza viruses change constantly. They do this in two ways: antigenic drift and antigenic shift.

Antigenic drift refers to small changes in the genes of influenza viruses that happen on a continual basis over time as the virus replicates. These genetic changes typically produce viruses that are closely related to each other. These viruses usually share the same antigenic properties. Thus, an immune system exposed to a similar virus will usually recognize and respond to it (CDC, 2017d).

However, these small genetic changes accumulate over time and eventually cause the development of viruses that are antigenically different. When this occurs, the body’s immune system may not recognize such viruses, and illness can occur. These viral changes are anticipated, so the composition of the flu vaccine must be evaluated every year and updated as needed. Pandemics are less likely to occur with antigen drift thanks to researchers who continually monitor virus evolution and update vaccines as needed and to the gradual nature of virus replication. Influenza type B viruses change only via the gradual process of antigenic drift (CDC, 2017d).

Antigenic shift is an abrupt, major change in influenza A viruses that causes the production of new proteins in the influenza viruses that infect humans. It is typically unexpected and unpredictable. Antigenic shift leads to a new influenza A subtype or one that has emerged from an animal population that is so different from the same subtype of viruses in humans that most people do not have immunity to the new type of virus. When this type of shift occurs, the new viruses infect people, spread rapidly, and lead to a pandemic (CDC, 2017d).

<table>
<thead>
<tr>
<th>COMPARING ANTIGENIC DRIFT AND SHIFT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antigenic Drift</strong></td>
</tr>
<tr>
<td>• Small, incremental build-up of changes</td>
</tr>
<tr>
<td>• Expected, researchers alert to potential</td>
</tr>
<tr>
<td>• Less likely to lead to pandemic</td>
</tr>
</tbody>
</table>
AVIAN FLU

Avian influenza viruses most commonly infect birds and rarely infect people. The subtypes of avian flu that most often infect humans are AH5, AH7, and AH9 viruses. These are nonhuman viruses (i.e., they are novel among humans, in that they do not at present readily infect humans) but they do circulate in birds in parts of the world. There is little to no immunity against these viruses among people. If any of these viruses were to change in such a way that it was able to infect humans easily and spread easily from person to person, an influenza pandemic could result.

Although avian influenza A viruses usually do not infect humans, rare cases of human infection with these viruses have been reported. Most human infections with avian influenza A viruses have occurred following direct or close contact with infected poultry.

- AH5 subtype H5N1 has been reported as infecting humans in 16 countries, frequently leading to severe pneumonia and greater than 50% mortality.
- Subtypes of AH7 viruses rarely infect humans, but when they do, severe respiratory illness and death have occurred.
- AH9 subtype H9N2 has infected people and generally caused mild upper respiratory tract illness. However, one such infection resulted in death.

The spread of avian influenza A viruses from one ill person to another has been reported very rarely. However, because of the possibility that avian influenza A viruses could change and gain the ability to spread easily between people, monitoring for human infection and person-to-person transmission is extremely important to public health.

Seasonal influenza vaccination will not prevent infection with avian influenza A viruses but can reduce the risk of infection with both human and avian influenza A viruses. It is also possible to make a vaccine that can protect people against avian influenza viruses. For example, the United States government maintains a stockpile of vaccine adequate to immunize 20 million persons against avian influenza A H5N1 (CDC, 2019a, 2017a, 2017c).

Seasonal Vaccine

Because viruses change constantly, the World Health Organization monitors the changes globally each season. The data obtained is then used to predict the strain that will be most prevalent during the next flu season and to publish vaccine recommendations to prevent what is called seasonal influenza (WHO, 2018).

In 2016, a new strategy was developed that can predict flu mutations before they occur in nature by simulating the changes in a laboratory. This new laboratory-based method of predicting how current viral strains of influenza will mutate can also be used to help select the strains to be included in the next seasonal flu vaccine (NIAID, 2016a).
Three types of vaccine-induced antibodies have been identified that can neutralize diverse strains of influenza virus that affect humans. This discovery will help in the future development of a universal influenza vaccine. Such a vaccine would be effective against multiple subtypes of influenza and would eliminate the need to update the vaccine each year. Dozens of vaccines are undergoing study around the world, and more than half of them are in the preclinical phase of study. As yet, it is uncertain when any of them will be ready for use (NIAID, 2016b).

HIGH-RISK POPULATIONS

Anyone can be infected with the flu virus, but the disease is more severe and the consequences more critical for some people than others. The most vulnerable are:

- Children under 5 years of age, especially those younger than 2 years of age
- Adults 65 years of age and older
- Pregnant women and women up to two weeks postpartum
- Residents of nursing homes and other long-term care facilities
- Native Americans and Alaska Natives

(CDC, 2018b)

Native Americans and Alaska Natives are more likely to be hospitalized from the flu than the general U.S. population. Experts are not sure exactly why, but reasons that these populations are at high risk of flu complications could include social and economic factors that often result in reduced access to healthcare and crowded living conditions (CDC, 2016a).

In addition, influenza can make chronic health problems worse. For example, individuals with asthma may suffer asthmatic attacks, and people with chronic congestive heart failure may experience an accumulation of fluid in the lungs, abdominal organs, and peripheral tissue. Generally speaking, people with the following medical conditions are more vulnerable to serious influenza-related complications:

- Asthma
- Neurological and neurodevelopmental conditions, including disorders of the brain, spinal cord, peripheral nerve, and muscles
- Chronic lung diseases such as chronic obstructive pulmonary disease (COPD) and cystic fibrosis
- Heart diseases such as congestive heart failure, congenital heart disease, and coronary artery disease
- Blood disorders such as sickle cell disease
- Endocrine disorders such as diabetes mellitus
• Kidney disorders
• Liver disorders
• Inherited metabolic disorders and mitochondrial disorders
• Weakened immune system due to disease or medication (HIV, AIDS, cancer, steroids)
• Morbid obesity (body mass index ≥40) (found to be a risk factor, independent from other chronic illnesses, resulting in greater hospitalization and death during the H1N1 pandemic)
• Any condition in children younger than 19 years of age that requires long-term aspirin therapy (related to Reye’s syndrome, see below)
  (CDC, 2018b)

RECOGNIZING INFLUENZA

Symptoms and Severity

Influenza is a highly contagious infection of the respiratory tract. The signs and symptoms of influenza can vary by age, immune status, and presence of underlying medical conditions. It should not be confused with a gastrointestinal illness sometimes referred to as the stomach flu. Uncomplicated influenza can cause mild to severe illness and may include any or all of these signs and symptoms:

• Fever (usually high, however, not everyone with the flu has a fever, especially elderly persons)
• Chills
• Dry cough
• Sore throat
• Runny or stuffy nose
• Muscle or body aches
• Headache
• Fatigue
• Cervical lymphadenopathy
• Conjunctivitis, rhinitis, and gastrointestinal symptoms (more common in infants and young children than adults)
  (CDC, 2016b; Brook, 2019)

The indicators of influenza are referred to as flu-like symptoms.
In the early stages of an infection, it may be difficult to distinguish between a common cold and influenza. However, the symptoms of flu are more severe and last longer than the common cold. A comparison of the usual symptoms of influenza and the common cold are listed below.

### INFLUENZA VS. THE COMMON COLD

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Influenza</th>
<th>Common Cold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Characteristic, high (100 °F–102 °F), lasts three to four days</td>
<td>Rare</td>
</tr>
<tr>
<td>Headache</td>
<td>Sudden onset, may be severe</td>
<td>Rare, usually mild</td>
</tr>
<tr>
<td>Muscle aches</td>
<td>Usual, often severe</td>
<td>Mild</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Often extreme, may last 2 to 3 weeks</td>
<td>Quite mild</td>
</tr>
<tr>
<td>Chills</td>
<td>In about 50% of cases</td>
<td>Not common</td>
</tr>
<tr>
<td>Rhinitis and runny nose</td>
<td>Sometimes</td>
<td>Common</td>
</tr>
<tr>
<td>Sneezing</td>
<td>Sometimes</td>
<td>Common</td>
</tr>
<tr>
<td>Sore throat</td>
<td>May occur</td>
<td>Common</td>
</tr>
<tr>
<td>Nausea, vomiting, diarrhea</td>
<td>Not usual; most often in children</td>
<td>Unusual</td>
</tr>
<tr>
<td>Cough</td>
<td>Dry cough (no phlegm) that may be severe; may last several weeks</td>
<td>Common, generally mild to moderate, usually produces phlegm</td>
</tr>
</tbody>
</table>

(CDC, 2019b)

### Diagnosis

The diagnosis of influenza is based on presenting symptoms and viral tests. However, **most individuals with flu symptoms do not require special testing because test results usually do not change their treatment**. The CDC offers a guide for practitioners in considering influenza virus diagnostic tests for individual patients when influenza viruses are circulating in the community.
GUIDE FOR CONSIDERING INFLUENZA VIRUS DIAGNOSTIC TESTING*

Does the patient have signs and symptoms suggestive of influenza, including atypical clinical presentation, or findings suggestive of complications associated with influenza?

- YES
  - Is the patient being admitted to the hospital?
    - YES
      - Test for influenza; start empiric antiviral treatment for hospitalized patients while results are pending (molecular assays should be used for influenza testing of hospitalized patients). Proper interpretation of testing results is important.
    - NO
      - Will influenza testing results influence clinical management?
        - YES
          - Influenza clinically diagnosed; start empirical antiviral treatment if patient is in high-risk group for influenza complication or has progressive disease; advise close follow-up if worsening
        - NO
          - Testing probably not indicated; consider other etiologies

- NO

* Refer to source document for additional explanatory text. (Source: CDC, 2019c.)

DIAGNOSTIC TESTS

There are a number of different tests used in diagnosing influenza. All of the following tests can be obtained from a mucus specimen collected from the back of the throat or nose by a healthcare provider (see “How to Obtain a Nasopharyngeal Specimen” below).

**Rapid influenza diagnostic tests (RIDT)** for antigen detection yield results in 15 minutes or less and display the results as “positive” or “negative.” However, these results are not foolproof and may give a false negative when the patient is actually infected or a false positive when the patient is not infected with influenza viruses. False negatives are more likely when influenza activity is high; during periods of low influenza activity, false positives may occur more often.
• RIDTs can help with diagnostic and treatment decisions for patients in clinical settings, such as whether to prescribe antiviral medications.

• Due to the possibility of a false negative result and/or the fact that this test is less likely to detect type B influenza, the decision to withhold antiviral medications from a symptomatic patient should not be based solely on a negative RIDT test result.

• Once the presence of influenza activity has been documented in a community or geographic area, a clinical diagnosis of influenza can be made for outpatients with signs and symptoms consistent with suspected influenza, especially during periods of peak influenza activity in the community.

RITDs are used to detect influenza virus as the cause of respiratory infections, and public health authorities should be notified promptly of any suspected outbreaks, especially in institutions such as nursing homes, hospitals, schools, etc. Respiratory specimens should then be collected for ill persons and sent to a public health laboratory for more accurate influenza testing (CDC, 2016c).

**Viral tissue cell culture** is a test on respiratory samples for determining the influenza A virus subtypes and influenza A and B virus strains causing illness. It is also used for surveillance of new virus strains that may need to be included in future vaccines (CDC, 2016d).

**Rapid cell culture** (shell vials, cell mixtures) yields live virus and takes one to three days.

**Reverse transcription-polymerase chain reaction (RT-PCR)** is a molecular assay that can identify the presence of influenza viral RNA or nucleic acid in respiratory secretions. It is used for hospitalized patients with suspected influenza and pneumonia if an upper respiratory tract specimen is negative and if positive testing would result in a change in clinical management. It is particularly useful in identifying influenza virus infection as a cause of respiratory outbreaks in institutions and in detecting novel influenza A strains. Results are generally available in one to eight hours (CDC, 2016d).

**Immunofluorescence**—direct (DFA) or indirect fluorescent-antibody (IFA) staining—is a type of antigen detection with results in two to four hours (CDC, 2016d).

**Rapid molecular assay** is a diagnostic test for upper respiratory tract specimens and takes approximately 20 minutes (CDC, 2019d).
HOW TO OBTAIN A NASOPHARYNGEAL SPECIMEN

- Explain the procedure to the patient in order to obtain their cooperation.

- Ask the patient to blow their nose just prior to specimen collection. Provide tissues and a place to dispose of the contaminated tissues. Then, ask the patient to wash or sanitize their hands with alcohol wipes.

- Gather equipment: appropriate swab; transport media; and personal protective equipment (PPE), including gloves, gown, respirator, and eye protection as prescribed by public health officials. Ideally, use a swab with a synthetic tip such as nylon. Specimen collection vials should contain 1 ml to 3 ml of viral transport medium containing protein stabilizer, antibiotics to discourage bacterial and fungal growth, and buffer solution.

- Wash or sanitize your hands and put on PPE.

- Tilt patient’s head back 70 degrees.

- Insert swab into nostril. (Swab should reach depth equal to the distance from nostrils to outer opening of the ear.) Leave swab in place for several seconds to absorb secretions.

- Slowly remove swab while rotating it. (Swab both nostrils with same swab.)

- Place tip of swab into sterile viral transport media tube and snap/cut off the applicator stick.

Proper technique for obtaining a nasopharyngeal specimen, with swab inserted to a depth equal to the distance from nostrils to outer opening of the ear. (Source: CDC, n.d.)
TREATING PATIENTS INFECTED WITH FLU

Comfort and Care

Very young children and older adults who are infected with virulent influenza viruses can be very ill. Such seriously ill people need rest, comfort, sleep, and extra fluids. They may benefit from analgesics and antipyretic medications such as ibuprofen (Advil) and acetaminophen (Tylenol). In spite of the misery for the first few days, most children and adults gradually recover in one to two weeks without complications or antiviral medications.

Children and adolescents under 19 years of age who are experiencing influenza symptoms should not be given any medication containing salicylates, such as acetylsalicylic acid (aspirin), because it has been linked with the risk of Reye’s syndrome, a rare, but potentially fatal neurological and/or hepatic disease.

Measures should be taken to reduce the spread of infection, including handwashing, covering the mouth and nose when sneezing or coughing, and avoiding crowds during peak flu season. If sick, the person should stay home for at least 24 hours after fever subsides (Mayo Clinic, 2019).

Antiviral Medications

Antiviral medications decrease the ability of influenza viruses to reproduce. These drugs are recommended for both treatment and prevention of influenza. Antiviral drugs work best when taken within 48 hours of influenza symptom onset. However, they may still offer benefits if taken later, especially if the patient is at high risk of serious influenza complications or is hospitalized with more illness. Healthcare providers may prescribe an antiviral medication if someone comes in close contact with someone who has influenza. The CDC does not recommend widespread or routine use of antiviral medications because that can lead to drug-resistant strains of the virus (CDC, 2019e, 2018c; WebMD, 2019).

RECOMMENDATIONS REGARDING MEDICATION TREATMENT

The CDC (2018c) recommends these drugs be given as early as possible to any patient who has confirmed or suspected influenza and:

- Is hospitalized
- Has severe, complicated, or progressive illness
- Is at higher risk for influenza complications (as listed earlier in this course), including:
  - Children younger than 2 years of age
  - Adults 65 years and older
  - Women who are pregnant or postpartum within two weeks of delivery during flu season
- Children and adolescents younger than 19 years who are receiving long-term aspirin therapy
- People with certain chronic medical conditions, including chronic pulmonary, cardiovascular, renal, hepatic, hematological, and metabolic disorders, or neurologic and neurodevelopment conditions
- People with immunosuppression, including those caused by medications or by HIV infection
- Native Americans/Alaska Natives
- Persons who are morbidly obese (body mass index ≥40)
- Residents of nursing homes and other chronic care facilities

Although all children younger than 5 years are considered at higher risk for complications from influenza, the highest risk is for those younger than 2 years, with the highest hospitalization and death rates among infants younger than 6 months. Because many children with mild febrile respiratory illness might have other viral infections (e.g., respiratory syncytial virus), knowledge of other respiratory viruses as well as influenza virus strains circulating in the community is important for treatment decisions (CDC, 2019e, 2018c; WebMD, 2019).

RECOMMENDED ANTIVIRAL DRUGS

Four antiviral drugs are approved by the U.S. Food and Drug Administration (FDA) and recommended by the CDC for use to prevent or treat influenza (CDC, 2018o). Antiviral drugs are not substitutes for annual flu vaccine. A summary of information regarding these drugs is as follows:

- **Oral oseltamivir phosphate (Tamiflu).** Oseltamivir is FDA-approved to treat influenza in people 2 weeks of age and older who have had symptoms for no more than two days. Although not part of the FDA-approved indications, use of oral oseltamivir in infants less than 2 weeks of age and in infants 3 months to 1 year is recommended by the CDC and the American Academy of Pediatrics. The most common side effects are nausea and vomiting. Other side effects include serious skin/hypersensitivity reactions and neuropsychiatric events; therefore, recipients should be monitored closely for signs of unusual behavior. The drug is available as a pill or liquid suspension. Oseltamivir is recommended for treatment of pregnant women with influenza because, compared to other antiviral drugs, it has the most studies available to indicate that the drug is beneficial during pregnancy (CDC, 2019e; Comerford & Durkin, 2019; Tamiflu, 2019).

- **Inhaled zanamivir (Relenza).** Zanamivir is administered to the respiratory tract via an oral disk inhaler device. It is approved to treat flu in people 7 years of age and older. Allergic reactions include oropharyngeal or facial edema. Common side effects are diarrhea; nausea; sinusitis; nasal signs and symptoms; bronchitis; cough; headache; dizziness; and ear, nose, and throat infections. It is contraindicated for those with underlying respiratory disease such as asthma or COPD and for those with a history of
allergy to milk protein (CDC, 2019e; Comerford & Durkin, 2019; RxList, 2016; WebMD, 2019).

- **Intravenous peramivir (Rapivab).** Peramivir may be used for treatment in people 2 years of age and older. It is not recommended for chemoprophylaxis. Side effects could include diarrhea and serious skin reactions as well as sporadic transient neuropsychiatric events. The drug is administered intravenously (CDC, 2019e; Comerford & Durkin, 2019; WebMD, 2019).

- **Baloxavir marboxil (Xofluza).** Baloxavir was approved in October 2018 by the FDA for the treatment of uncomplicated influenza in people 12 years of age and older who have had flu symptoms for less than two days. Baloxavir is a pill, given as a single-dose tablet by mouth. The CDC does not recommend use of baloxavir in pregnant women, breastfeeding mothers, outpatients with complicated or progressive illness, or hospitalized patients because of the lack of information on the use of baloxavir in these populations (CDC, 2018k).

Antiviral drugs work best when started within 48 hours of the onset of symptoms (without waiting for laboratory confirmation of the disease). Treatment duration depends on the antiviral drug prescribed. Oseltamivir and zanamivir are typically prescribed to be taken twice daily for five days. People who are hospitalized with influenza may need antiviral treatment for longer than five days. Peramivir is given one time intravenously over a period of 15 to 30 minutes. Baloxavir is given as a single oral dose (CDC, 2019e).

**PREVENTING FLU TRANSMISSION**

The most common way influenza viruses spread from person to person is by droplet infection. Infected people exhale, cough, or sneeze, and virus-containing droplets fly through the air into the nose and throat of others or onto some intermediate surface such as a doorknob. When other people touch a contaminated surface, viruses may stick to their fingers. When they touch the mucous membranes of their body, they then inoculate themselves with the virus (CDC, 2018l).

Influenza viruses can survive on hard surfaces for 24 hours and can also survive for several hours as droplets in the air. Low temperatures increase their airborne survival. Infectious flu viruses can survive on tissues for only 15 minutes (NHS, 2018).

Sick adults are able to infect others beginning one day before symptoms appear and up to five to seven days after they become ill. Sick children may be able to infect others beginning one day before symptoms appear and for more than seven days after they become ill (NYSDH, 2016).

Symptoms develop one to four days after the virus enters the body. That means people may be able to pass on the flu virus to others even before they know they are sick. **Any individual who is infected with viruses can infect others whether they show symptoms or not** (NYSDH, 2016).
The Chain of Infection

The process of transmission of an infectious agent such as the influenza virus can be best explained by the epidemiologic model called the chain of infection. An infectious disease results from specific interactions between the organism, host, and environment. Transmission occurs when the infectious organism leaves the reservoir or host through a portal of exit, travels by some mode of transmission, and enters through a portal of entry to infect another susceptible host (APIC, 2017).

- **Infectious agent** is the pathogenic organism that causes diseases.
- A **reservoir** is the habitat where the infectious agent normally lives and grows. Reservoirs may be humans, animals, insects, or the environment.
- The **portal of exit** is the path by which the infectious agent leaves its host (e.g., respiratory tract, open wounds).
- **Means of transmission** is the mode in which the infectious agent is transmitted from its natural reservoir to a susceptible host (e.g., touching a doorknob that contains infectious particles or droplet spread). Transmission can occur in a mode that is direct or indirect.
- The **portal of entry** refers to the way in which the infectious agent enters the host (e.g., through one’s nose into the respiratory tract when breathing in airborne particles, broken skin, mucous membranes, catheters, and tubes). The portal of entry must provide access to tissues in a way that allows the infectious agent to multiply and thrive.
- The final link is the **vulnerable or susceptible host**. Susceptibility of a host depends on many factors, including immunity and the individual’s ability to resist infection. (APIC, 2017)
By breaking any link of the chain of infection, healthcare professionals can prevent the occurrence of new infection. Infection prevention measures are designed to break the links and thereby prevent new infections. The chain of infection is the foundation of infection prevention.

<table>
<thead>
<tr>
<th>Link</th>
<th>Influenza Implications</th>
<th>Healthcare Provider Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious agent</td>
<td>Present in environment during flu season</td>
<td>Be aware of current strains and case reporting requirements</td>
</tr>
<tr>
<td>Reservoir</td>
<td>Potentially everyone, some higher risk</td>
<td>Promote vaccinations</td>
</tr>
<tr>
<td>Portal of exit</td>
<td>Droplets</td>
<td>Teach/reinforce sneeze/cough etiquette and correct use/disposal of tissues</td>
</tr>
<tr>
<td>Transmission</td>
<td>Organism can remain active on environmental surfaces</td>
<td>Teach disinfection techniques</td>
</tr>
<tr>
<td>Portal of entry</td>
<td>Nose/mouth</td>
<td>Teach/reinforce handwashing, not touching eyes/face, wearing masks</td>
</tr>
<tr>
<td>Vulnerable hosts</td>
<td>Everyone; some people at greater risk</td>
<td>Promote vaccinations among high-risk groups</td>
</tr>
</tbody>
</table>

**CDC Prevention Recommendations**

Because influenza produces such serious symptoms, the CDC has issued these prevention recommendations to the public:

1. Take time to get flu vaccinations.
2. Take every-day preventative actions:
   - Try to avoid close contact with sick people.
   - While sick with the flu, limit contact with others as much as possible to keep from infecting them.
   - When sick with flu-like illness, stay home for at least 24 hours after your fever is gone except to get medical care or for other necessities. (Your fever should be gone for 24 hours without the use of a fever-reducing medicine.)
   - 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.
   - Clean and disinfect surfaces and objects that may be contaminated with germs like the flu.
3. Take flu antiviral drugs if recommended by a primary care provider.

4. If an outbreak of flu occurs in your area, follow the advice given by public health officials. Such information may include how to increase distance between people and other measures.
   (CDC, 2018d)

**ADHERENCE TO DROPLET PRECAUTIONS**

Standard Precautions should be carefully adhered to when healthcare professionals provide care to patients with influenza. Additionally, the CDC (2018e) recommends the following adherence to **Droplet Precautions**:

- Implement Droplet Precautions for patients with either suspected or confirmed influenza for seven days after the onset of the illness or until 24 hours after symptoms of fever and respiratory symptoms have subsided. Droplet Precautions may remain in place for more than seven days based on clinical assessment.

- Place patients in a private room.

- Healthcare staff members should wear face masks when in the room with patients who have suspected or confirmed influenza. After leaving the room, remove the mask, dispose of it in appropriate waste containers, and perform hand hygiene.

- If patients need to be moved outside of their rooms, they should wear face masks and adhere to respiratory and cough precautions as well as hand hygiene.

- Inform personnel in the areas patients are transported to (e.g., radiology) that patients with confirmed or suspected influenza will be arriving in their departments.

Routine cleaning and disinfection strategies can also help prevent the spread of influenza. Management of laundry, utensils, and medical waste should be performed in accordance with established procedures.

**CASE**

John Smith, a 57-year-old man with a history of asthma, had been experiencing flu-like symptoms for three days. He was running a fever and, despite using his inhaler more frequently, found himself increasingly short of breath. At the urging of his wife, he went to the emergency department (ED) to be checked.

The ED intake staff noticed that Mr. Smith was frequently coughing, so they responded per facility policy by offering him a face mask to wear while he sat in the waiting room. As is consistent with their usual practice, the staff performed frequent hand hygiene. A few minutes later he was brought into triage, where the nurse noted that his symptoms were consistent with a contagious phase of influenza.
During triage, the nurse allowed Mr. Smith to remove his face mask for his comfort but donned a face mask herself to minimize the risk that she might become infected and transmit the virus to family or other patients who had not yet been vaccinated. After sending the patient to the ED, the nurse remembered to clean all surfaces near the patient in the triage room, including the doorknobs, with an alcohol-based wipe prior to the next patient’s arrival.

During further diagnostic testing, the ED team continued the practice established by the triage nurse of wearing face masks when they were within three feet of the patient while allowing him the comfort of not wearing a face mask.

Mr. Smith was admitted to the hospital with a diagnosis of left lower lobe pneumonia and influenza. On the advice of the infection prevention nurse, he was presumed to be infectious and was asked to wear a face mask when out of his room or being transported, while healthcare workers and visitors donned face masks when they expected to come within three feet of him.

The infection prevention nurse explained to Mr. Smith and his family that the use of face masks is a prudent measure to decrease the spread of the virus.

Public Education

Prevention of epidemics and pandemics depends on education of the public about the importance of vaccination and personal hygiene. The greater the number of vaccinated individuals, the fewer the cases of influenza. With increased prevention by individuals—such as covering a sneeze or cleansing the hands—the flu virus will be less likely to infect other people. For these reasons, healthcare providers have a special responsibility to encourage the general public to be vaccinated and to practice preventative measures.

SEASONAL FLU VACCINATION FOR 2019–2020

Routine annual influenza vaccination of all persons 6 months of age and older who do not have contraindications is recommended. Vaccination is especially important for vulnerable individuals with chronic medical conditions, healthcare workers, others who live with or care for high-risk people, pregnant women, adults age 65 and older, children younger than 5 years (especially children younger than 2 years old), and those who care for children younger than 6 months (Grohskopf et al., 2019).

Children age 6 months through 8 years should receive a second dose four weeks or more after the first dose 1) if they are receiving influenza vaccine for the first time, 2) if they did not receive a total of at least two doses of trivalent or quadrivalent influenza vaccine before July 1 of the current year, or 3) if their vaccination history is unknown (Grohskopf et al., 2019).
Possible Contraindications for Vaccination

Those who should not be vaccinated before talking to their primary care provider include:

- Those who have had a severe allergic reaction to an influenza vaccination in the past (e.g., anaphylaxis) after previous dose of influenza vaccine or to vaccine component
- Persons with moderate to severe acute illness with or without fever until symptoms are relieved
- Those who have had Guillain-Barré syndrome
  (U.S. DHHS, 2018)

Vaccination and Persons with Egg Allergy

The recommendations for people with a history of egg allergies include the following:

- People who have experienced only hives after exposure to egg can get any licensed flu vaccine (IIV, RIV4, or LAIV4) that is otherwise appropriate for their age and health.
- People who have symptoms other than hives after exposure to eggs (such as angioedema, respiratory distress, lightheadedness, or recurrent emesis) or who have needed epinephrine or any other emergency medical intervention also can get any licensed flu vaccine that is appropriate for their age and health, but the vaccine should be given in a medical setting and be supervised by a healthcare provider who is capable of recognizing and managing severe allergic conditions. Such settings include hospitals, clinics, health departments, and physician offices.
- People with egg allergies no longer have to wait 30 minutes for observation after receiving their vaccine.
  (U.S. DHHS, 2018)

Timing of Vaccination

The optimal time period when vaccination should occur is before the onset of influenza activity in a community. Healthcare providers should begin offering vaccination by the end of October whenever possible. Studies have shown that the vaccination is still beneficial even if given in December or later. Most adults will have a protective antibody response within two weeks following immunization. The vaccine should be offered continually as long as the influenza viruses are circulating and unexpired vaccine is available (CDC, 2018g).

Children aged 6 months through 8 years who require two doses of vaccine should receive their first dose as soon as possible after the vaccines becomes available to allow the second dose, which must be administered 4 weeks or later, to be received by the end of October. For those requiring only one dose for the season early vaccination (i.e., in July and August) is probably
linked with suboptimal immunity before the end of the influenza season, especially among older adults (Grohskopf et al., 2019).

**Vaccines for the 2019–2020 Flu Season**

There are many different flu viruses that are constantly changing. Vaccine composition is reviewed annually and updated as needed to match circulating influenza viruses (CDC, 2019f).

**NEW FOR THE 2019–2020 SEASON**

- Flu vaccines have been updated to better match circulating viruses.
- The A(H1N1)pdm09 vaccine component was updated from an A/Michigan/45/2015 (H1N1)pdm09-like virus to an A/Brisbane/02/2018 (H1N1)pdm09-like virus.
- The A(H3N2) vaccine component was updated from an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus to an A/Kansas/14/2017 (H3N2)-like virus.
- Both B/Victoria and B/Yamagata virus components from the 2018–2019 flu vaccine remain the same for the 2019–2020 flu vaccine. (CDC, 2019g)

**FLU VACCINE OPTIONS FOR THE 2019–2020 SEASON**

Vaccine options for the 2019–2020 season are quite similar to those from last year (2018–2019 season).

- Providers may choose to administer any licensed, age-appropriate flu vaccine.
- Standard-dose flu shots are given intramuscularly, usually with one needle.
- Various higher-dose vaccines are available for adults 65 and older. Since the effectiveness of the immune system decreases with age, a higher dose of antigen may give older people a better immune response and better protection against influenza.
- Adjuvants can be added to enhance immune response.
- Cell-based vaccine may be administered. (Cell-based vaccine was developed as an alternative to the egg-based manufacturing process.)
- Live attenuated influenza vaccine (LAIV), or nasal spray vaccine, is an option for persons whom it is otherwise appropriate.
- The American Academy of Pediatrics advises families to vaccinate their children against influenza for the 2019–2020 flu season with either the flu shot or the nasal spray vaccine. The AAP board of directors approved both options after reviewing the latest data on the inactivated vaccine (which is injected) and the quadrivalent live attenuated influenza vaccine (which is the nasal spray given to healthy patients aged at least 2 years).
- No preferential recommendation is made for one influenza vaccine product over another for persons for whom more than one licensed, recommended, and appropriate product is available.
  (CDC, 2018g, 2018h; AAP, 2019; Grohskopf et al., 2019)

**VIRUSES THAT THE 2019–2020 FLU VACCINE PROTECTS AGAINST**

Flu vaccines protect against the three or four viruses (depending on the vaccine) that research suggests will be most common. For 2019–2020, trivalent (three-component) vaccines are recommended to contain:

- A/Brisbane/02/2018 (H1N1)pdm09-like virus (updated)
- A/Kansas/14/2017 (H3N2)-like virus (updated)
- B/Colorado/06/2017-like (Victoria lineage) virus

**Quadrivalent (four-component) vaccines**, which protect against a second lineage of B viruses, are recommended to contain:

- The three recommended viruses above, plus B/Phuket/3073/2013-like (Yamagata lineage) virus
  (CDC, 2019f, 2019g; Grohskopf et al., 2019)

Clinicians who expect to be providing influenza vaccines should familiarize themselves with the CDC references and obtain copies of the most current vaccine dosing and administration tables so that, in consultation with medical providers, they are prepared to quickly ascertain the best vaccine options for their patients. (See “Resources” at the end of this course.)

**TIPS FOR INTRAMUSCULAR VACCINE ADMINISTRATION**

- Follow standard medication administration guidelines for site assessment/selection and site preparation.
- Prepare vaccine out of line of sight of patient and/or parents (for children).
- Position patient so that the muscle is as relaxed as possible. If using the deltoid, allow the arm to swing freely and not rest on the patient’s lap, chair arm, or any other surface.
- Allow skin disinfectant to dry completely before injecting; this ensures adequate skin contact time and minimizes secondary pain from disinfectant.
- To avoid injection into subcutaneous tissue, spread the skin of the selected vaccine administration site taut between the thumb and forefinger, isolating the muscle. Another technique, acceptable for pediatric and geriatric patients, is to grasp the tissue and “bunch up” the muscle.
• Insert the needle fully into the muscle at a 90° angle and inject (do not attempt aspiration).

• Withdraw the needle and apply light pressure to the injection site for several seconds with a dry cotton ball or gauze pad.

(CDC, 2018h)

Possible Side Effects Following Flu Vaccination

Following vaccination, some individuals experience mild side effects. These mild side effects may include:

• Soreness, redness, and swelling at the injection site
• Headache
• Fever
• Muscle aches
• Fainting

(CDC, 2018f)

Because these mild side effects mimic some influenza symptoms, some people believe the vaccine causes them to contract influenza. But the injectable influenza vaccine produced in the United States has never been capable of causing influenza. This is because the only type of licensed vaccine available is made from inactivated influenza viruses, which cannot cause infection, or with no flu viruses at all, which is the case for the recombinant influenza vaccine (CDC, 2017e).

Signs of a severe reaction to the flu vaccine include:

• High fever
• Behavioral changes
• Difficulty breathing
• Hoarseness or wheezing
• Swelling around the eyes of lips
• Hives
• Paleness
• Weakness
• Tachycardia
• Dizziness

(CDC, 2017e)
If signs of a severe reaction occur outside a healthcare setting, emergency medical intervention should be immediately obtained by calling 911.

**Flu Vaccination for Healthcare Workers**

The CDC, the Advisory Committee on Immunization Practices (ACIP), and the Healthcare Infection Control Practices Advisory Committee recommend that all U.S. healthcare workers be vaccinated annually against influenza. Healthcare workers include (but are not limited to):

- Physicians
- Nurses
- Nursing assistants
- Therapists
- Technicians
- Emergency medical service personnel
- Dental personnel
- Pharmacists
- Laboratory personnel
- Autopsy personnel
- Students and trainees
- Contractual staff not employed by the healthcare facility
- Persons not directly involved in patient care but potentially exposed to infectious agents:
  - Clerical
  - Dietary
  - Housekeeping
  - Laundry
  - Security
  - Maintenance
  - Administrative
  - Billing
  - Volunteers

(CDC, 2018m)
CASE

On a Friday afternoon in early September, Jeanine, a 55-year-old female patient, asked Dwayne Jones, RN, when she should receive her annual flu shot and if she could have the nasal spray so she didn’t need to have a shot. Dwayne told her he thought it was still a little early but did not yet have the information for the recommendations for this season. He reassured Jeanine that he would look into it and give her a call with further information.

Over the weekend, Dwayne went to the CDC website and read about the new recommendations for seasonal influenza vaccinations. He found a table that showed types of vaccines available, dosing, and route information. He also located information regarding when vaccinations should be provided. Dwayne printed the table and presented it to his nurse and physician coworkers when he came to work Monday morning. Together, they used the tables to determine the best option for a variety of their patients.

With a confirmation from the physician, Dwayne was then able to call the patient. He told Jeanine that the CDC recommends vaccines be given as soon as they are available and that the clinic expected to have their first doses available in early October. Dwayne informed her that a nasal spray form would be available this year and that Jeanine would be meeting with her healthcare provider to determine the best vaccine option for her.

PNEUMOCOCCAL VACCINE RECOMMENDATIONS FOR PERSONS AGE 65 AND OLDER

A serious complication of influenza is pneumococcal pneumonia caused by *Streptococcus pneumoniae*. It is the leading cause of vaccine-preventable illness and death in the United States. Adults 65 years and older are at greater risk for contracting this disease. Also, because some strains of this bacterium have become resistant to drugs that were effective in the past, prevention through vaccination has become even more important.

Two vaccines are available to prevent pneumococcal disease:

- PCV13
- PPSV23

The CDC (2018n) recommends two pneumococcal vaccines for all adults 65 years of age or older. Further recommendations state:

- Administer a dose of PCV13 first, followed by a dose of PPSV23, at least 1 year later.
- In those who already received any doses of PPSV23, administer the dose of PCV13 at least 1 year after the most recent PPSV23 dose.
- In those who already received a dose of PCV13 at a younger age, CDC does not recommend an additional vaccination.
CONCLUSION

Influenza still has the potential to be a deadly disease, but due to the work of scientists and clinicians, people can be protected from infection by the ever-changing influenza viruses. With vaccination and protective sanitary measures, infections can be reduced; and with antiviral medications, vulnerable individuals and those who are infected can be treated. Healthcare professionals play an important role in delivering this message to those they serve.

RESOURCES

Frequently Asked Flu Questions (CDC)

Influenza (Flu) (CDC)
https://www.cdc.gov/flu

Influenza (National Institute of Allergy and Infectious Diseases)
https://www.niaid.nih.gov/diseases-conditions/influenza

REFERENCES


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TEST

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1. Which is a **true** statement about influenza viruses?
   a. Type A viruses are the most virulent of the influenza types.
   b. Type B viruses affect animals as well as humans.
   c. Antigenic shift, or abrupt change, only occurs in influenza C viruses.
   d. Antigenic drift, or gradual change, only occurs in influenza A viruses.

2. Seasonal influenza vaccines are updated annually because:
   a. Last season’s vaccine may no longer protect against this year’s viral strains.
   b. Influenza A viruses always undergo an annual, abrupt antigenic shift.
   c. Influenza B viruses replace influenza A viruses.
   d. The previous season’s flu vaccine expires after 12 months.

3. The nurse working in a community health clinic is **least** concerned about influenza risk among which patient population?
   a. Patients with weakened immune systems
   b. Patients with sickle cell disease
   c. Adults with diabetes mellitus
   d. Adults under the age of 55 years

4. If a patient with symptoms of influenza is being admitted to a hospital:
   a. Empiric antiviral treatment is started while influenza testing results are pending.
   b. Testing is not indicated if the patient is hospitalized.
   c. Even positive diagnostic test results will not influence clinical management.
   d. Antiviral treatment is contraindicated if the patient is over the age of 65.

5. Which form of diagnostic testing for influenza provides the most rapid results?
   a. Viral tissue culture
   b. Rapid cell culture
   c. Rapid influenza diagnostic tests
   d. Reverse transcription-polymerase chain reaction
6. Aspirin is **not** administered to children and adolescents with flu-like symptoms because it is:
   a. Ineffective as an analgesic.
   b. Less effective than ibuprofen (Advil) or acetaminophen (Tylenol).
   c. Undesirable as an alternating drug with other antipyretics.
   d. Linked with the risk of Reye’s syndrome.

7. Antiviral drugs for influenza work best when started within what time frame from symptom onset?
   a. 7 days
   b. 5 days
   b. 72 hours
   d. 48 hours

8. To prevent transmission of the influenza virus, the clinician instructs patients who are **not** infected with the virus to:
   a. Wear protective masks whenever leaving home during the flu season.
   b. Avoid close contact with sick people.
   c. Avoid eating high-risk meat, such as pork and lamb.
   d. Wash clothing and linens in strong detergent.

9. Children 6 months to 8 years old who are receiving an influenza vaccine for the first time require an additional dose if:
   a. They have been exposed to someone who has influenza.
   b. They are receiving influenza vaccine for the first time.
   c. They have had an allergic reaction to a vaccine in the past.
   d. They have parents who disapprove of vaccine administration.

10. Receiving the influenza vaccine is contraindicated for:
    a. People who develop hives after exposure to eggs.
    b. Those who have had a severe allergic reaction to an influenza vaccination in the past.
    c. Those who faint after receiving an injection.
    d. Those who develop soreness, redness, and swelling at the injection site.
11. Which is a true statement about the 2019–2020 seasonal influenza vaccines?
   a. Flu vaccines protect against three or four viruses.
   b. Quadrivalent (four-component) vaccines have been discontinued.
   c. A/Brisbane/02/2018 (H1N1)pdm09-like virus (updated) is contraindicated for the 2019–2020 season.
   d. The vaccine containing the B/Colorado/06/2017-like (Victoria lineage) virus is recommended only for people who have allergies to eggs.

12. CDC recommendations for pneumococcal vaccines for all adults 65 years of age or older state that they should receive:
   b. An additional dose of PCV13 even if they previously received a dose of PCV13 at a younger age.
   c. Doses of both the PCV13 and the PPSV23 within a month of each other.
   d. A dose of PCV13 at least 1 year after the most recent PPSV23 if they have already received any doses of PPSV23.