Section I: Influenza 101

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What is Influenza?

Influenza, more commonly referred to as the flu, is a respiratory disease caused by influenza viruses. Influenza can range from mild to severe illness and even death (*1*). Symptoms of influenza may include fever or feeling feverish/chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches and fatigue. Among children, otitis media, nausea, vomiting and diarrhea are also commonly reported. Influenza is usually a self-limiting infection, but in people with chronic medical conditions such as heart or lung disease, it can lead to pneumonia and other life-threatening complications. Adults over 65 years of age account for approximately 90% of deaths attributed to pneumonia and influenza. An estimated 23,607 (range 3,349-48,614) deaths associated with influenza occur every year in the United States (*2*).

Influenza is an infectious disease that is easily transmitted from person to person (*1*). Transmission occurs via "droplet spread." After a person infected with influenza coughs, sneezes or talks, influenza viruses contained in the respiratory droplets travel through the air; other persons nearby can become infected if these droplets land in their noses or mouths. These droplets can also contaminate surfaces, and people can become infected when they touch an object or a surface on which these droplets have landed and then touch their noses or mouths. Transmission may also occur by direct contact, such as kissing. Symptoms of influenza usually come on suddenly, one to four days after the virus enters the body (*3*). Infected persons can start shedding virus up to 24 hours before the onset of symptoms (*1*). Additionally, some persons who become infected with influenza remain asymptomatic.

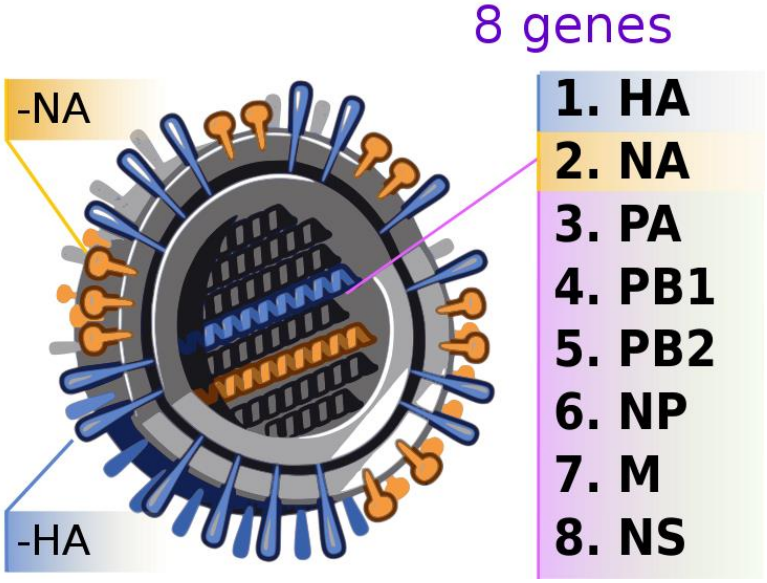
Some people are at higher risk of severe illness or complications from influenza, including people who (*1,4*):

- are less than 5 years of age
- are 65 years of age or older
- have chronic pulmonary (including asthma), cardiovascular (excluding hypertension), endocrine, renal, hepatic, neurologic, hematologic or metabolic disorders
- are immunosuppressed
- are or will become pregnant during the influenza season
- are younger than 19 years who are receiving long-term aspirin therapy
- are residents of nursing homes and other long-term care facilities
- are morbidly obese (body mass index $\geq$40)

Types of Influenza

Influenza viruses are single-stranded RNA viruses that belong to the family Orthomyxoviridae (*5*). There are four types of influenza viruses: Influenza A, B, C and D (*6*). Influenza A and B are the viruses seen during the regular influenza season in the United States. Influenza C is also present, but not very common. Influenza C causes a mild or subclinical illness and is not associated with epidemics. Influenza D viruses primarily affect cattle and are not known to infect or cause illness in people (*6*).

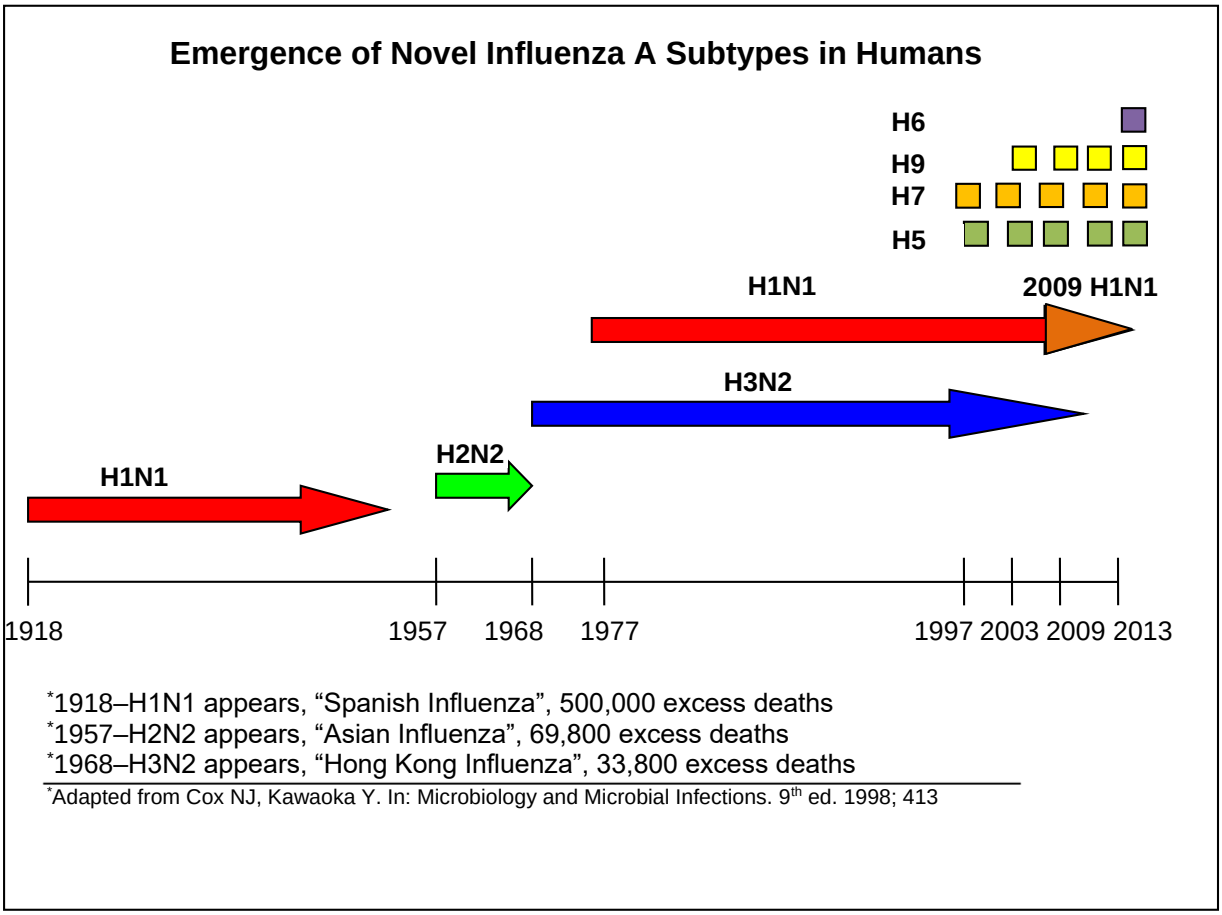
Influenza A viruses are further divided into subtypes based on differences in surface proteins. Influenza A has two surface proteins on the virus capsule called neuraminidase (11 variations) and hemagglutinin (18 variations), as seen in the diagram below. Different combinations of these surface proteins result in many subtypes of influenza A including H3N2 and H1N1, the subtypes currently circulating in humans. Influenza A viruses are unique in that they are able to cause infection in animal species as well as in humans. All known subtypes of influenza A viruses have been isolated from avian species except subtype H17N10 and H18N11 which have only been found in bats (*7*). Influenza A subtypes have also been found in pigs, horses, seals and whales, as well as many other animal species. Influenza B and C infections are primarily associated with illness in humans and are not often found in animals. Influenza B viruses are not subtyped; instead influenza B viruses are divided into lineages (i.e., Yamagata and Victoria) (*8*).



Source: http://commons.wikimedia.org/wiki/File:2009_H1N1_influenza_virus_genetic-num.svg

Influenza viruses undergo two different methods of antigenic change: antigenic drift and antigenic shift (*3,9*). Antigenic drift is the result of point mutations that occur during viral replication resulting in new virus strains. Antigenic drift is the reason that the influenza vaccine must be updated each year. Antigenic shift is a more dramatic change resulting in a novel subtype of influenza. Antigenic shift can lead to a pandemic because the majority of the population would have little or no immunity to novel subtypes created through reassortment. A pandemic could also occur through antigenic drift that allows an animal influenza virus to infect humans, followed by an "adaptive mutation" that allows the virus to spread readily within the human population (*10*).

The chart below demonstrates the changes in circulating subtypes of influenza A. New subtypes of influenza A may dramatically emerge as part of a pandemic such as in 1918. Sometimes the new subtypes will continue to circulate though the specific strains may vary, such as with H1N1. Other times the new subtypes eventually quit circulating, such as with H2N2.

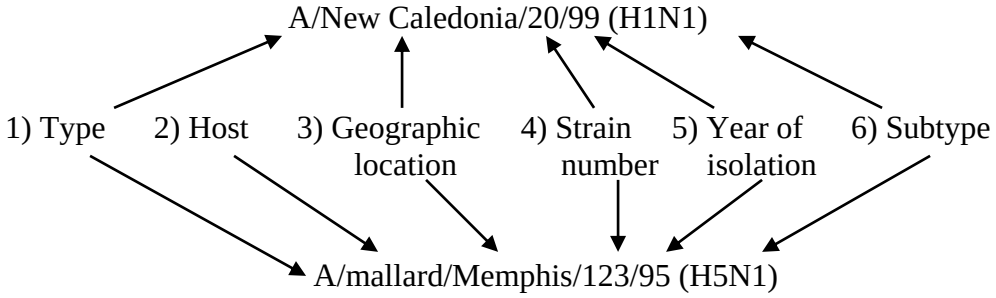


Influenza Naming Convention

Influenza viruses are often called by common names such as Spanish influenza, Hong Kong Flu or Russian Flu (*3*). These names are easily recognizable by the general public and usually refer to a specific strain of influenza associated with a large epidemic or pandemic. Referring to influenza viruses by their subtypes (e.g., H1N1, H3N2, etc.) is also becoming fairly mainstream. One challenge with referring to influenza viruses by subtype is that the general public does not understand that there are different strains of influenza associated with each subtype. One strain of H1N1 may be very different from another strain of H1N1, as seen with the 2009 pandemic strain of H1N1 compared with the "seasonal" strain of H1N1 that was circulating prior to 2009.

Terms like "swine flu" and "avian flu" are also used to describe influenza but are frequently misused. Both of those terms refer to influenza subtypes that normally circulate among pig and bird populations, respectively (*7*). While a person may become infected with an avian or swine strain of influenza, it is no longer considered to be avian or swine influenza once it has adapted to spread easily among humans.

It is important for public health professionals to be familiar with the technical names of influenza viruses to help distinguish between current and novel strains as well as between strains that are included in the vaccine and those that are not. Naming influenza viruses is a fairly simple procedure. First, the virus type is classified. Influenza A is indicated with an "A" and influenza B is indicated with "B" (*11*). Second, the host origin is identified. This is omitted if the virus has a human origin. Third, the geographic location in which the strain was first isolated is indicated. Fourth, the strain number is indicated; this is followed by the year the strain was isolated. The year is marked with two digits if isolated during the 1900s and four digits if isolated in or after the year 2000. Last, influenza A viruses will be followed with the virus subtype (H#N#). The number symbol indicates which of the 18 subtypes of hemagglutinin and the 11 subtypes of neuraminidase is present.



Human origin examples:

A/New Caledonia/20/99 (H1N1)
A/Perth/16/2009 (H3N2)
A/California/07/2009 (H1N1)
B/Brisbane/60/2008

Non-human origin example:

A/mallard/Memphis/123/95 (H5N1)

Testing

Note: Influenza Signs and Symptoms and the Role of Laboratory Diagnostics, Rapid Diagnostic Testing for Influenza: Information for Health Care Professionals and Rapid Diagnostic Testing for Influenza: Information for Clinical Laboratory Directors are from the *Resource Manual for Seasonal and Pandemic Influenza Testing in Texas*, Texas Department of State Health Services. Unless otherwise indicated, the material was taken from the Centers for Disease Control and Prevention (CDC) website:
http://www.cdc.gov/flu/professionals/diagnosis/labrolesprocedures.htm (*12*)
http://www.cdc.gov/flu/professionals/diagnosis/rapidclin.htm (*13*)
http://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm (*14*)

Influenza Signs and Symptoms and the Role of Laboratory Diagnostics
The signs and symptoms of influenza can vary by age, immune status, and presence of underlying medication conditions. Uncomplicated influenza can include any or all of these signs and symptoms: fever, muscle aches, headache, lack of energy, dry cough, sore throat, nasal congestion, and possibly runny nose. Fever is not always present, especially in elderly persons. The fever and body aches can last 3-5 days and the cough and lack of energy may last for 2 or more weeks, especially in elderly. Influenza can be difficult to diagnose based on clinical signs and symptoms alone because the signs and symptoms of influenza can be similar to those caused by other infectious agents including, but not limited to, *Mycoplasma pneumoniae*, adenovirus, respiratory syncytial virus, rhinovirus, parainfluenza viruses, and *Legionella* spp.

Appropriate treatment of patients with respiratory illness depends on accurate and timely diagnosis. Early diagnosis of influenza can reduce the inappropriate use of antibiotics and provide the option of using antiviral therapy. However, because certain bacterial infections can produce signs and symptoms similar to influenza, bacterial infections should be considered and appropriately treated, if suspected. In addition, bacterial co-infection can occur as a complication of influenza.

Influenza surveillance information about the prevalence of circulating influenza viruses and diagnostic testing can aid clinical judgment and help guide treatment decisions. The accuracy of clinical diagnosis of influenza on the basis of signs and symptoms alone is limited because symptoms from illness caused by other pathogens can overlap considerably with influenza. Influenza surveillance by state and local health departments and CDC can provide information regarding the presence of influenza viruses in the community. Surveillance can also identify the predominant circulating types, influenza A subtypes, and strains of influenza viruses.

Diagnostic tests available for influenza include viral culture, serology, rapid antigen testing, reverse transcription polymerase chain reaction (RT-PCR), immunofluorescence assays, and rapid molecular assays. Sensitivity and specificity of any test for influenza might vary by the laboratory that performs the test, the type of test used, the time from illness onset to specimen collection, and the type of specimen tested. Among respiratory specimens for viral isolation or rapid detection of human influenza viruses, nasopharyngeal specimens typically have higher yield than nasal or throat swab specimens. As with any diagnostic test, results should be evaluated in the context of other clinical and epidemiologic information available to health-care

providers. Please see Table 1 on pages I.11-I.12 for basic descriptions of common influenza testing types.

Commercial rapid diagnostic tests are available that can detect influenza viruses within 20 minutes. Some tests are approved for use in any outpatient setting, whereas others must be used in a moderately complex clinical laboratory. These rapid tests differ in the types of influenza viruses they can detect and whether they can distinguish between influenza types. Different tests can detect 1) only influenza A viruses; 2) both influenza A and B viruses, but not distinguish between the two types; or 3) both influenza A and B and distinguish between the two types.

None of the rapid influenza diagnostic tests provide any information about influenza A virus subtypes. The types of specimens acceptable for use (i.e., throat, nasopharyngeal, or nasal aspirates, swabs, or washes) also vary by test. The specificity and, in particular, the sensitivity of rapid influenza diagnostic tests are lower than for viral culture and RT-PCR and vary by test. Because of the lower sensitivity of the rapid influenza diagnostic tests, physicians should consider confirming negative tests with RT-PCR, viral culture or other means, especially in hospitalized patients or during suspected institutional influenza outbreaks because of the possibility of false-negative rapid test results, especially during periods of peak community influenza activity. In contrast, false-positive rapid test results are less likely, but can occur during periods of low influenza activity. Therefore, when interpreting results of a rapid influenza diagnostic test, physicians should consider the positive and negative predictive values of the test in the context of the level of influenza activity in their community. Package inserts and the laboratory performing the test should be consulted for more details regarding use of rapid influenza diagnostic tests.

Despite the availability of rapid diagnostic tests, collecting clinical specimens for viral culture is critical, because only culture isolates can provide specific information regarding circulating strains and subtypes of influenza viruses. This information is needed to compare current circulating influenza strains with vaccine strains, to guide decisions regarding influenza treatment and chemoprophylaxis, and to formulate vaccine for the coming year. Virus isolates also are needed to monitor the emergence of antiviral resistance and of novel influenza A subtypes that might pose a pandemic threat.

Rapid Diagnostic Testing for Influenza: Information for Healthcare Professionals

Rapid diagnostic tests for influenza can provide timely results that may be helpful with patient management. It is important to understand how the conditions under which these tests are used affect their reliability. To minimize false results:

- Use rapid diagnostic tests with high sensitivity and specificity.
- Collect specimens as early in the illness as possible (within 3-4 days of illness onset).
- Follow manufacturer's instructions, including handling of specimens, as described in the device package insert.
- Consider sending respiratory specimens for RT-PCR to confirm results of rapid tests especially when community influenza activity is low and the rapid diagnostic test result is positive and when the rapid diagnostic test result is negative but influenza activity is high.

Rapid Diagnostic Testing for Influenza: Information for Clinical Laboratory Directors

The availability and use of influenza rapid diagnostic tests by laboratories and clinics have substantially increased in recent years.

- Rapid influenza diagnostic tests (RIDTs) are screening tests for influenza virus infection that can provide results within 15 minutes.
- More than 10 RIDTs have been approved by the U.S. Food and Drug Administration (FDA).
- RIDTs tests differ in some important respects:
    - Some tests identify influenza A and B viruses and distinguish between the two types.
    - Some tests identify influenza A and B viruses but cannot distinguish between the two types.
    - Some tests are waived from requirements under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).
    - Most tests can be used with a variety of specimen types, but the accuracy of the tests can vary based on the type of specimen collected (for example, throat swab versus nasal swab).
- FDA approval is based upon specific specimen types.
- RIDTs vary in terms of sensitivity and specificity when compared with viral culture or RT-PCR. Product insert information and research publications indicate that:
    - Sensitivities are approximately 50-70%
    - Specificities are approximately 90-95%
- Specimens to be used with RIDTs generally should be collected as close as is possible to the start of symptoms (e.g., less than 4 days after illness onset). In very young children, influenza viruses can be shed for longer periods; therefore, in some instances, testing for a few days after this period may still detect influenza viruses. Immunosuppressed persons may have detectable influenza viruses in respiratory specimens for prolonged periods (weeks to months).

Predictive Value Depends Upon Prevalence

The positive and negative predictive values vary considerably depending upon the prevalence of influenza (level of influenza activity) in the patient population being tested.

- False-positive (and true-negative) influenza test results are more likely to occur when disease prevalence is low, which is generally at the beginning and end of the influenza season.
- False-negative (and true-positive) influenza test results are more likely to occur when disease prevalence is high, which is typically at the height of the influenza season.

Clinical Considerations of Testing When Influenza Prevalence is Low

When influenza prevalence is relatively low, the positive predictive value (PPV) is low and false-positive test results are more likely. By contrast, when influenza prevalence is low, the negative predictive value (NPV) is high, and negative results are more likely to be true.

If Flu Prevalence is…	And Specificity is…	Then PPV is…	False Pos. rate is…
VERY LOW (2.5%)	MODERATE (80%)	VERY LOW (6-12%)	VERY HIGH (88-94%)
VERY LOW (2.5%)	HIGH (98%)	LOW (39-56%)	HIGH (44-61%)
MODERATE (20%)	MODERATE (80%)	LOW (38-56%)	HIGH (44-62%)
MODERATE (20%)	HIGH (98%)	HIGH (86-93%)	LOW (7-14%)

The interpretation of positive results should take into account the clinical characteristics of the patient and the prevalence of influenza in the patient population being tested (e.g., level of influenza activity in the community). If an important clinical decision is affected by the test result, the rapid test result should be confirmed by another test, such as reverse transcription polymerase chain reaction (RT-PCR).

Clinical Considerations of Testing When Influenza Prevalence is High
When influenza prevalence is relatively high, the NPV is low and false-negative test results are more likely. When influenza prevalence is high, the PPV is high and positive results are more likely to be true.

If Flu Prevalence is…	And Sensitivity is…	Then NPV is…	False Neg. rate is…
MODERATE (20%)	LOW (50%)	MODERATE (86-89%)	MODERATE (11-14%)
MODERATE (20%)	HIGH (90%)	HIGH (97-99%)	LOW (2-3%)
HIGH (40%)	LOW (50%)	MODERATE (70-75%)	MODERATE (25-30%)
HIGH (40%)	HIGH (90%)	HIGH (93-94%)	LOW (6-7%)

The interpretation of negative results should take into account the clinical characteristics of the patient and the prevalence of influenza in the patient population being tested (e.g., level of influenza activity in the community). If an important clinical decision is affected by the test result and influenza is still suspected, then the rapid test result should be confirmed by another test, such as RT-PCR.

Selecting Tests
Many factors should be considered when selecting a test, including the following:

- Tests with high sensitivity and specificity will provide higher positive and negative predictive values.
- Types of specimens that provide the most accurate results.

Information about these characteristics can be found in product inserts and scientific articles, and by contacting the manufacturer.

Changes in Recommended Procedures Can Affect Test Results
Modification by the user can affect test performances and increase false-positive and/or false-negative rates. Such modifications include:

- Using specimens for which the test is not optimized
- Using swabs that did not come with the rapid test kits [unless recommended].

- Improper storage or prolonged storage before specimens are tested

When Is Use of Rapid Diagnostic Tests Beneficial?

- Testing during an outbreak of acute respiratory disease can determine if influenza is the cause.
- During influenza season, testing of selected patients presenting with acute respiratory illnesses compatible with influenza can help establish whether influenza is present in a specific patient population and help health-care providers determine how to use their clinical judgment for diagnosing and treating respiratory illness. (Testing need not be done for all patients.)
- Otherwise, rapid influenza diagnostic tests do not address the public health need for influenza virus isolates that can only be obtained through the collection of specimens for viral culture. Influenza virus isolates are essential for determining the match between circulating influenza virus strains and those virus strains contained in the vaccine and for aiding in the selection of new vaccine strains.

Rapid influenza antigen testing have unknown sensitivity and specificity to detect human infection with a novel influenza A virus in clinical specimens. Some studies suggest that antigen detection tests have low sensitivity to detect H5N1 viruses. Therefore, negative results from this type of testing does not exclude novel influenza virus infection. In addition, a rapid antigen test may give a positive influenza A result, but it cannot distinguish between seasonal and novel influenza A viruses (*15*).

Table 1. Descriptions of common influenza testing types (*14,16-17*)

Test Name	Test Description	Identifies*	Minimum Testing Time†	Notes
Viral culture‡§ (aka viral isolation)	The patient specimen is inoculated into cell culture in a laboratory in order to grow the influenza virus, if present in the patient sample. Following virus isolation, confirmation and identification tests--such as immunofluorescence and hemagglutination inhibition--are performed to further classify the virus.	Type Subtype Lineage	3-10 days**	• Traditionally considered the "gold standard" for influenza testing • Test requires that the virus be able to infect a host cell and multiply • Allows identification of viruses other than influenza if host cell line is sensitive to the specific virus
Real-time reverse transcription polymerase chain reaction (rRT-PCR)‡§	Portions of the influenza virus's genetic code, if present in the patient sample, are amplified and detected using sophisticated laboratory equipment.	Type Subtype	1-8 hours	• "The most sensitive and specific influenza diagnostic test" (*17*) • Can detect viruses no longer capable of causing infection as long as the target genetic sequences are present and intact • Can detect viruses present in a sample at low numbers
Serology	The patient's serum is tested for influenza-specific antibodies in a laboratory.	Type	≥ 2 weeks	• Requires paired acute and convalescent sera • Not recommended for routine patient diagnosis; special studies only (*14*)
Hemagglutination inhibition‡§	Antisera specific for either subtypes or strains and guinea pig blood are added to virus isolated in cell culture. The absence of agglutination (inhibition) indicates a positive result.	Subtype Lineage	3-6 hours	• Requires a cell culture isolate
Immunofluorescence‡§ [Direct Fluorescent Antibody (DFA) or Indirect Fluorescent Antibody (IFA) Staining]	An antibody with a fluorescent tag (direct method) recognizes and binds to influenza antigen in the patient sample, if present; the fluorescent antibody-antigen complex can be visualized under a laboratory microscope (*16*). IFA testing can be used to detect influenza antigen or specific antibody isotypes in the patient sample.	Type Subtype	1-4 hours	• "Sensitivity is usually higher than rapid tests but lower than culture or rRT-PCR" (*17*) • Specificity is high (*17*)

Test Name	Test Description	Identifies*	Minimum Testing Time†	Notes
Enzyme Immunoassay (EIA or ELISA)	There are two categories of EIA tests--the antigen detection method (direct or indirect) and the antibody detection method (competitive or noncompetitive) (*16*). The antigen detection testing method detects influenza antigens present in the patient sample when they bind to antibodies fixed to the test kit plate. The antibody detection testing method detects antibodies present in the patient sample when they bind to antigens fixed to the test kit plate. In both methods, another molecule that recognizes or competes with the target influenza antigen or antibody from the patient sample is added, along with an enzyme label. A chemical is added, it interacts with the enzyme label, and produces a signal (e.g., color, fluorescence, etc.) which can be measured using laboratory equipment; the intensity of the signal is compared to a standard cutoff value for the specific test to determine whether the sample is positive or negative.	Type	2 hours	• Indirect EIA antigen detection tests are more sensitive than direct versions of the test (*16*).
Rapid Diagnostic Tests	Monoclonal antibodies in the test kit are used to detect influenza antigens in the patient specimen, if present.	Type only; some tests cannot distinguish between influenza A and B	< 15 min.	• Point-of-care (CLIA-waived) tests can be performed in a doctor's office; moderately complex tests (not CLIA-waived) must be performed in a laboratory (*14*). • Specificity is 90-95% (*14*) • Sensitivity is 50-70%; however, reported sensitivities for 2009 pandemic influenza A H1N1 ranged from 10%-70% (*14*,*17*)

*Type = influenza A or B; Subtype = H1N1, H3N2, H5N1, or other subtype that can be detected by current diagnostic testing methods (for influenza A viruses only); Lineage = Victoria or Yamagata (for influenza B viruses only). Testing for other uncommon or novel influenza A subtypes is available at the CDC Influenza Laboratory.

†Minimum testing time does not include time to rerun a specimen, if necessary, or time to report the results to the submitter, and is a best case scenario where no other competing laboratory duties are present. Actual testing turnaround times vary by laboratory.

‡Testing performed in the DSHS Austin Laboratory; please see Section VI: Laboratory Support for more information on DSHS testing capabilities and testing turnaround times

§ Not all laboratories that can perform these tests have the capability to subtype and/or determine influenza B lineage.

**Time required for traditional viral culture; shell vial culture, if available, may produce a more rapid result (*14*)

Note: The CDC Influenza Laboratory can perform additional tests to further identify influenza strains and antiviral resistance markers.

Prevention

It is especially important for people who are at higher risk of severe illness or complications from influenza and for close contacts of higher risk individuals to take steps to prevent the spread of influenza. There are several actions that can be taken to protect oneself and to prevent the spread of influenza (*18*):

- Get vaccinated for influenza every year
- Wash hands frequently with soap and water, especially after coughing or sneezing
- Use alcohol-based hand sanitizers when facilities are not available for hand washing
- Cover coughs and sneezes with disposable tissues or your arm/sleeve
- Avoid touching your eyes, nose or mouth
- Avoid close contact with people who are sick
- When you are sick, limit contact with others and stay home until fever free for 24 hours without the use of fever-reducing medications
- Take antiviral medications if prescribed by your doctor

Educational materials for preventing the spread of influenza can be found at:

- http://texasflu.org/materials.htm
- http://www.cdc.gov/flu/freeresources/

Vaccinations

Vaccination is the primary method of preventing influenza infection. There are two ways a vaccine can be administered: injection or nasal spray (*19*). The "flu shot" contains a dead virus [known as inactivated influenza vaccine (IIV)] while the nasal spray contains a weakened virus [known as live, attenuated influenza vaccine (LAIV)]. The nasal spray (LAIV) should not be used for the 2017-2918 season. Although there are a few mild side effects, neither method of vaccination causes influenza illness in the vaccine recipient.

There are several categories of influenza vaccine available including inactivated influenza vaccine (IIV); recombinant influenza vaccine (RIV); and live attenuated influenza vaccine (LAIV) (*20*). Within the IIV category, there are the traditional egg-based trivalent inactivated influenza vaccines (IIV3), cell culture-based quadrivalent inactivated influenza vaccines (ccIIV4), and the egg-based quadrivalent inactivated influenza vaccines (IIV4). There are also several other vaccine options within the IIV3 category, including standard dose and high-dose formulations (the latter for adults 65 years and older), as well as an intradermal vaccine with a smaller needle. The RIV category currently contains a recombinant trivalent hemagglutinin influenza vaccine (RIV3) that is not produced using eggs and therefore can be given to individuals with egg allergies (*21*). The LAIV category contains the trivalent live, attenuated influenza vaccine (LAIV3) and the quadrivalent live, attenuated influenza vaccine (LAIV4); however, beginning in the 2013-2014 season, only the LAIV4 formulation will be manufactured. Vaccines are licensed for specific age groups and health statuses.

Every year a new influenza vaccine is developed for each hemisphere; strain recommendations for each vaccine are made using virologic data collected by World Health Organization (WHO) Collaborating Laboratories located throughout the world (*22*). Recommended strains for the Northern Hemisphere's influenza vaccine are chosen by the WHO each February; strains for the Southern Hemisphere's influenza vaccine are chosen each September. Until recently, the seasonal influenza vaccine has been available solely as a trivalent vaccine, containing three strains of the influenza virus—two influenza A components, usually an H1N1 and an H3N2, and one influenza B virus component. Beginning in the 2013-2014 influenza season, some influenza vaccines will be available in quadrivalent formulations, containing four strains of the influenza virus—two influenza A components, usually an H1N1 and an H3N2, and two influenza B components representing each influenza B lineage (*20*).

It has been recommended that all persons ≥ 6 months of age be vaccinated annually for influenza since 2010 (*20*). There are certain groups of people who have a higher risk of contracting influenza or developing severe, life-threatening illness from influenza. It is important for high risk individuals and their close contacts to protect themselves and others by getting vaccinated. The Advisory Committee on Immunizations Practices (ACIP) considers the following categories of people as high risk or close contacts of people at high risk:

- all children aged 6 months to 4 years (59 months);
- all persons aged ≥50 years;

- adults and children who have chronic pulmonary (including asthma), cardiovascular (except isolated hypertension), renal, hepatic, neurological, hematologic or metabolic disorders (including diabetes mellitus);
- persons who have weakened immune systems (including immunosuppression caused by medications or by HIV);
- women who are or will be pregnant during the influenza season;
- children and adolescents (aged 6 months to 18 years) who are receiving long-term aspirin therapy and who might be at risk for experiencing Reye syndrome after influenza virus infection;
- residents of nursing homes and other long term care facilities;
- American Indians/Alaska Natives;
- persons who are morbidly obese (BMI ≥40);
- healthcare professionals (HCPs);
- household contacts and caregivers of children aged <5 years and adults aged ≥50 years, with particular emphasis on contacts of children aged <6 months; and
- household contacts and caregivers of persons with medical conditions that put them at higher risk for severe complications from influenza.

Some people should not be vaccinated for influenza (*23*). These include people who:

- are less than 6 months of age
- have severe, life-threatening allergies to flu vaccine or any ingredient in the vaccine

Some people should talk to their doctor before getting vaccinated for influenza (23). These include people who:

- have an allergy to eggs or any of the ingredients in the vaccine
- have ever had Guillain-Barré Syndrome (a severe paralyzing illness, also called GBS)
- are not feeling well (these people should talk to their doctor about their symptoms)

Influenza vaccines are not equally effective in all persons. Vaccine effectiveness varies depending on each person's age and general health; it also depends on how well circulating influenza strains match the current season's vaccine strains (*24-25*). Influenza vaccine efficacy may be reduced for some immunocompromised persons and persons over 65 years of age (*24*). However, even when influenza vaccine effectiveness is reduced, influenza vaccination provides protection against severe influenza-related complications, hospitalizations, and deaths, especially in the elderly (*24*).

Antivirals

Antiviral medications are prescription medications given to persons in order to treat an influenza illness or to prevent influenza illness from occurring; however, antiviral medications are not a replacement for the annual influenza vaccine.

Two classes of antiviral medications are currently available for clinical use—the adamantanes and the neuraminidase inhibitors. The adamantanes, amantadine and rimantadine, inhibit viral replication by interacting with the viral M2 protein (*3*). Influenza B viruses lack an M2 protein; therefore, the adamantanes are not effective against them.

The neuraminidase inhibitors, oseltamivir and zanamivir, interact with neuraminidase and eventually reduce the amount of virus released by host cells (*3,26*). During the 2009 influenza A (H1N1) pandemic, another neuraminidase inhibitor, intravenous peramivir, temporarily was made available by the FDA for emergency use in certain hospitalized patients (*27*). On December 19, 2014, the FDA approved intravenous peramivir to treat influenza infections in adults (*28*). Antiviral medications are typically available either in pill or liquid form for oral administration, an inhaled powder, or an intravenous solution (*29*).

An antiviral medication given within the first 48 hours of illness may shorten the duration and severity of illness (*29*). Antiviral medications also may be given for illness prevention to persons who were exposed to someone with an influenza illness and can be 70% to 90% effective in preventing illness (*30*). Antiviral medications are usually recommended only for those persons who have a severe illness or those who are at higher risk for developing serious illness or complications due to influenza (*29*). Antivirals also may be considered for chemoprophylaxis in settings where persons live in close proximity. First responders and public health workers involved in response to an investigation of very severe illnesses due to novel influenza A subtypes and strains may be given antivirals for illness prevention.

The CDC recommends influenza antiviral medications should be given to the following groups of people (*31*):

- Hospitalized patients with suspected or confirmed influenza;
- Persons with severe, complicated, or progressive illness;
- Outpatients who are at high risk for influenza complications (for example, young children, people 65 and older, pregnant women, and persons with certain underlying chronic medical conditions) (For a full list of people at high risk of influenza complications, see: http://www.cdc.gov/flu/about/disease/high_risk.htm); and
- Persons with uncomplicated influenza who are not in a high risk group and who present within 48 hours of illness onset. These persons can be treated with antiviral medications based upon clinical judgment, because reviews of RCTs and observational studies have found consistent clinical benefit of early oseltamivir treatment in reducing the risk of lower respiratory tract complications such as those requiring antibiotics.

An important reason for limiting the use of antiviral medications is the increasing development of antiviral resistance to currently available medications. A large percentage of circulating influenza A (H3N2) viruses and some influenza A (H1N1) viruses have been shown to be resistant to adamantanes; therefore, the CDC continues to recommend the use of neuraminidase inhibitors over adamantanes (*8*). In the 2007-2008 season, 10.9% of influenza A (H1N1) viruses from across the nation tested by the CDC demonstrated resistance to oseltamivir, compared to only 0.7% in the 2006-2007 influenza season. In the 2008-2009 season, oseltamivir resistance was observed in almost all (99.6%) of the seasonal influenza A (H1N1) viruses tested by CDC; additionally, a small percentage (0.5%) of 2009 pandemic influenza A (H1N1) viruses tested positive for resistance to oseltamivir (*32*). Throughout the 2009-2010 influenza season, the number of oseltamivir-resistant 2009 pandemic influenza A (H1N1) viruses detected by CDC remained low (1.3%); almost all of the 2009 pandemic influenza A (H1N1) viruses have shown resistance to the adamantanes (*33*). In the 2011-20012 season, a cluster of 2009 pandemic influenza A (H1N1) viruses with resistance to oseltamivir was detected through routine surveillance in Texas Health Service Region 11. Resistance trends will continue to be monitored.

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