



# Influenza and Influenza Vaccines

Epidemiology and Prevention of Vaccine-Preventable Diseases  
(Pink Book) Webinar Series

September 25, 2019

# Influenza

- Highly infectious viral illness
- First pandemic in 1580
- At least 4 pandemics in 19th century
- Three pandemics in the 20<sup>th</sup> century
  - Estimated 50 million deaths worldwide in pandemic of 1918-1919
  - Pandemics of 1957 and 1968 of lesser severity
- Most recent pandemic (H1N1) in 2009-2010
- Virus first isolated in 1933

# Influenza Virus

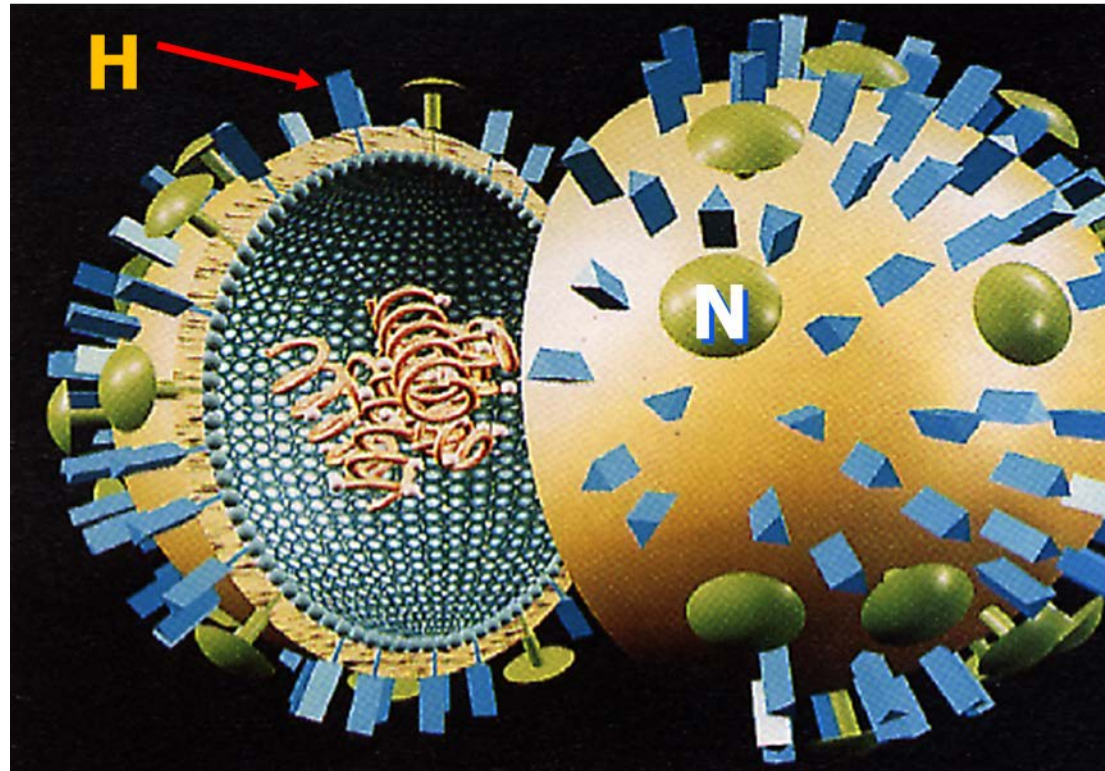
- Single-stranded RNA virus
- Orthomyxoviridae family
- 3 types: A, B, C
- Subtypes of type A are determined by hemagglutinin and neuraminidase

# Influenza Virus Strains

- Type A
  - Moderate to severe illness
  - All age groups
  - Humans and other animals
- Type B
  - Milder epidemics
  - Primarily affects children
  - Humans only
- Type C
  - Rarely reported in humans
  - No epidemics

# Influenza Type A Subtypes

Subtypes of type A determined by hemagglutinin (H) and neuraminidase (N)



A/California/7/2009 (H1N1)

Virus type    Geographic origin    Strain number    Year of isolation    Virus subtype

# Influenza Antigenic Changes

- Antigenic Drift
  - minor change, same subtype
  - caused by point mutations in gene
  - may result in epidemic
  
- Antigenic Shift
  - major change, new subtype
  - caused by exchange of gene segments
  - may result in pandemic

# WHO declares first flu pandemic in 41 years

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By Fabrice Coffrini, AFP/Getty Images

World Health Organization Director General Margaret Chan sits before Assistant Director General Keiji Fukuda at a Geneva news conference announcing that the WHO decided to raise the

By [Steve Sternberg](#), USA TODAY

The World Health Organization scaled up its flu warning to its highest level Thursday, declaring the first global influenza pandemic in 41 years as cases of H1N1 continued to mount in the USA, Europe, Latin America and Australia.

"The scientific criteria for a pandemic have been met," said [Margaret Chan](#), director general of the WHO. "The world is now at the start of the 2009 influenza pandemic."

**PHOTOS:** [Schools closed in Hong Kong, Vermont \(and more\)](#)

**INTERACTIVES:** [World map, how H1N1 strain emerged](#)

**FAQ:** [What you should know about swine flu](#)

**VIDEO:** [Reporters answer your questions](#)

The decision marks the agency's formal recognition of the magnitude of the challenge posed by a novel, H1N1 flu virus now spreading unchecked among people who, because the virus is new, are virtually all susceptible to it.

The WHO is working closely with vaccine makers, who are just wrapping up production of seasonal flu vaccine for fall and gearing up to produce the first doses of an H1N1 vaccine by September. The agency urged member nations to maintain their vigilance to detect ominous changes in the virus's

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# Influenza Pathogenesis

- Respiratory transmission of virus
- Replication in respiratory epithelium with subsequent destruction of cells
- Viremia rarely documented
- Virus shed in respiratory secretions for 5-10 days



# Influenza Clinical Features

- Incubation period 2 days (range 1-4 days)
- 50% of infected persons develop classic symptoms
- Abrupt onset of fever (usually 101° - 102°F), myalgia, sore throat, nonproductive cough, headache

# Influenza Complications

- Pneumonia
  - Secondary bacterial pneumonia
  - Primary influenza pneumonia
- Reye syndrome
- Myocarditis
- Death reported in <1 per 1,000 cases

# Impact of Influenza – Death - United States, 2010-2014

- Number of influenza-associated deaths varies substantially by year, influenza virus type and subtype, and age group
- Annual influenza-associated deaths ranged from 12,000 to 56,000 between 2010 and 2014, with an average of 23,607 annual deaths
- Persons 65 years of age and older account for 70% to 85% of deaths
- 2.7 times more deaths during seasons when A(H3N2) viruses were prominent

# Impact of influenza, - Hospitalization – United States - 2010-2016

- Highest rates of complications and hospitalization among persons 65 years and older, young children, and persons of any age with certain underlying medical conditions
- 2010-2011 to 2015-2016:
  - Flu-related hospitalizations in the United States ranged from a low of 140,000 (during 2011-2012) to a high of 710,000 (during 2014-2015).
  - During the 2015-2016 flu season, CDC estimated 310,000 people were hospitalized for flu-related illness.
- About 50% of hospitalizations among persons younger than 65 years of age
- Greater number of hospitalizations during years that A(H3N2) is predominant

# Influenza Among School-Aged Children

- School-age children
  - typically have the highest attack rates during community outbreaks of influenza
  - serve as a major source of transmission of influenza within communities

# Influenza Epidemiology

- Reservoir
  - human, animals (type A only)
- Transmission
  - respiratory, probably airborne
- Temporal pattern
  - peak December – March in temperate climate
  - may occur earlier or later
- Communicability
  - 1 day before to 5 days after onset (adults)

# Influenza Diagnosis

- Clinical and epidemiological characteristics
- Isolation of influenza virus from clinical specimens (e.g., throat, nasopharynx, sputum)
- Significant rise in influenza IgG by serologic assay

# Influenza Virus Testing Methods

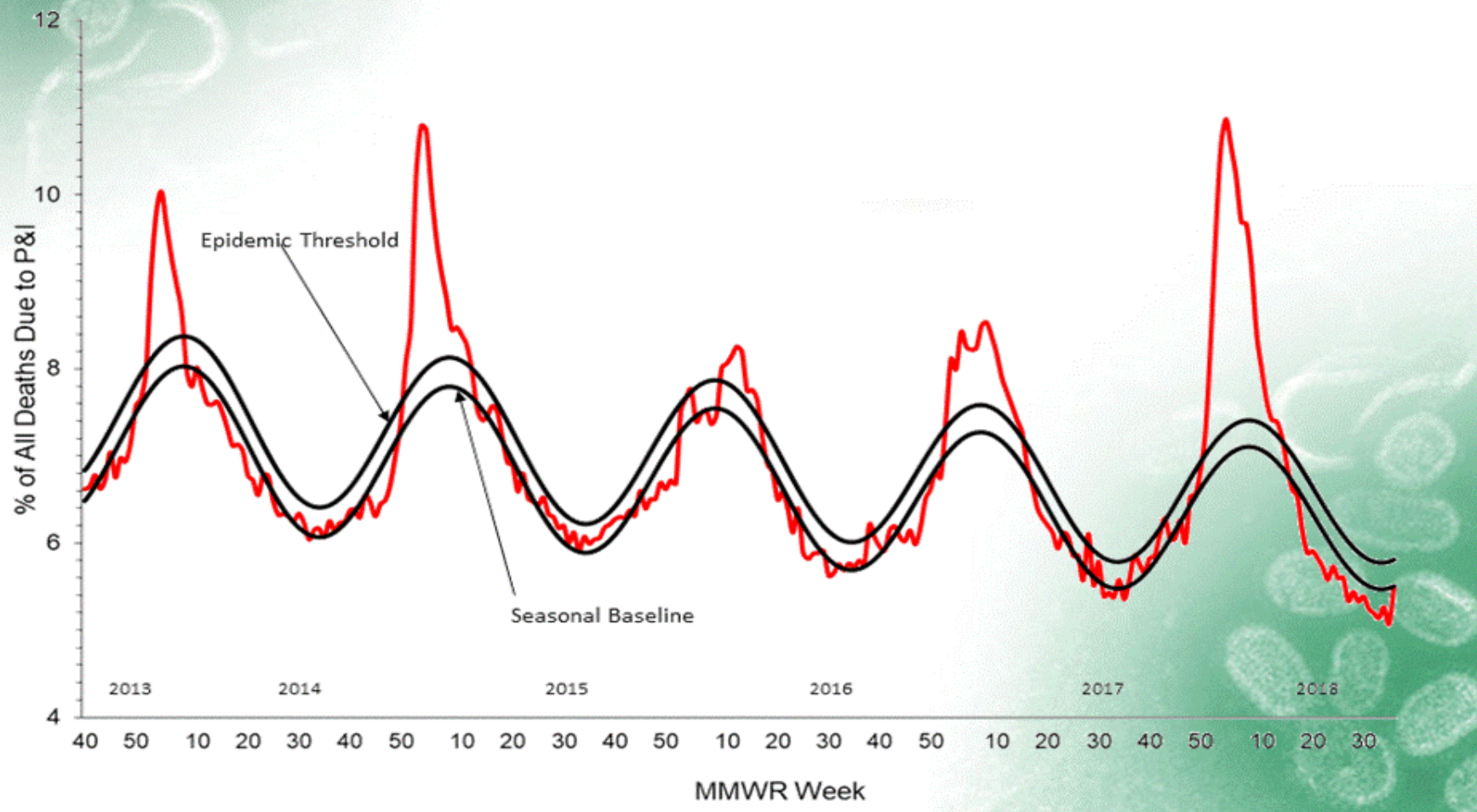
Method	Types Detected	Test Time
<u>Viral tissue cell culture</u>	<u>A and B</u>	<u>3-10 days</u>
Rapid cell culture (shell vials; cell mixtures; yields live virus)	A and B	1-3 days
Immunofluorescence, Direct (DFA) or Indirect (IFA) Florescent Antibody Staining	A and B	1-4 hours
<u>Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and other molecular assays [influenza viral RNA or nucleic acid detection]</u>	<u>A and B</u>	<u>Varies by assay (Generally 60-80 minutes and 4-8 hours)</u>
Rapid Molecular Assay [influenza viral RNA or nucleic acid detection]	A and B	15 to 30 minutes
<u>Rapid Influenza Diagnostic Tests (antigen detection)</u>	<u>A and B</u>	<u>&lt;15 min.</u>



A Weekly Influenza Surveillance Report Prepared by the Influenza Division

## Pneumonia and Influenza Mortality from the National Center for Health Statistics Mortality Surveillance System

Data through the week ending September 8, 2018, as of September 27, 2018



# Influenza Surveillance

- Monitor prevalence of circulating strains and detect new strains
- Estimate influenza-related morbidity, mortality and economic loss
- Rapidly detect outbreaks
- Assist disease control through rapid preventive action

# Inactivated Influenza Vaccine Effectiveness

- 40%-60% effective among all age groups.
- 74% effective in preventing PICU admissions
- 40% effective in preventing hospitalization among adults
- 82% effective in preventing ICU admissions
- 80% effective in preventing death among elderly persons

# 2019-2020 Influenza Vaccine Recommendations

# 2019-2020 Influenza Vaccine Composition

## ■ Trivalent vaccines:

- An A/Brisbane/2/2018 (H1N1)pdm09-like virus (updated)
- An A/Kansas/14/2017 (H3N2)-like virus (updated)
- B/Colorado/06/2017-like virus

## ■ Quadrivalent vaccines:

- The above three viruses
- A B/Phuket/3073/2013-like virus

# Abbreviations

- IIV = Inactivated influenza vaccine
- LAIV = Live attenuated influenza vaccine
- RIV = Recombinant influenza vaccine
- Prefixes: SD = standard dose  
HD = high dose  
a = adjuvanted  
cc = cell culture-based
- Numeric suffixes (e.g., RIV3, IIV4) indicate trivalent or quadrivalent, respectively

# Influenza Vaccines

- IIV:
  - Contain inactivated virus, split or subunit
    - High Dose or Standard Dose
    - Trivalent or quadrivalent
    - Unadjuvanted or adjuvanted
    - Egg- or cell culture-based
  - Many brands, some approved for those as young as 6 months of age
  - Most are intramuscular
- RIV
  - Contain recombinant HA
  - Egg-free
  - quadrivalent
- LAIV
  - Live attenuated virus
  - Recommended again in 2018-19

# Quick Aside about Influenza Vaccines for 6 Months – 35 Months of Age

- Two potential points of confusion
  - Four licensed products, but the dose volume differs
    - Afluria Quadrivalent: 0.25 mL – newly licensed down to 6 months
    - Fluarix Quadrivalent: 0.5 mL
    - FluLaval Quadrivalent: 0.5 mL
    - Fluzone Quadrivalent: 0.25 mL
    - Fluzone Quadrivalent: 0.5 mL – newly licensed formulation
- Dose volume is distinct from number of doses needed
  - A child 6 months through 35 months who is recommended for two doses of influenza vaccine and receives FluLaval Quadrivalent 0.5 mL still needs the second dose of vaccine 4 weeks later



# Groups Recommended for Vaccination

- Routine annual influenza vaccination is recommended for all persons  $\geq 6$  months of age who do not have contraindications
- While vaccination is recommended for everyone in this age group, there are some for whom it is particularly important:
  - People age  $\geq 6$  months who are at high risk of complications and severe illness
  - Contacts and caregivers of these people, and of infants under age 6 months (because there is no vaccine approved for children this age)

# Groups at Increased Risk for Influenza Complications and Severe Illness

- Children age 6 through 59 months and adults age  $\geq 50$  years (children under 6 months of age are also at high risk, but cannot be vaccinated)
- Persons with chronic pulmonary (including asthma) or cardiovascular (except isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)
- Immunosuppressed persons
- Women who are or will be pregnant during the influenza season
- Children and adolescents (age 6 months–18 years) who are receiving 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 extremely obese (BMI  $\geq 40$ )

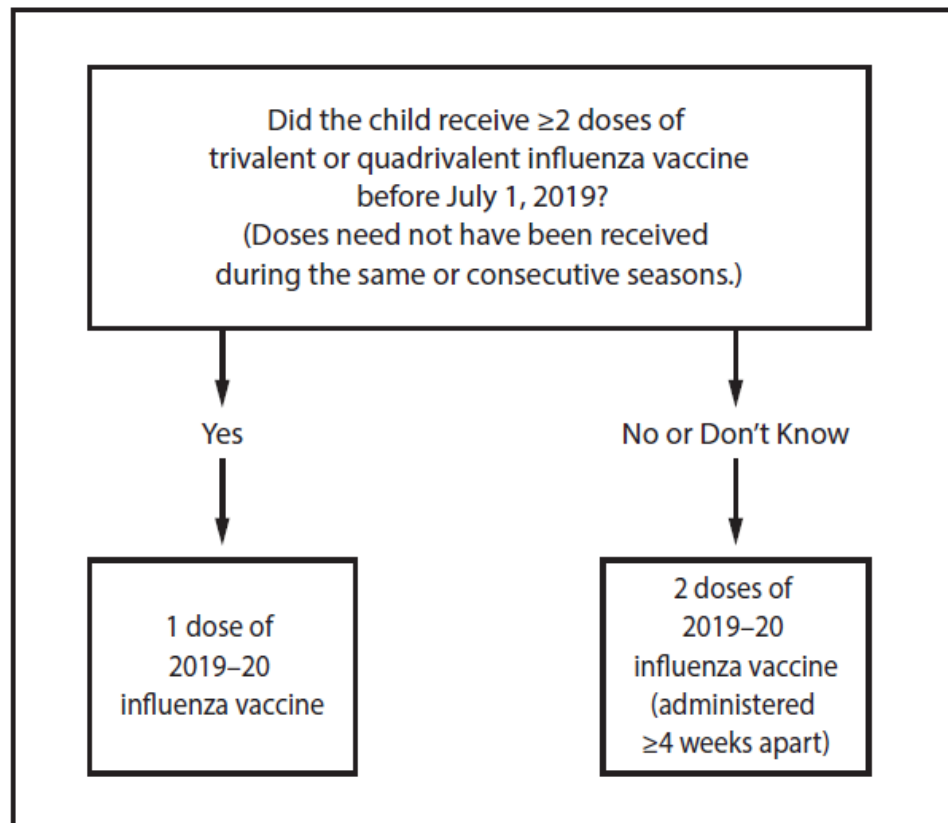
# Influenza Vaccination of Pregnant Women

- Influenza vaccination recommended by ACIP for women who will be pregnant during influenza season since 2004
  - Increased risk for severe influenza illness in pregnant women, particularly during second and third trimesters;
- Previous language stated pregnant women should receive inactivated influenza vaccine (IIV)
- For 2018-19, pregnant women may receive any licensed, recommended, age-appropriate influenza vaccine
  - IIV or RIV
  - LAIV not recommended for pregnant women

# Timing of Vaccination

- Vaccination should occur before onset of influenza activity. Health care providers should offer vaccination by the end of October, if possible.
- To avoid missed opportunities for vaccination, providers should offer vaccination during routine health care visits and hospitalizations when vaccine is available
- Organized campaigns should occur throughout the season
- Vaccination in July and August might result in suboptimal immunity

FIGURE. Influenza vaccine dosing algorithm for children aged 6 months through 8 years\* — Advisory Committee on Immunization Practices, United States, 2019–20 influenza season



## Dosing Algorithm for Children Age 6 Months Through 8 Years, 2019–2020

- ❑ Similar to past two seasons
- ❑ If 2 cumulative doses received prior to July 1, 2019, only 1 dose needed for 2019-2020
- ❑ Only 1 dose needed after the 9th birthday
- ❑ For children aged 8 years who require 2 doses of vaccine, both doses should be administered even if the child turns age 9 years between receipt of dose 1 and dose 2.

# Inactivated Influenza Vaccine (IIV) Adverse Reactions

- Local reactions (soreness, redness)
  - 15% - 20%
- Fever, malaise, myalgia
  - Less than 1%
- Allergic reactions (hives, angioedema, anaphylaxis)
  - Rare
- Guillain-Barré syndrome

# Live Attenuated Influenza Vaccine (LAIV)

## Adverse Reactions

- Children
  - No significant increase in URI symptoms, fever, or other systemic symptoms
  - Increased risk of wheezing in children 6-23 months of age
- Adults
  - Significantly increased rate of cough, runny nose, nasal congestion, sore throat, and chills reported among vaccine recipients
  - No increase in the occurrence of fever
- No serious adverse reactions identified

# Inactivated Influenza Vaccine (IIV) and RIV

## Contraindications and Precautions

### Contraindication

- Severe allergic reaction (e.g., anaphylaxis) to a vaccine component or following a prior dose of inactivated influenza vaccine

### Precaution

- Moderate or severe acute illness
- History of Guillain-Barré syndrome (GBS) within 6 weeks following a previous dose of influenza vaccine



# LAIV Contraindications and Precautions

## Contraindications

- History of severe allergic reaction to any component of the vaccine† or after a previous dose of any influenza vaccine
- Concomitant aspirin or salicylate-containing therapy in children and adolescents
- Children aged 2 through 4 years who have received a diagnosis of asthma or whose parents or caregivers report that a health care provider has told them during the preceding 12 months that their child had wheezing or asthma or whose medical record indicates a wheezing episode has occurred during the preceding 12 months
- Children and adults who are immunocompromised due to any cause (including immunosuppression caused by medications or by HIV infection)
- Close contacts and caregivers of severely immunosuppressed persons who require a protected environment
- Pregnancy
- Receipt of influenza antiviral medication within the previous 48 hours

## Precautions

- Moderate-to-severe acute illness with or without fever
- History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine
- Asthma in persons aged  $\geq 5$  years
- Other underlying medical conditions that might predispose to complications after wild-type influenza infection (e.g., chronic pulmonary, cardiovascular [except isolated hypertension], renal, hepatic, neurologic, hematologic, or metabolic disorders [including diabetes mellitus])

# Influenza Vaccination of Persons with Egg Allergy




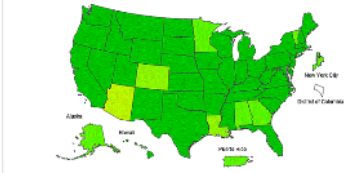
- ❑ **Mostly unchanged from last few seasons**
  - LAIV is an option again this season
- ❑ **Egg allergic persons can receive any licensed, recommended vaccine that is otherwise appropriate (IIV, RIV4, or LAIV4)**
  - However, RIV not licensed for persons under 18 years of age
- ❑ **For persons with a history of severe allergic reaction to egg (i.e., any symptom other than hives)**
  - “The selected vaccine should be administered in an inpatient or outpatient medical setting (including but not necessarily limited to hospitals, clinics, health departments, and physician offices). Vaccine administration should be supervised by a health care provider who is able to recognize and manage severe allergic conditions.”
- ❑ **No specific post-vaccination observation period recommended**
  - However, per the ACIP General Best Practices guidelines, providers should consider observing all recipients of any vaccine for 15 minutes to avoid injury due to syncope

# Influenza Antiviral Agents

- Amantadine and rimantadine
  - Not recommended because of documented resistance in U.S. influenza isolates
- Zanamivir, oseltamivir, peramavir, baloxavir
  - Neuraminidase inhibitors
  - Effective against influenza A and B
  - Oseltamavir and zanamavir approved for prophylaxis

# CDC website on influenza:

## <https://www.cdc.gov/flu/index.htm>

			
<b>PREVENT FLU</b>	<b>SYMPTOMS &amp; DIAGNOSIS</b>	<b>TREATMENT</b>	<b>FLU ACTIVITY &amp; SURVEILLANCE</b>
Everyone 6 months & older should receive a yearly flu vaccine.	Flu can cause mild to severe illness. Learn the symptoms of flu.	Prescription medications called antiviral drugs can be used to treat flu.	The 2016-2017 flu season is over. Flu activity is low in the U.S.
<a href="#">More &gt;</a>	<a href="#">More &gt;</a>	<a href="#">More &gt;</a>	<a href="#">More &gt;</a>

 <b>ABOUT FLU</b> Learn about flu season and get answers to questions.	 <b>COMMUNICATION RESOURCES</b> Find resources to promote flu prevention.
 <b>FLU SEASON</b> Find information about current and past flu seasons.	 <b>HEALTH PROFESSIONALS</b> Learn what CDC recommends this season.
 <b>PEOPLE AT HIGH RISK</b> Understand who is at high risk from flu.	 <b>FLU NEWS &amp; SPOTLIGHTS</b> Read about CDC's work with flu.

### Flu Vaccine Finder



Everyone **six months of age or older** needs a flu vaccine.

Find the flu shot near you.

  
[GO](#)

# Influenza Resources



- ACIP's Influenza Recommendations web page  
[www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/flu.html](http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/flu.html)
- CDC's Influenza web page  
[www.cdc.gov/flu/index.htm](http://www.cdc.gov/flu/index.htm)
- Immunization Action Coalition Influenza web page  
[www.immunize.org/influenza/](http://www.immunize.org/influenza/)
- Children's Hospital of Philadelphia Vaccine Education Center Influenza web page  
<http://www.chop.edu/centers-programs/vaccine-education-center/vaccine-details/influenza-vaccine#.VgHMa3YpCAU>



How to avoid Influenza  
Gargle Daily

**...and get a flu  
vaccination!**

How to avoid Influenza  
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