

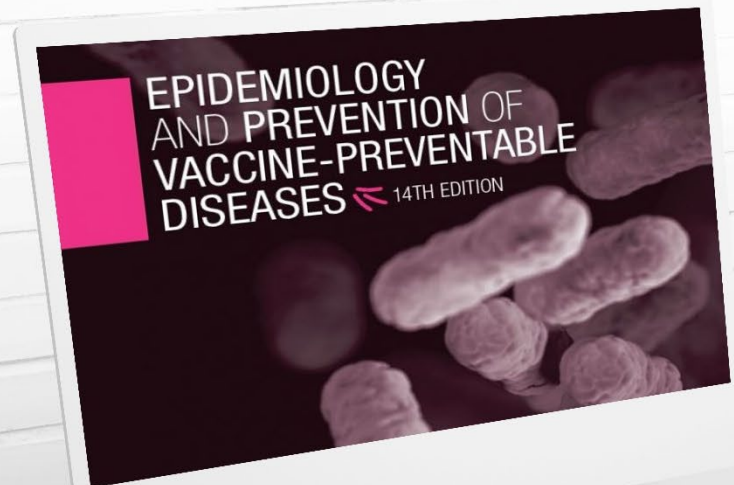
Influenza Vaccines

Pink Book Web-on-Demand Series

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Medical Officer

Immunization Services Division





Learning Objectives

- Describe the fundamental principles of the immune response.
- Describe immunization best practices.
- Describe an emerging immunization issue.
- For each vaccine-preventable disease, identify those for whom routine immunization is recommended.
- For each vaccine-preventable disease, describe characteristics of the vaccine used to prevent the disease.
- Locate current immunization resources to increase knowledge of team's role in program implementation for improved team performance.

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1

Influenza

Influenza

Highly infectious viral illness

- **1930s: Influenza A and B viruses isolated**
- **1930s and 1940s: First non-live vaccines**

- **Has led to multiple pandemics**
 - 1580: First pandemic
 - 1918–1919: Estimated 21 million deaths worldwide
 - 2009–2010: Most recent pandemic (H1N1)



2009 - CDC activated the Emergency Operations Center (EOC) during the H1N1 Pandemic

Influenza Virus Antigenic Changes

- **Antigenic drift**

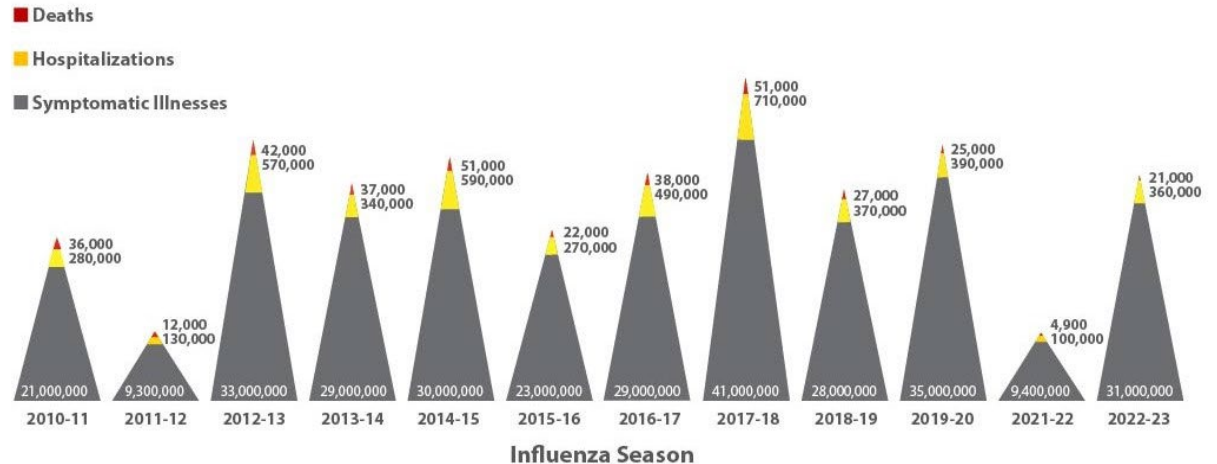
- Small mutations over time
 - Result in novel strains
 - Drift occurs in all types
- Reason people can get influenza more than once
- Requires that changes in the viruses represented in the vaccine be considered each year

- **Antigenic shift**

- Abrupt, major change in influenza A virus surface antigen(s):
 - Hemagglutinin (H)
 - Neuraminidase (N)
- May lead to pandemic (rare)

Estimated Annual Burden of Flu in the United States, 2010–2023

- Burden varies widely from year to year
- Public health impact always substantial



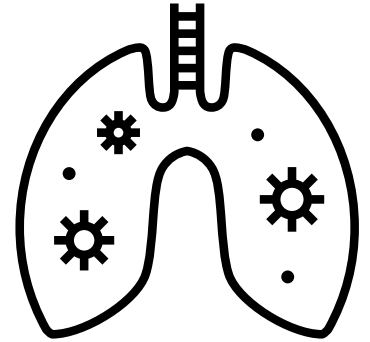
Influenza Virus Transmission



- Spreads from person to person mainly by droplets when people cough, talk or sneeze.
- May be spread by touching an infected surface then touching your mouth, nose or possibly eyes.

Influenza Pathogenesis

- **Following inhalation, influenza viruses can**
 - Attach to and penetrate respiratory epithelial cells in trachea and bronchi.
 - Replicate, destroying host cells.
- **Regeneration of epithelium takes about 3 to 4 weeks**
- **Viremia (presence of virus in the blood) rarely seen**
- **Virus is shed in respiratory secretions for 5 to 7 days, peaking 1 to 3 days after illness onset.**



Influenza Temporal Pattern

Northern hemisphere:

October through April or May,
most often peaks in February



Southern hemisphere:
April through September

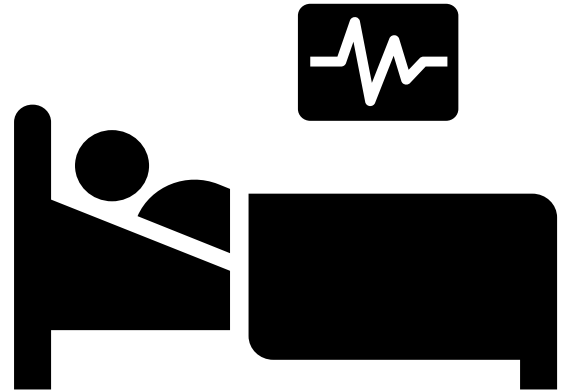
Influenza Clinical Features

- Incubation period 2 days (range 1–4 days)
- 50% of infected persons develop classic symptoms:
 - Fever
 - Feeling feverish/chills
 - Cough
 - Sore throat
 - Runny or stuffy nose
 - Muscle or body aches
 - Headaches



Influenza Complications

- **Pneumonia**
 - Secondary bacterial pneumonia
 - Primary influenza pneumonia
- **Myocarditis, myositis, encephalitis**
- **Multi-organ failure**
- **Reye syndrome**
- **Worsening of chronic medical conditions**



Populations at Higher Risk for Medical Complications Attributable to Severe Influenza

- Children younger than 5 years of age
- Adults 65 years of age and older
- People with certain chronic medical conditions
- People younger than 19 years of age who are receiving aspirin- or salicylate-containing medications
- People who are immunocompromised
- People who are or will be pregnant during the influenza season
- Residents of nursing homes and other long-term care facilities
- American Indian or Alaska Native persons

Chronic Medical Conditions That Increase Risk for Influenza Complications

- **Chronic lung disease, including asthma**
- **Neurologic and neurodevelopmental conditions**
- **Blood disorders, including sickle cell disease**
- **Chronic heart disease**
- **Severe obesity (BMI of 40 or greater)**
- **Kidney diseases**
- **Endocrine disorders, including diabetes**
- **Liver disorders**
- **Inherited metabolic disorders**
- **Immune suppression**
- **History of stroke**

Influenza Antiviral Medications

- **Recommended when patients with suspected or confirmed influenza are:**
 - Hospitalized
 - Severely ill
 - At higher risk for complications
- **Recommended options effective against influenza A and B viruses:**
 - Neuraminidase inhibitors: oseltamivir, zanamivir, peramivir
 - Endonuclease inhibitor: baloxavir
- **Adamantanes (amantadine and rimantadine) *not recommended* due to documented resistance among circulating influenza A viruses.**

2

Influenza Vaccine

Influenza Vaccine Abbreviations

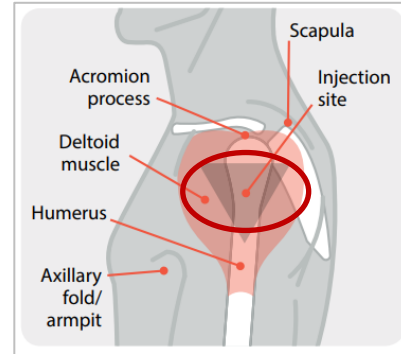
- **Main influenza vaccine types**
 - **IIV** = Inactivated Influenza **V**accine
 - **RIV** = Recombinant Influenza **V**accine
 - **LAIV** = Live-**A**ttenuated Influenza **V**accine
- **Prefixes identify specific IIVs**
 - **a** = **adjuvanted**: aIIV
 - **cc** = **cell culture-based**: ccIIV
 - **HD** = **High-Dose**: HD-IIV
 - **SD** = **Standard-Dose**: SD-IIV
- **Numeric suffixes indicate valency**
 - **3** = **trivalent**: e.g., aIIV3
 - **4** = **quadrivalent**: e.g., HD-IIV4

Transition to Only Trivalent Vaccines in 2024–2025

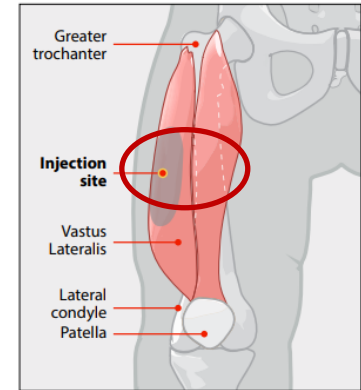
- **Quadrivalent influenza vaccines had been available since 2013–2014.**
- **In March 2024, FDA’s Vaccines and Related Biological Products Advisory Committee (VRBPAC) recommended that all 2024–2025 influenza vaccines be trivalent vaccines.**
 - One influenza A(H1N1), one influenza A(H3N2), and one influenza B/Victoria-lineage vaccine virus
 - Influenza B/Yamagata-lineage viruses have not been detected in global virologic surveillance since March 2020.
- **In June 2024, ACIP recommendations included this decision.**

Inactivated Influenza Vaccines (IIVs)

- **Non-live vaccine**
- **Standard-dose or high-dose**
- **Most egg-based**
 - Vaccine viruses incubated in chicken eggs prior to inactivation
- **One cell-culture based**
- **One adjuvanted**
- **Intramuscular (IM) administration**



Deltoid muscle for adults and older children



Anterolateral thigh for infants and younger children

Standard-dose Nonadjuvanted Egg-Based IIV3s

Vaccine	Age Indication and Approved Dose Volume
Afluria Trivalent	<ul style="list-style-type: none">• Children ages 6 through 35 months: 0.25 mL per dose• All persons ages 36 months and older: 0.5 mL per dose
Fluarix Trivalent	<ul style="list-style-type: none">• All persons ages 6 months and older: 0.5 mL per dose
FluLaval Trivalent	<ul style="list-style-type: none">• All persons ages 6 months and older: 0.5 mL per dose
Fluzone Trivalent	<ul style="list-style-type: none">• Children ages 6 through 35 months: 0.25 mL or 0.5 mL per dose• All persons ages 36 months and older: 0.5 mL per dose

High-Dose Egg-Based IIV3

Vaccine	Age Indication and Approved Dose Volume
Fluzone High-Dose Trivalent (HD-IIV)	<ul style="list-style-type: none">• For persons 65 years of age and older• 0.5 mL per dose

Contains four times the antigen as standard dose influenza vaccines

Can be used in persons 19 through 64 years with a solid organ transplant on immunosuppressive medications

Adjuvanted Egg-Based IIV3

Vaccine	Age Indication and Approved Dose Volume
Fluad Trivalent (aIIV)	<ul style="list-style-type: none">• For persons 65 years of age and older• 0.5 mL per dose

Standard dose with M59 adjuvant

Can be used in persons 19 through 64 years with a solid organ transplant on immunosuppressive medications

Cell Culture-based IIV3

Vaccine	Age Indication and Approved Dose Volume
Flucelvax (ccIIV)	<ul style="list-style-type: none">• For persons 6 months of age and older• 0.5 mL per dose

- **Manufactured without use of eggs**
- **Grown in cell culture prior to inactivation**

Recombinant Influenza Vaccine (RIV3)

Vaccine	Age Indication and Approved Dose Volume
Flublok Trivalent	<ul style="list-style-type: none">• For persons 18 years of age and older• 0.5 mL per dose

- **Non-live vaccine**
- **Manufactured without use of influenza viruses or eggs**
- **Contains recombinant hemagglutinin antigen produced using genetic sequences**
- **IM administration**

Live, Attenuated Influenza Virus Vaccine (LAIV3)

Vaccine	Age Indication and Approved Dose Volume
FluMist Trivalent	<ul style="list-style-type: none">• For persons ages 2 through 49 years• 0.1 mL each nostril (0.2 mL total)

- **Live vaccine**
- **Egg-based manufacturing**
- **Intranasal (NAS) administration**
 - Replicates in the nasopharynx; necessary for immune response

Intranasal (NAS) Administration for LAIV

- **LAIV the only vaccine administered by the intranasal route.**
- **Administration:**
 - 0.2mL divided between both nostrils



[Live, Attenuated Influenza Vaccine \(LAIV\) \(youtube.com\)](#)

[ACIP Vaccine Administration Guidelines for Immunization | CDC](#)

2024–2025 Influenza Vaccine Composition

Egg-based IIVs and LAIV3:

- A/Victoria/4897/2022
(H1N1)pdm09-like
- A/Thailand/8/2022
(H3N2)-like virus (updated)
- B/Austria/1359417/2021
(Victoria lineage)-like virus

Cell Culture-based IIV3 and RIV3:

- A/Wisconsin/67/2022
(H1N1)pdm09-like virus
- A/Massachusetts/18/2022
(H3N2)-like virus (updated)
- B/Austria/1359417/2021
(Victoria lineage)-like virus

All 2024–2025 influenza vaccines are trivalent.

Vaccine Effectiveness: How Well Do Flu Vaccines Work?

- **Varies from season to season, depending on factors such as:**
 - Characteristics of the recipient (such as their age and health)
 - How well the viruses represented in the vaccine match those circulating in the community
- **Flu vaccine has been shown to reduce the risk of having to go to the doctor with flu by 40% to 60%**
 - During seasons when flu vaccine viruses are similar to circulating flu viruses

Vaccine Effectiveness: How Well Do Flu Vaccines Work?

- Flu vaccination has been shown in several studies to reduce severity of illness in people who get vaccinated but still get sick.
- Flu vaccination can reduce the risk of flu-associated hospitalization.

3

Clinical Considerations

Influenza Vaccine Recommendations: Children and Adolescents

Table 1 Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2024

These recommendations must be read with the notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars. To determine minimum intervals between doses, see the catch-up schedule (Table 2).

Vaccine and other immunizing agents	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs
Influenza (IIV4)					Annual vaccination 1 or 2 doses										Annual vaccination 1 dose only		
OR																	
Influenza (LAIV4)					Annual vaccination 1 or 2 doses										Annual vaccination 1 dose only		

- Range of recommended ages for all children
- Range of recommended ages for catch-up vaccination
- Range of recommended ages for certain high-risk groups
- Recommended vaccination can begin in this age group
- Recommended vaccination based on shared clinical decision-making
- No recommendation/not applicable

Influenza Vaccine Dosing for Children 6 Months Through 8 Years of Age, 2024–2025

- **During first influenza vaccination season:
2 doses of influenza vaccine administered a minimum of 4 weeks apart**
 - Children requiring 2 influenza vaccine doses who receive their first dose at age 8 years should receive a second dose even if they turn 9 before getting it.

Influenza Vaccine Recommendations: Adults

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2024

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
Influenza inactivated (IIV4) or Influenza recombinant (RIV4)	1 dose annually			
Influenza live, attenuated (LAIV4)				

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of immunity

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

No recommendation/ Not applicable

Groups Recommended for Vaccination

- **Routine annual influenza vaccination is recommended for all persons 6 months of age or older with no contraindications.**
- **Influenza vaccination particularly important for:**
 - People 6 months of age and older who are at risk of complications and severe illness
 - Contacts and caregivers of people at risk of complications and severe illness
 - Contacts and caregivers of infants younger than 6 months
 - People who are or will be pregnant during the influenza season.

Timing of Vaccination

- **Vaccination should occur before onset of influenza activity.**
- **Vaccination should ideally be offered during September or October.**
- **Organized campaigns should continue throughout the season so long as influenza viruses are circulating.**
- **To avoid missed opportunities for vaccination, offer vaccination during routine health care visits and hospitalizations when vaccine is available.**
- **Vaccination in July and August might result in suboptimal immunity later in influenza season.**
 - Not recommended for those 65 years old and older, or for persons in the first or second trimester of pregnancy in July or August.

Vaccination Timing: May Consider Early Vaccination in July and August



Children 6 months–8 years who need 2 doses should get first dose as soon as vaccine is available.



May be considered for children of any age who need only 1 dose for the season



May be considered for people in 3rd trimester of pregnancy during July–August

Influenza Vaccination is Recommended for Pregnant Persons

- Includes persons who are pregnant, might be pregnant, or postpartum
- Higher risk of flu complications during 2nd and 3rd trimesters
- Protects infants during first few months of life when too young for vaccination
- Influenza vaccine can be administered during any trimester.
- Age-appropriate IIV3 or RIV3 may be used.

X LAIV3 should **NOT** be given during pregnancy.



Age-Appropriate IIV3 or RIV3 Recommended for Immunocompromised Persons

- **Includes but is not limited to people:**
 - With congenital and acquired immunodeficiency states
 - Who are immunocompromised due to medications
 - Additional flexibility for solid organ transplant recipients
 - With anatomic or functional asplenia

 LAIV3 should **NOT** be given to people with compromised immunity, or with anatomic or functional asplenia.

High-dose, Adjuvanted, or Recombinant Influenza Vaccines Preferentially Recommended for Persons 65 Years of Age and Older

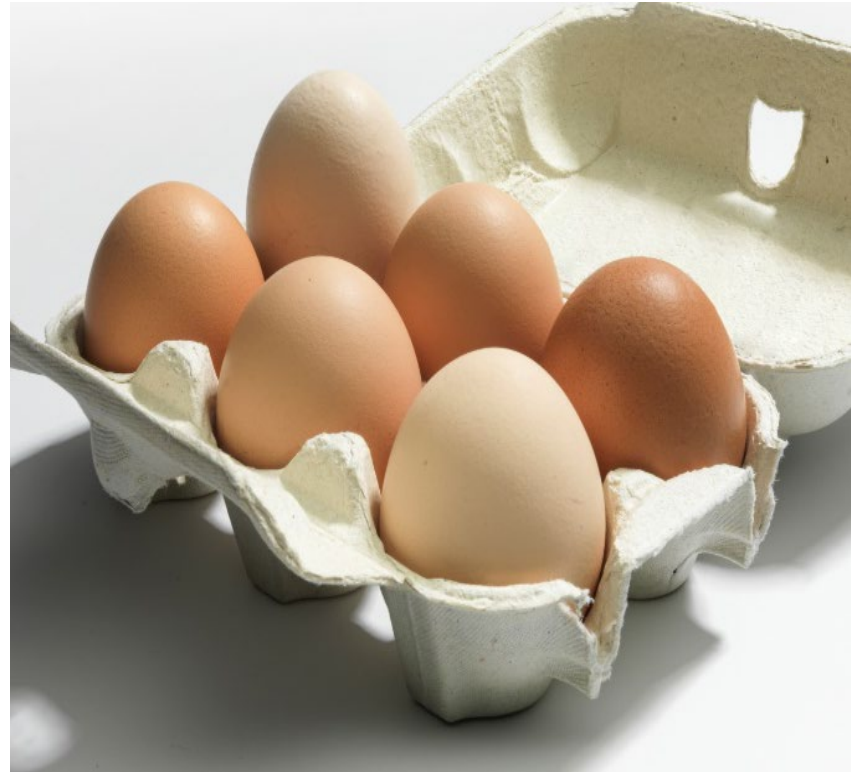
- **Includes Fluzone High-Dose (HD-IIV), Flud (aIIV), and Flublok (RIV)**
 - No preference between these three
- **Persons 65 years of age and older do not mount as strong of an immune response, so they benefit from one of these three vaccines.**
- **If none of the three are available, vaccinate with another age-appropriate influenza vaccine.**

Vaccine Options for Solid Organ Transplant Recipients on Immunosuppressive Therapy

- **A new recommendation beginning in 2024-2025**
- **High-dose or adjuvanted influenza vaccines are acceptable options for solid organ transplant recipients aged 18 through 64 years who are receiving immunosuppressive medication regimens.**
 - No preference over other age-appropriate IIVs or RIV3
 - This is an off-label ACIP recommendation.
- **Persons who receive solid organ transplants on immunosuppressive therapy mount a lower immune response to vaccination and so will benefit from high-dose or adjuvanted vaccines.**

Influenza Vaccination Recommended for All Persons with Egg Allergy

- Any appropriate influenza vaccine (egg-based or non-egg) can be used.
- Egg allergy alone necessitates no additional safety measures.
- All vaccines should be administered in settings with trained personnel and needed equipment needed for recognizing and managing acute hypersensitivity reactions.



Coadministration of Influenza and Other Vaccines

- **IIV3s and RIV3 can be administered with other inactivated or live vaccines.**
- **LAIV3 can be administered simultaneously with other live or inactivated vaccines.**
 - *Reminder:* allow at least 4 weeks between doses when two or more live vaccines are given non-simultaneously.
- **Limited data regarding coadministration with newer nonaluminum adjuvanted vaccines**
 - If aIV is indicated, another non-adjuvanted influenza vaccine may be considered, but do not delay if a specific vaccine is not available.



Influenza Vaccine Administration Errors – Example 1

- **What if a smaller dose (e.g., 0.25 mL) is inadvertently administered to a person 36 months or older?**
- **What steps should be taken?**
 - Remaining volume needed to make a full dose should be administered during the same vaccination visit

or

 - If measuring the remaining volume is a challenge, administering a repeat dose at the full volume is acceptable.

Influenza Vaccine Administration Errors – Example 2

- **What if the error is discovered later, after the recipient has left the vaccination setting?**
- **What steps should be taken?**
 - A full dose should be administered as soon as the recipient can return.

4

Safety

Adverse Reactions: IIV

Local reactions (soreness, redness)	15–20%
Fever, malaise, myalgia	Less than 1%
Allergic reactions (hives, angioedema, anaphylaxis)	Rare
Guillain-Barré syndrome	1–2 per million

Adverse Reactions

- **RIV3, like all injectable vaccines, can cause:**
 - Pain, redness, and swelling at the injection site
 - Fever, malaise, and myalgia
- **Some side effects more common with HD-IIV and aIIV compared to SD-IIV, but are mild and temporary:**
 - Pain, redness at injection site
 - Headache, myalgia, malaise

Adverse Reactions: LAIV

- **Children**

- Rhinitis (runny nose), fever greater than 100°F, and nasal congestion
- Increased risk of wheezing in children 6–23 months of age

- **Adults**

- Rhinitis (runny nose), nasal congestion, headache, sore throat, tiredness/weakness, muscle aches, cough, chills, sinusitis
- No increase in the occurrence of fever

Contraindications: IIV

- **Severe allergic reaction (e.g., anaphylaxis) after previous dose of any influenza vaccine or to vaccine component**

Contraindications: cclIV and RIV

- **cclIV**

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of cclIV of any valency or to any component of cclIV3

- **RIV**

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of RIV of any valency or to any component of RIV3

Precautions: IIV

- **GBS less than 6 weeks after a previous dose of influenza vaccine**
- **Moderate or severe acute illness with or without fever**

Precautions: cclIV and RIV

- **cclIV**

- GBS less than 6 weeks after previous dose of influenza vaccine
- Moderate or severe acute illness with or without fever
- Severe allergic reaction (e.g., anaphylaxis) after previous dose of any other influenza vaccine (any egg-based IIV, RIV, or LAIV)

- **RIV**

- GBS less than 6 weeks after previous dose of influenza vaccine
- Moderate or severe acute illness with or without fever
- Severe allergic reaction (e.g., anaphylaxis) after previous dose of any other influenza vaccine (any egg-based IIV, cclIV, or LAIV)

Contraindications: LAIV

- **All ages**

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component
- Pregnancy
- Active communication between cerebrospinal fluid/oropharyngeal communications/leaks
- Cochlear implants
- Altered immunocompetence
- Anatomic or functional asplenia (e.g., sickle cell disease)

- Close contact or caregiver of severely immunosuppressed persons who require a protected environment
- Recent receipt of antivirals: oseltamivir or zanamivir (48 hours), peramivir (5 days), baloxavir (17 days)

- **Children and adolescents**

- Concomitant use of aspirin or salicylate-containing medication
- Ages 2 through 4 years: diagnosed asthma or a recorded wheezing episode in the preceding 12 months

Precautions: LAIV

- **GBS less than 6 weeks after previous dose of influenza vaccine**
- **Asthma in persons aged 5 years old or older**
- **Other medical conditions that might predispose to higher risk of complications attributable to influenza**
- **Severe or moderate acute illness with or without fever**



Knowledge Check

A child just turned 9 years old yesterday. One month ago, he received his first ever dose of influenza vaccine. Should he receive another dose of influenza vaccine this season?

- A. Yes
- B. No



Knowledge Check

A child just turned 9 years old yesterday. One month ago, he received his first ever dose of influenza vaccine. Should he receive another dose of influenza vaccine this season?

A. Yes ←

B. No



Knowledge Check

Which condition is a contraindication to LAIV for a 10-year-old?

- A. Asthma
- B. Cognitive impairment
- C. Cochlear implant
- D. History of influenza infection this year



Knowledge Check

Which condition is a contraindication to LAIV for a 10-year-old?

- A. Asthma
- B. Cognitive impairment
- C. Cochlear implant** ←
- D. History of influenza infection this year

5

Storage and Handling

Influenza Vaccine Storage and Handling

- **IIV and LAIV**
 - Store between 2°C and 8°C (36°F and 46°F)
 - No diluent
- **Never expose vaccine to freezing temperatures.**
- **General rule for all vaccines:**
Never store vaccine in the door of the refrigerator or freezer.

6

Resources

Influenza Resources



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H5N1 Bird Flu: Current Situation Summary

Influenza Updates:

- Seasonal influenza activity remains low nationally.
- CDC continues to recommend vaccination as long as flu viruses are spreading.
- There are [antiviral drugs](#) to treat flu illness.

[Flu Report](#)

Prevent Flu



Everyone 6 months & older should receive a yearly flu vaccine.

[Prevention](#)

Symptoms & Diagnosis



Flu can cause mild to severe illness. Learn the symptoms of flu.

[Symptoms](#)

Treatment



Prescription medications called antiviral drugs can be used to treat flu.

[Treatment](#)

Flu Activity & Surveillance



Read this week's FluView report for the latest information on flu activity.

[Activity](#)

Influenza Vaccine Resources

- **ACIP's influenza vaccine recommendations web page**
 - <https://www.cdc.gov/acip-recs/hcp/vaccine-specific/flu.html>
- **Immunize.org influenza web page**
 - <https://www.immunize.org/influenza/>
- **Children's Hospital of Philadelphia Vaccine Education Center influenza web page**
 - <https://www.chop.edu/vaccine-education-center/vaccine-details/influenza-vaccine>

CDC Clinical Resources

- www.cdc.gov/vaccines/
 - Advisory Committee on Immunization Practices (ACIP) Vaccine Recommendations and Guidelines
 - Recommended Immunization Schedules
 - Vaccine Storage and Handling Toolkit
 - Vaccine Information Statements

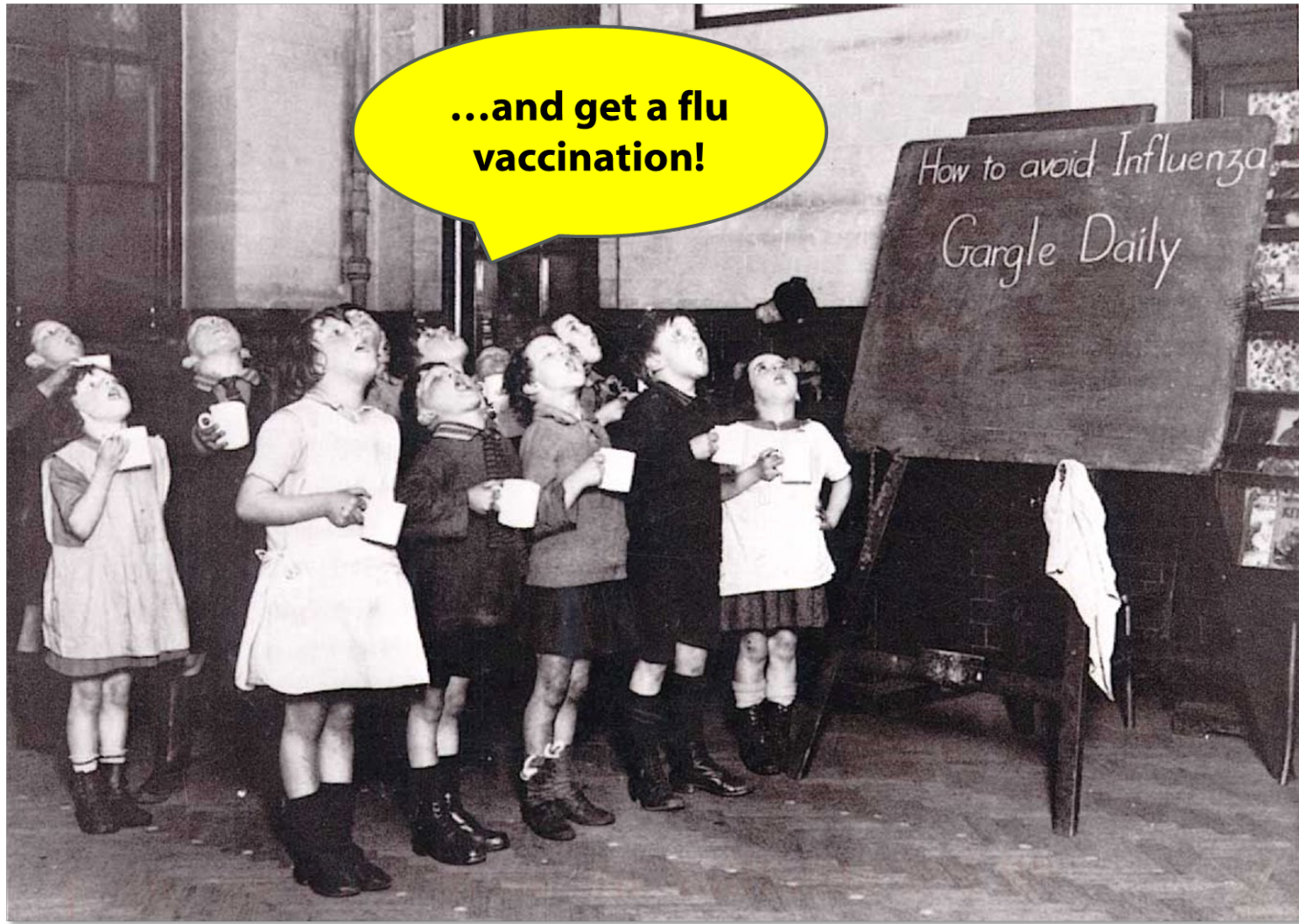
Pink Book Training
Materials





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

How to avoid Influenza
Gargle Daily



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