Proposed Recommendations 2016-17 Influenza Season

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Persons Recommended for Vaccination

Reiteration of core recommendation:

Annual influenza vaccination is recommended for all persons of persons 6 months of age and older.

- A licensed, age-appropriate influenza vaccine should be used
- Recommendations for different vaccine types and specific populations discussed in the ACIP statement

Timing of Vaccination

Minor changes in wording:

- 2015-16:

  Optimally, vaccination should occur before onset of influenza activity in the community. Healthcare providers should offer vaccination by October, if possible. Vaccination should continue to be offered as long as influenza viruses are circulating. Children aged 6 months through 8 years who require 2 doses (see "Vaccine Dose Considerations for Children Aged 6 Months through 8 Years") should receive their first dose as soon as possible after vaccine becomes available, and the second dose ≥4 weeks later.

- 2016-17 (proposed):

  Optimally, vaccination should occur before onset of influenza activity in the community. Healthcare providers should offer vaccination by the end of October, if possible. Children aged 6 months through 8 years who require 2 doses (see "Vaccine Dose Considerations for Children Aged 6 Months through 8 Years") should receive their first dose as soon as possible after vaccine becomes available, and the second dose ≥4 weeks later. Vaccination should continue to be offered as long as influenza viruses are circulating and unexpired vaccine is available.

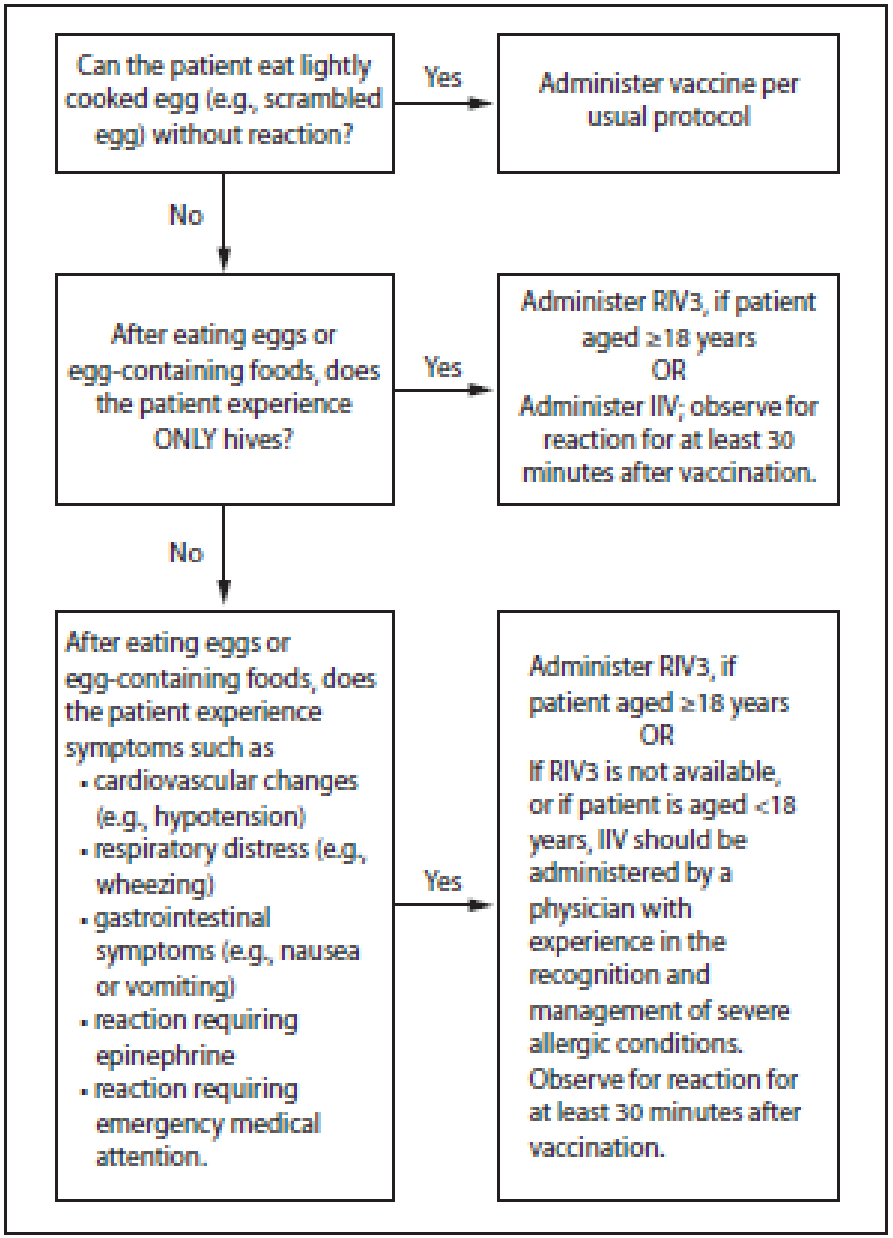
Influenza Vaccination of Persons with Egg Allergy

Per current (2015-16) recommendations:

- Stratified approach based on symptoms following egg exposure
  - hives only to eggs=mild allergy;
  - any other symptoms=severe allergy)
- LAIV not recommended for egg allergy
  - Until recently, little specific data on LAIV in this population
- 30 minute post-vaccination period to observe for signs of allergic reaction

MMWR 2015; 64(30):818-825

FIGURE 2. Recommendations regarding influenza vaccination of persons who report allergy to eggs*† — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season



Influenza Vaccination of Persons with Egg Allergy

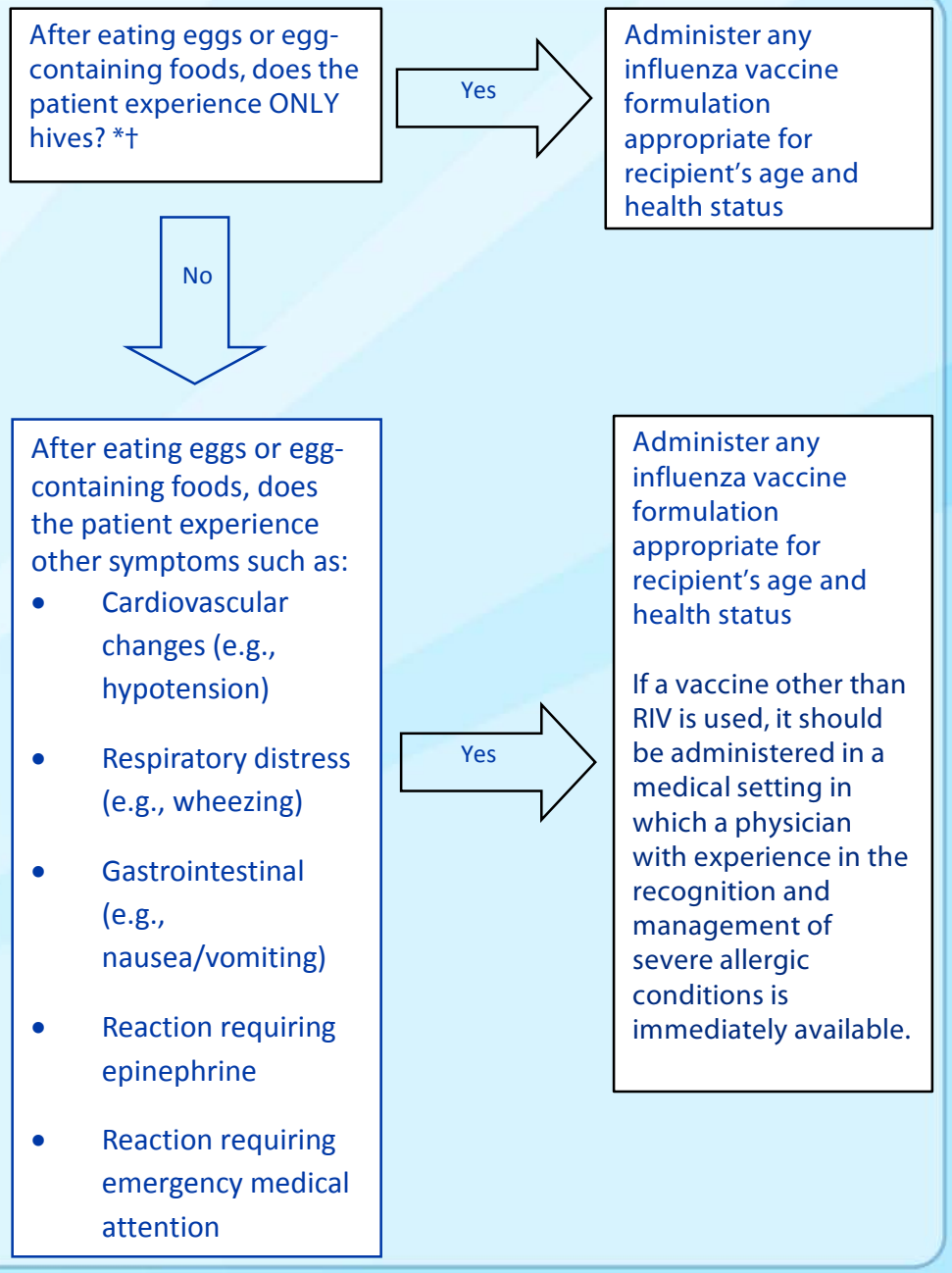
- Published data and potential language discussed in Influenza WG and with investigators of the Clinical Immunization Safety Assessment (CISA) project.
- Considerations
  - Overall rarity of anaphylaxis following vaccination in general; events may be missed in small studies
    - McNeil 2015: 33 anaphylaxis cases after 25,173,965 doses (all vaccines combined); rate=1.31 (95% CI 0.90-1.84) per million doses
    - For IIV3 administered alone, 10 anaphylaxis cases after 7,434,628 doses; rate=1.83 (95% CI 0.22-6.63) per million doses
  - 30 minute postvaccination observation period may miss reactions
    - McNeil 2015: symptom onset within 30 minutes in only 8 of 33 cases
  - Occasional VAERS reports of anaphylaxis following influenza vaccination of egg-allergic individuals
    - Stepwise approach permits assessment of additional reports over seasons subsequent to change in recommendations

McNeil MM et al, J Allergy Clin Immunol 2015

Influenza Vaccination of Persons with Egg Allergy

Proposed recommendations for 2016-17:

- LAIV included as an option for individuals with egg allergy of any severity
- Removal of 30 minute post-vaccination observation period (15 minutes recommended for all persons, particularly adolescents, in case syncope occurs)
- Persons with a history of severe reaction to eggs should be vaccinated in a medical setting with a physician immediately available



Influenza Vaccination of Persons with Egg Allergy

NO ALGORITHM (FIGURE 2)

1. Regardless of a recipient's allergy history, all vaccines should be administered in settings in which personnel and equipment for rapid recognition and treatment of anaphylaxis are available.

2. A previous severe allergic reaction to influenza vaccine, regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the vaccine.

3. Persons with a history of egg allergy who have experienced only hives after exposure to egg should receive influenza vaccine. Any licensed influenza vaccine (i.e., any form of IIV, LAIV, or RIV) that is otherwise appropriate for the recipient's age and health status may be used.

Influenza Vaccination of Persons with Egg Allergy

4. Persons who report having had reactions to egg involving symptoms other than hives, such as angioedema, respiratory distress, lightheadedness, or recurrent emesis; or who required epinephrine or another emergency medical intervention, may similarly receive any licensed influenza vaccine (i.e., any form of IIV, LAIV, or RIV) that is otherwise appropriate for age and medical conditions. The selected vaccine should be administered in a medical setting in which a healthcare provider with experience in the recognition and management of severe allergic conditions is immediately available.
5. ~~A 30 minute postvaccination observation period, previously recommended following vaccination of egg-allergic recipients, is no longer recommended. However, regardless of allergy history, vaccine providers should consider observing all patients, particularly adolescents, with patients seated or lying down for 15 minutes after vaccination to decrease the risk for injury should syncope occur (24).~~

Influenza Vaccination of Persons with Egg Allergy

6. For persons with no known history of exposure to egg, but who are suspected of being egg-allergic on the basis of previously performed allergy testing, the recommendations in 3) immediately above may be followed.

Anaphylaxis following administration of Live Attenuated Influenza Vaccine in Persons with a History of Egg Allergy

US Vaccine Adverse Event Reporting System (VAERS)

June 2003 – February 2016

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Background

- Currently ACIP does not recommend use of Live attenuated Influenza Vaccine (LAIV) in persons with egg allergy "because relatively few data are available for use of LAIV is this setting."[1]
- ACIP is reviewing current data on the safety of LAIV use in persons with egg allergy
- A retrospective analysis of post-vaccination anaphylaxis in the Vaccine Safety Datalink (VSD) for children and adults showed no case of anaphylaxis after 530,737 doses LAIV3[2]
- Since the 2011-2012 influenza season, enhanced surveillance for reports of anaphylaxis after influenza vaccine in persons with egg allergy has been conducted through the Vaccine Adverse Event Reporting System (VAERS).
- Reports of anaphylaxis after LAIV vaccination in VAERS were reviewed to provide additional information

1 CDC. Prevention and control of seasonal influenza with vaccines. recommendations of the Advisory Committee on Immunization Practices—United States, 2015–16. MMWR ;64(30):818-825

2 Risk of anaphylaxis after vaccination in children and adults J Allergy Clin Immunol. 2015 Sep 28. pii: S0091-6749(15)01160-4

Vaccine Adverse Event Reporting System (VAERS)

- National spontaneous reporting system for adverse events† (AE) after US-licensed vaccines
  - Accepts reports from healthcare providers, manufacturers and the public via mail, fax, secured online and telephone
  - Signs/symptoms of adverse event are coded using MedDRA* preferred terms (PTs) and entered into database
  - More than one code may be assigned to a single event; one VAERS report may include more than one symptom
- Jointly administered by CDC and FDA since 1990
- A reports is codes as a serious event if one of the following is reported
  - Defined as death, life-threatening illness, hospitalization, prolongation of hospitalization, or permanent disability

† Any untoward medical occurrence that follows vaccination and which does not necessarily have a causal relationship with the use of the vaccine

* http://www.meddra.org/

Vaccine Adverse Event Reporting System (VAERS)-Continued

Strengths

- Rapid signal detection
- Can detect rare adverse events
- Generates hypothesis
- Encourages reports from healthcare providers and accepts reports from patients and others
- Data available to the public

Limitations

- Reporting bias (e.g., underreporting, stimulated reporting)
- Inconsistent data quality and completeness
- Not designed to assess if vaccine caused an adverse event (AE)
- Lack of unvaccinated comparison group

VAERS website: http://vaers.hhs.gov

Methods

1. Automated search in VAERS database
   - United States domestic reports from June 2003 – February 2016
   - MedDRA* Preferred Terms (PTs):

     ANAPHYLACTIC REACTION

     ANAPHYLACTOID REACTION

     ANAPHYLACTIC SHOCK

     ANAPHYLACTOID SHOCK
   - Text string search-"egg" in symptom text, lab data, medical history and pre-existing illness sections
   - Vaccines- LAIV (trivalent or quadrivalent) with or without concomitant administration of other vaccines
   - Age and onset of symptoms : No restriction
2. Clinical review: available medical records of all VAERS reports of anaphylaxis following LAIV vaccination in persons with history of egg allergy (6/2003 – 2/2016) reviewed by CDC medical officers

*Medical Dictionary for Regulatory Activities

Summary of Anaphylaxis Cases in Persons with Egg Allergy following LAIV Vaccination

Age/ Gender	Influenza Season	Vaccine	Onset Interval	Signs/Symptoms Diagnosis/Brighton Level	Medical History	Allergy Test Result	Treatment/Out come
8Y/M	2011-12	LAIV3	5 hrs	• Diffuse urticarial rash • Dyspnea, wheezing Diagnosis: acute allergic reaction/anaphylactic shock Brighton Level 1	• Asthma, eczema, intolerance to cow's milk (recurrent emesis and angioedema) • History of egg ingestion on day of vaccination; ingested previously and appeared to tolerate eggs	• Positive skin prick • Positive allergen-specific test to egg white	Intramuscular epinephrine, oral Benadryl, intravenous Solumedrol and albuterol aerosol Treated in emergency department (ED). Recovered and discharged home

Case previously discussed at
(1) 2014 Vaccine Research Conference
(2) Clinical Immunization Safety Assessment (CISA) Project:
CISA's assessment: Anaphylaxis in a person with egg allergy. Causality of anaphylaxis and association with LAIV could not be determined due to concomitant ingestion of egg a few hours prior to vaccination

Summary of Anaphylaxis Cases in Persons with Egg Allergy following LAIV Vaccination (contd)

Age/ Gender	Influenza Season	Vaccine	Onset Interval	Signs/Symptoms Diagnosis/ Brighton level	Medical History	Allergy Test Result	Treatment/ Outcome
31Y/ F	2015-16	LAIV4	1hour	Itchy throat, facial swelling, difficulty swallowing, respiratory distress and oropharyngeal swelling. No wheeze Diagnosis: anaphylaxis Brighton Level 1	Asthma, Egg allergy (anaphylaxis*)	No documentation in VAERS report or medical records	Treated in ED with intramuscular epinephrine, albuterol, oral prednisone and oral Benadryl. Recovered and discharged home

No documentation if she consumes or avoids eggs/egg containing foods
No documentation of prior influenza vaccination
*Medical records unclear if this indicates a prior history of anaphylaxis after ingestion of eggs

Summary of Anaphylaxis Cases in Persons with Egg Allergy following LAIV Vaccination (contd)

Age/ Gender	Influenza Season	Vaccines	Onset Interval	Signs/Symptoms Diagnosis/ Brighton level	Medical History	Allergy Test Result	Treatment/ Outcome
4Y/ M	2015-16	LAIV4#1 DTaP#5 IPV#4 MMR#2 and VZV#2	10 mins	Abdominal pain Vomiting Pruritus in head, ears Urticarial rash in face, trunk and groin Wheezing Diagnosis: anaphylaxis Brighton Level 1	Asthma Allergic rhinitis	skin prick test* "reacted a bit" to tree pollen, cats, dogs, eggs, and pork	Diphenhydramine albuterol aerosol, intramuscular epinephrine, oral steroids and ranitidine. Transferred to ED. Recovered and discharged home

Previous influenza vaccination with IIV on 11/2012, 12/2012, 11/2013 and 10/2014
No documentation if he consumes or avoids eggs/egg containing foods
* Done 1 month after anaphylaxis event

Brighton Criteria: Anaphylaxis

- For all levels of diagnostic certainty

  Anaphylaxis is a clinical syndrome characterized by
  - Sudden onset AND
  - Rapid progression of signs and symptoms AND
  - Involving multiple (≥2) organ systems as follows:
- Level 1
  - ≥1 major dermatologic AND
  - ≥1 major cardiovascular AND/OR ≥1 major respiratory
- Level 2
  - ≥1 major cardiovascular AND ≥1 major respiratory

  OR
  - ≥1 major cardiovascular OR respiratory AND
  - ≥1 minor criterion involving ≥1 different system (other than cardiovascular or respiratory)

  OR
  - (≥1 major dermatologic) AND (≥1 minor cardiovascular AND/OR minor respiratory)
- Level 3
  - ≥1 minor cardiovascular OR respiratory AND
  - ≥1 minor criterion from each of ≥2 different systems/categories

[€]Anaphylaxis: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine 2007 Aug 1;25(31):5675-84

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