

Use of influenza vaccines in egg-allergic recipients

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Outline

- Background
 - Risk of withholding influenza vaccine
 - Safety of IIV in egg-allergic recipients
- Current guidelines regarding IIV and LAIV in egg-allergic recipients
- New studies on administration of LAIV to egg-allergic recipients
- Summary and my personal recommendations

Risk of *Withholding* Influenza Vaccine

- An average of 294,128 persons are hospitalized each year in the United States because of influenza, including an average of 21,156 hospitalizations in children less than 5 years of age.
- An average of 23,607 deaths occur each year in the United States as a result of influenza, including an average of 124 children.

Risk of *Withholding* Influenza Vaccine

- Egg allergy affects 1.3 % of children and 0.2 % of adults ¹ (self/parent reported rates much higher)
- There are 73.7 million children in the US ²
- As many as 958,100 egg-allergic children

1. The Center for Food Safety and Applied Nutrition Food and Drug Administration US Department of Health and Human Services

2. www.childstats.gov/americaschildren

Influenza vaccine contains measurable quantities of egg protein (ovalbumin); Does this cause systemic reactions when injected into egg-allergic patients?

- 27 published studies involving >4100 egg-allergic subjects getting influenza vaccine (IIV) without *any* serious reactions (no respiratory distress or hypotension)
- Very low rate of minor reactions (hives, mild wheezing), but *same in non-egg-allergic controls*
- So, the answer is no

Des Roches A, et al. Egg-allergic patients can be safely vaccinated against influenza. *J Allergy Clin Immunol* 2012;130:1213-1216.

But what about patients with severe egg allergy?

- Most studies have specifically *included* patients with histories of severe anaphylaxis (n = 513) with egg ingestion and these patients also tolerate the vaccine
- So, even these patients are not at risk of serious reaction

Why are there no serious reactions being reported?

- Manufacturers of injectable inactivated influenza vaccine (IIV) report the maximum amount of ovalbumin < 1 µg per 0.5 mL dose
- The measured amounts in independent laboratories are usually much lower than the claimed amounts
- Thus, the vaccine does not contain enough ovalbumin to cause a reaction

Current US allergy guidelines

The Joint Task Force on Practice Parameters. Update on influenza vaccination of egg allergic patients.

Annals of Allergy, Asthma & Immunology
2013; 111:301-2.

“All patients with egg allergy of any severity, including anaphylaxis, should receive IIV annually, using any age-approved brand of IIV in an age-appropriate dose.”

“Special precautions regarding medical setting and waiting periods after administration of IIV to egg-allergic recipients beyond those recommended for any vaccine are not warranted.”

Current international allergy guidelines

- International Consensus (ICON): Allergic Reactions to Vaccines (draft)
 - World Allergy Organization (WAO)
 - European Academy of Allergy and Clinical Immunology (EAACI)
 - American Academy of Allergy, Asthma, and Immunology (AAAAI)
 - American College of Allergy, Asthma, and Immunology (ACAAI)

“Egg allergy does not impart increased risk of anaphylactic reaction to immunization with either inactivated or live attenuated influenza vaccines”

“Although cases of immediate hypersensitivity reactions such as urticaria may occur, they are no more common in egg-allergic than non-egg-allergic vaccine recipients ”

Current Canadian vaccine guidelines

An Advisory Committee Statement (ACS)

National Advisory Committee on
Immunization (NACI)

Canadian Immunization Guide Chapter on
Influenza and Statement on Seasonal
Influenza Vaccine for 2015-2016

Current Canadian vaccine guidelines

- “Regarding administration of influenza vaccine to egg allergic persons, after careful review, NACI has concluded that egg allergic individuals may be vaccinated against influenza using TIV without prior influenza vaccine skin test and with the full dose, *irrespective of a past severe reaction to egg and without any particular consideration, including immunization setting.*”

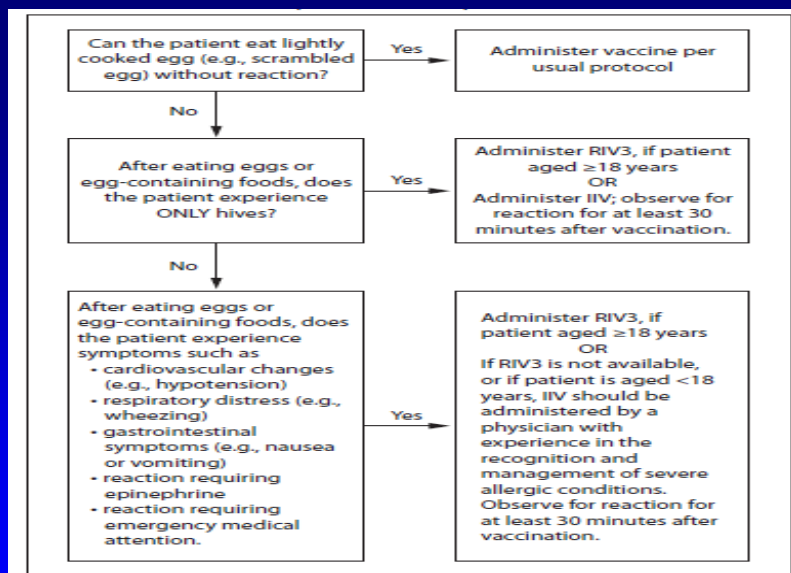
Current Canadian vaccine guidelines

- These guidelines have been in place since 2014
- No uptick in adverse reactions or safety signals in monitoring
- Most of the small number of anaphylaxis cases do not mention egg allergy

Current ACIP guidelines

Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2015-16 Influenza Season.

MMWR Morb Mortal Wkly Rep 2015;
64:818-25.



“Other measures, such as dividing and administering the vaccine by a two-step approach and skin testing with vaccine, are not necessary”

Current ACIP guidelines

- “ACIP will continue to review safety data for use of LAIV in the setting of egg allergy.”

Safe vaccination of patients with egg allergy by using live attenuated influenza vaccine

Des Roches A, Samaan K, Graham F, Lacombe-Barrios J, Paradis J, Paradis L, et al.

J Allergy Clin Immunol Pract
2015; 3:138-9.

LAIV and egg allergy

SUBJECTS

- 68 children age 2 to 16 years (median 6.5) with egg allergy = history of symptoms within 1 hour of egg ingestion *and* ongoing sensitization confirmed by skin test or specific IgE
 - 27/68 (40%) with anaphylaxis
- 55 children without egg allergy

LAIV and egg allergy

METHODS

- Administered LAIV (FluMist, <0.24 µg of ovalbumin per dose) in usual manner
- Observed for 1 hour

LAIV and egg allergy

RESULTS

- No patients developed an allergic sign or symptom during the hour of observation

LAIV and egg allergy

CONCLUSIONS

- “LAIV is a safe alternative to TIV in children with known egg allergy. It was not surprising that there were no immediate IgE-mediated reactions after vaccination of the children with egg allergy because the quantity of ovalbumin in LAIV is comparable with that of TIV, which has previously been shown to be safe in patients with egg allergy”

Safety of live attenuated influenza vaccine in atopic children with egg allergy

Turner PJ, Southern J, Andrews NJ, Miller E, Erlewyn-Lajeunesse M, Doyle C, et al.

J Allergy Clin Immunol
2015; 136:376-81.

LAIV and egg allergy

SUBJECTS

- 282 children age 2 to 17 years (median 4.9) with egg allergy =
 - (1) positive food challenge result to egg within the last 12 months under medical supervision
 - (2) previous convincing clinical reaction within 12 months and current sensitization (skin test or specific IgE)
 - (3) current sensitization with a greater than 95% likelihood of clinical reaction
- 115/282 (41%) prior anaphylaxis

LAIV and egg allergy

METHODS

- Administered LAIV (FluMist, <math><0.24\ \mu\text{g}</math> of ovalbumin per dose) in usual manner
- Observed for 1 hour
- 151/282 received a 2nd dose 4 weeks later = total of 433 doses given

LAIV and egg allergy

RESULTS

- No anaphylaxis
- 8/282 (2.8%) with possible allergic reactions within one hour (6 rhinitis, 1 localized urticaria, 1 gastrointestinal discomfort) all mild and self-limiting

LAIV and egg allergy
CONCLUSIONS

- “These data have demonstrated a safety profile in terms of systemic allergic reactions to LAIV in children with egg allergy, including those with a prior history of anaphylaxis, similar to that previously reported for children without egg allergy.”

Safety of live attenuated influenza vaccine in young people with egg allergy: multicentre prospective cohort study

Turner PJ, Southern J, Andrews NJ, Miller E, Erlewyn-Lajeunesse M.

BMJ 2015;351:h6291

LAIV and egg allergy

SUBJECTS

- 779 children age 2 to 18 years (median 5.3) with current doctor diagnosis of egg allergy
 - 270 (34.7%) with a history of anaphylaxis to egg

LAIV and egg allergy

METHODS

- Administered LAIV in usual manner
- Observed for 30 minutes

LAIV and egg allergy

RESULTS

- No systemic allergic reactions occurred
- 9/779 (1.2%) with possible allergic reactions within 30 minutes (4 rhinitis, 4 localized/contact urticaria, 1 oropharyngeal itch) all mild and self-limiting

LAIV and egg allergy

CONCLUSIONS

- Children with an egg allergy can be safely vaccinated with LAIV in any setting

LAIV and egg allergy SUMMARY

- Published reports now describe 1129 children with egg allergy, including 412 with history of anaphylaxis to egg ingestion, given LAIV without any immediate systemic reactions
- As with IIV, this is likely due to the very low amount of egg protein in the vaccine

LOAEL: Lowest observed-adverse effect level (ingestion)

- The lowest amount of the offending food that would elicit mild, objective symptoms (e.g., mild urticaria, erythema, and oral angioedema) in the most sensitive individuals.
- 0.35% of patients allergic to egg may react to 130 µg of egg-white proteins
- This is more than 100 fold more than the amount in influenza vaccine

Taylor SL, et al. Factors affecting the determination of threshold doses for allergenic foods: how much is too much?
J Allergy Clin Immunol 2002;109:24-30.

**Allergic reactions after
egg-free recombinant
influenza vaccine: reports
to the US Vaccine Adverse
Event Reporting System.**

Woo EJ.

Clin Infect Dis 2015;60:777-780.

- Twelve reports described signs and symptoms that were consistent with acute hypersensitivity reactions after administration of RIV3.
- The cases were all considered to be possible anaphylaxis.

Anaphylaxis after influenza vaccine

- Rate of about 1 per million like other vaccines
 - *whether recipient is egg-allergic or not*
 - *whether vaccine contains egg or not*
- A patient with a history of a prior allergic reaction *to influenza vaccination (not egg)* should be evaluated prior to subsequent vaccinations.

Kelso JM. Administering influenza vaccine to egg-allergic persons. *Expert Rev Vaccines* 2014;13:1049-57.

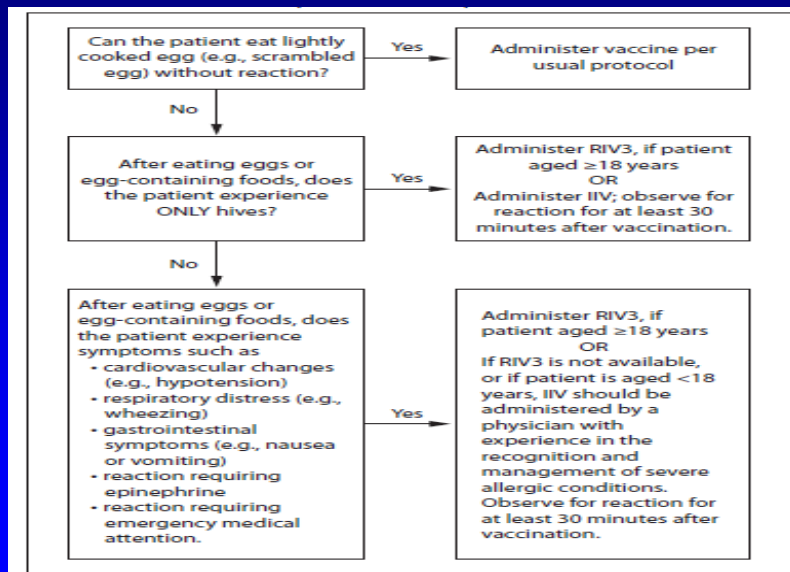
What precautions are advised to mitigate the risk of anaphylaxis with any vaccine?

General Recommendations on Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Recommendations and Reports
January 28, 2011 / 60(RR02);1-60

- “Although anaphylactic reactions are rare after vaccination, their immediate onset and life-threatening nature require that all personnel and facilities providing vaccinations have procedures in place for anaphylaxis management. All vaccination providers should be familiar with the office emergency plan and be currently certified in cardiopulmonary resuscitation. Epinephrine and equipment for maintaining an airway should be available for immediate use.”

Do we need the algorithm?



Do we need the algorithm?

- It implies that egg allergy increases the risk for an anaphylactic reaction after influenza immunization, but an extensive body of data says this is not the case.
- It implies that children with severe reactions to egg ingestion are at increased risk for reactions, but hundreds of such children have been vaccinated uneventfully.
- It implies that RIV is safer than IIV or LAIV for egg-allergic recipients, but all vaccines rarely cause anaphylaxis

Do we need the algorithm?

- For those with severe egg allergy requires a “physician with experience in the recognition and management of severe allergic conditions” = allergist, to whom a consult in some communities takes months
- It is inconsistent with US and international allergy guidelines
- It is inconsistent with Canadian vaccine guidelines

Do we need the algorithm?

- It is an unnecessary barrier to immunization
- Egg-allergic children (and some adults) are going unimmunized because practitioners don't want to take the "risk"
- Many hospitalizations and some deaths occur among the unimmunized

Influenza vaccine and egg allergy

My Recommendation ("Pearl of Wisdom")

1. No restriction on the use of the LAIV in egg-allergic recipients, i.e. treat LAIV like IIV.
2. No special precautions for the administration of any influenza vaccine (IIV or LAIV) to any egg-allergic recipient, i.e. no special medical setting or waiting period *beyond those recommended for any vaccine recipient*
3. *No algorithm.*