Influenza vaccine safety in patients with egg allergy
Katie A. Croegaert, Marwa M. Ithman, Andrew L. Spurgin, Susan S. Vos, and Gary Milavetz

Egg allergy is one of the most common food allergies in pediatric patients, with a parent-reported prevalence ranging from 1.6% to 2.6% of children in the general population. An egg allergy early in life has been correlated with respiratory allergic symptoms (asthma and/or rhinitis). In addition, adult patients with asthma are at a high risk for complications from influenza. Until recently, all influenza vaccines had been prepared by inoculation of virus into chicken eggs. In 2012, the Food and Drug Administration announced the approval of Flucelvax (Novartis), the first influenza vaccine produced using cultured animal cells instead of fertilized chicken eggs. Therefore, understanding the current recommendations and concerns for influenza vaccination in patients with egg allergy is important.

Egg intolerance versus allergy to eggs
Egg intolerance occurs when the body is not able to properly digest or reacts adversely to certain components of the egg. This happens if a person lacks specific enzymes or if he/she has a gastrointestinal reaction to a component of the egg product. People with egg intolerance usually can eat small amounts of egg without having a serious reaction. Individuals with food intolerance to egg typically can get the influenza vaccine without any risks or harm.

A true egg allergy is a systemic immune response and occurs when the body produces immunoglobulin E (IgE) antibodies to a protein in the egg. The individual must have been exposed to the substance causing the allergic reaction previously. The exposure could have been through diet or previous vaccination. IgE recognizes and binds an egg protein. With the allergen bound, the IgE crosslinks on the mast cell, releasing potent chemicals such as histamine and cytokines. These chemicals mediate an allergic reaction in the body that can present as a variety of symptoms (e.g., urticaria, angioedema, pruritus, vomiting, diarrhea, dyspnea, wheezing, swelling of the mouth and throat). Although some symptoms of egg intolerance and allergy overlap, an egg allergy is much more serious.

The allergic response to exposure to the allergy-causing food usually occurs within minutes. Individuals react at varying levels of severity during a food allergy reaction. Classification of the allergic reaction is important when considering vaccination. Mild symptoms of egg allergy are defined as hives only. Severe symptoms (e.g., anaphylaxis) generally require epinephrine or emergency treatment and involve cardiovascular changes (e.g., hypotension), respiratory symptoms (e.g., wheezing, dyspnea), and gastrointestinal symptoms (e.g., nausea, vomiting). Individuals requiring epinephrine must be sent for further medical evaluation.

Current recommendations
The Advisory Committee on Immunization Practices recommends administering the influenza vaccine with caution to patients with mild egg allergy; it is no longer contraindicated. Patients with a mild allergic reaction to egg can receive the injectable influenza vaccine with careful observation for 30 minutes after vaccination. Patients with a history of a severe allergic reaction to egg should be referred to a physician with expertise in managing allergic conditions. The safety of live attenuated influenza vaccine (LAIV; FluMist—MedImmune) in patients with egg allergy has not been established; therefore, LAIV should not be used in this population at this time (Figure 1). In addition, procedures such as skin prick testing and dividing the injectable vaccine into a two-step dose have been found to be unnecessary.

Evaluating egg protein content of influenza vaccines
Ovalbumin is used as a marker for the egg protein content in influenza vaccines. A number of studies have reported the content of ovalbumin safely administered to egg-allergic patients to be as high as 1.4 µg/mL (0.7 µg/0.5 mL dose). Ovalbumin content in vaccines can vary among seasons, manufacturers, and lots. However, the maximum threshold of safe ovalbumin concentration is unknown.
Unfortunately, a single source of information regarding ovalbumin content does not exist. Currently, three sources of information on ovalbumin content are available. The most readily available sources are the various package inserts. However, some manufacturers do not include ovalbumin content on the package insert. Second, pharmacists can contact the vaccine manufacturer and request ovalbumin content of the product. Third, the Centers for Disease Control and Prevention publishes vaccination recommendations each summer/fall with updated information for individuals with egg allergy.4

**Precautions when administering vaccination**

Patients with mild egg allergy may be vaccinated by a pharmacist familiar with the potential manifestations of egg allergy and trained to manage an anaphylactic reaction.4 Before administering the vaccine, a thorough medical history should be taken, with special attention focused on previous vaccines and the patient’s response. Patients should be observed on site for at least 30 minutes following administration of the vaccine dose for signs and symptoms of allergic reaction. The pharmacist should be able to recognize a severe allergic reaction at its early stages and must have emergency resuscitative equipment available for immediate treatment in case of anaphylaxis. This should include injectable epinephrine and an oral antihistamine, such as diphenhydramine or hydroxyzine.10 Because of the severe nature of the reaction, some community pharmacies may not be appropriate sites for this approach. Pharmacists should offer advice and refer patients with an egg allergy who may benefit from influenza immunization.

Figure 1. Pharmacists’ algorithm for patients with suspected egg allergy

<table>
<thead>
<tr>
<th>History of allergic reaction to eggs?</th>
<th>Administer influenza vaccine per routine procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Is the pharmacist allowed to administer vaccine to an egg allergic patient?</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Was reaction to eggs hives only?</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

References

4. Precautions when administering influenza vaccine include observation for 30 minutes and appropriate resuscitative equipment available.

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