

Letter to the Editor

Higher-ovalbumin-content influenza vaccines are well tolerated in children with egg allergy*To the Editor:*

The risk of vaccinating children who are allergic to egg with the influenza vaccine is unclear. We report our results with a 2-step influenza vaccine protocol to both the seasonal and H1N1 vaccines.

Influenza infections account for significant morbidity and mortality in the United States and abroad. The influenza vaccine decreases symptoms, outpatient visits, and hospitalizations^{1,2} and is now recommended for all children aged 6 months to 18 years.³ Because the influenza vaccine contains egg protein, whether patients with egg allergy can be safely vaccinated is unclear. The American Academy of Pediatrics and US Centers for Disease Control and Prevention^{4,5} recommend not vaccinating children with severe egg allergy, which is defined by the American Academy of Pediatrics as a history of hives, angioedema, allergic asthma, or anaphylaxis.

Although anaphylaxis has been described, recent studies suggest vaccination might be safe in patients with egg allergy. In 1998, James et al⁶ vaccinated 83 subjects with egg allergy (23 of whom had egg-induced anaphylaxis) with a 2-step protocol to the influenza vaccine (0.01-0.6 µg of ovalbumin/0.5-mL dose) without any significant reactions. More recently, Esposito et al⁷ vaccinated children with egg allergy and asthma and children with asthma alone in a 1-dose protocol (1 ng of ovalbumin/0.5-mL dose) after having negative skin prick test (SPT) results, with 1 wheezing episode in each group. Gagnon et al⁸ vaccinated 830 children with egg allergy (<8 ng of ovalbumin/0.5-mL dose) and had no cases of anaphylaxis. Chung et al⁹ found a 3% to 5% systemic reaction rate among children with egg allergy given the influenza vaccine by means of a 2-step challenge protocol regardless of whether SPTs were performed.⁹

We report our experience using a 2-dose graded protocol to administer influenza vaccine in patients with egg allergy. We conducted a retrospective chart review of patients with egg allergy who received the influenza vaccine, either seasonal, H1N1, or both, in our allergy/immunology clinic during 2009-

2010. We included all known patients with egg allergy who received an influenza vaccine during that time using a 2-step protocol. Written consent was obtained before vaccine administration. Egg allergy was defined as having (1) a clinical history of egg reaction with confirmatory positive results on either egg-specific IgE measurement or positive SPT results (ie, egg-specific IgE level >0.35 kUA/L or an SPT wheal response 3 mm or larger than that elicited by the saline control) or (2) positive test results (SPT or egg-specific IgE measurement) without a history of egg consumption. Patients currently consuming egg directly (eg, scrambled eggs) were excluded from this study because they were not considered to have egg allergy. We recorded parameters of age, sex, atopic history, asthma, previous egg reaction, SPTs, egg-specific IgE levels, total IgE levels, type of influenza vaccine (seasonal or H1N1), type of reaction, and vaccine lot number and producer for all patients, if available. Three patients were excluded from our study, 1 who received the vaccine in a single dose and 2 who received the vaccine in a graded protocol using more than 2 steps. None of these patients had a reaction. The 2 patients who received a greater than 2-step protocol did not appear to be at higher risk for an allergic reaction based on history and were vaccinated early in the season before implementation of the 2-step protocol.

Our vaccine protocol provided the influenza vaccine in a 2-step protocol first as a 10% aliquot and then the remaining 90% with a 15- to 30-minute observation period between doses and after the final dose. The Sanofi-Pasteur seasonal (Fluzone) and H1N1 influenza vaccine were exclusively used in our clinic for vaccination. All patients were observed for signs of both local (injection-site erythema) and systemic (hives, wheezing, and vomiting) reactions and were considered to have an allergic reaction if they had any of these objective symptoms.

Four mild allergic reactions occurred among 64 patients and 96 total vaccinations, resulting in a reaction rate of 6.2% of patients (95% CI, 4.4% to 7.8%) and 4.2% of vaccinations (95% CI, 3.4% to 5.0%), respectively. No patients had anaphylaxis as all reactions were mild cutaneous symptoms of urticaria or erythema. There were no significant differences between patients who did and did not react to vaccination. The average egg-specific

TABLE I. Demographics and reaction details for patients experiencing an allergic reaction to the influenza vaccine

Age (y)	Sex	Asthma	Other food allergies	Previous egg reaction	SPT egg	IgE egg (kUA/L)	Eats egg	Total IgE (kUA/L)	Reaction and timing	Dose
1	Male	No	Peanut	Vomiting	Not done	7.02	Baked goods	Not done	Small area of erythema with papule at diaper line, resolved with observation	90% Seasonal
1	Male	No	Milk	Hives	3-mm Wheal/5-mm flare	1.28	Baked goods	25	Multiple hives on chest, given diphenhydramine with resolution	Simultaneous administration of 10% H1N1 and 10% seasonal
6	Female	No	None	Hives, vomiting	Not done	>100	None	>2000	Large local erythema, resolved with observation.	10% H1N1
3	Male	No	Peanut, tree nut, milk	None	Not done	6.26	Baked goods	1099	Single prominent hive, resolved with diphenhydramine	10% Seasonal

IgE levels were higher (28.6 kUA/L) in patients who reacted than in those who did not (19.1 kUA/L), but this did not reach statistical significance and was driven by one reacting patient with an egg-specific IgE level of greater than 100 kUA/L. Two patients reacted to the seasonal vaccine, 1 reacted to the H1N1 vaccine, and 1 reacted when both were administered simultaneously. Three of 4 of the patients with reactions tolerated egg in baked goods, and 3 of 4 reacted to the 10% dose (the remaining 90% dose was withheld from these patients). **Table I** lists the characteristics of patients experiencing an allergic reaction.

These data further support that the influenza vaccine is well tolerated when given in a 10%/90% protocol to patients with egg allergy. Recent studies demonstrated that the Sanofi-Pasteur seasonal and H1N1 vaccines contained higher ovalbumin content than other influenza vaccines available last year, up to 0.7 µg/0.5-mL dose for the seasonal and 0.032 µg/0.5-mL dose for the H1N1 vaccination, respectively.^{10,11} It is reassuring that even with these higher-ovalbumin-content vaccines, no patients in our cohort had anaphylaxis, which is consistent with earlier studies.⁶

Our results provide further support to the concept that influenza vaccines are well tolerated in patients with egg allergy using a 10%/90% protocol. This tolerance is tempered somewhat by the fact that 3 of 64 patients reacted to 10% of the normal dose. Whether they would have had a more severe reaction to the 90% dose is unknown, although the low rate and mild degree of reactions with vaccines containing relatively high amounts of ovalbumin provide support that the 100% dose might be tolerated by patients with egg allergy. Further research is needed to evaluate whether a 2-step protocol is necessary or whether patients with egg allergy can receive the influenza vaccine in a single dose.

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