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Single-dose influenza vaccination of patients with egg allergy in a multicenter study

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To the Editor

Studies have suggested that the ovalbumin content in recent years' influenza vaccines is extremely low[1,2] and that most individuals with egg allergy can be safely vaccinated.[3,4] Although there are more conservative approaches, the majority of published studies use a 2-step protocol in which 10% of the dose is administered, followed 30 minutes later by the remaining 90%, a strategy used in the pivotal study by James et al[5] in 1998 and confirmed in several studies since then.[3,6] Some, however, have documented the safety of a single full dose when the vaccine contains a very low amount of ovalbumin.[7] Even patients with a history of severe egg allergy have been safely vaccinated by both strategies.

On average, 36,000 people die each year in the United States because of complications of influenza infection. Children under the age of 2 years are 9 times more likely to be hospitalized because of complications from influenza than children older than 5 years.[8] Vaccination remains the single most important tool available for prevention. Unnecessary avoidance of the influenza vaccine places undue risk on a significant proportion of one of our most vulnerable populations.

We performed a retrospective review of the safety of seasonal and H1N1 influenza vaccinations in patients with egg allergy at 4 university-based allergy and immunology clinics during the 2009 to 2010 influenza season to determine the tolerability of these vaccines in this population. The diagnosis of egg allergy was confirmed by an allergist and based on a clinical history consistent with an allergic reaction within 2 hours of the ingestion of egg and evidence of egg-specific IgE by skin or serum testing, or by an egg-specific IgE level or skin prick test (SPT) with >95% predictive value for type I hypersensitivity.[9]

A full-strength vaccine SPTwas performed along with positive and negative controls. Patients who tolerated baked egg were only skin tested at the clinician's discretion; otherwise they were given the full dose in a single injection because individuals tolerant of baked egg regularly tolerate small amounts of egg protein. If SPT was negative, the patient was given a single injection containing 100% of the required dose on the basis of age. If the

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SPT was positive or equivocal, the patient was given the vaccine in a 2-step protocol (10% of the total dose followed 30 minutes later by the remaining 90%). If a patient required a booster dose and the first dose was tolerated without adverse reaction, the vaccine from the same manufacturer but not necessarily the same lot was administered as a single dose with no antecedent SPT. No intradermal testing was performed at any time. All patients were observed for 30 minutes after the final dose, and all patients or parents were contacted the next clinic day to ensure that no delayed reactions occurred. Only injectable influenza vaccines were used in this study.

A total of 292 vaccinations with seasonal and/or H1N1 influenza were performed on 152 patients. Thirty-four (22%) of the 152 patients had a convincing history of anaphylaxis to egg involving a drop in blood pressure or a combination of respiratory compromise, skin involvement, or prolonged gastrointestinal symptoms as defined by the Second Symposium on the Definition and Management of Anaphylaxis.[10] Eighty-seven (57%) patients had a history of immediate-type allergic reaction to egg affecting the skin or gastrointestinal system alone. Thirty-one (20%) patients had not knowingly consumed egg or no reaction was documented in the medical record, but had a level of egg IgE by SPT, serum *in vitro* test, or both that was >95% predictive of egg allergy.[9] The age of patients ranged from 7 months to 30 years with a median age of 3 years. The most recent SPT to egg showed a median wheal size of 8 mm (range, 0-28 mm). The median serum IgE to egg was 6.01 kU/mL (range, <0.35->100 kU/L) using the Phadia ImmunoCAP system (Phadia, Uppsala, Sweden).

Skin prick testing was performed before 85% of challenges. One patient had a positive SPT, and 6 were equivocal. One child received the vaccine in split dosing because of parent preference, despite a negative SPT. The only positive SPT occurred to the seasonal FluZone (Sanofi Pasteur Inc, Swiftwater, Pa) vaccine in a 22-month-old who had never knowingly ingested egg but who had a 15-mm wheal to egg SPT and serum egg IgE 2.57 kU/L. The child tolerated the full dose of the seasonal vaccine administered by split dosing. Of note, this same child with a positive SPT to the seasonal vaccine had a negative SPT to the H1N1 vaccine and tolerated the latter in a single dose on 2 occasions, including a booster H1N1 dose.

Two hundred eighty-five vaccinations were performed by using single-dosing (97%), including 65 vaccinations (23%) in patients with a history of severe egg allergy. One of the 34 patients with severe egg allergy received the vaccine in a divided dose because of an equivocal SPT to the seasonal FluZone vaccine. There were no systemic reactions in any of the patients undergoing vaccination in our study, including those with severe egg allergy. Two patients with negative vaccine SPT developed mild local reactions, both to the single 100% dose of seasonal FluZone vaccine. One of these patients was a 7-year-old with a history of anaphylaxis to egg characterized by both skin and gastrointestinal symptoms with an egg SPT 28 mm and serum egg-specific IgE 7.8 kU/L. The second was a 5-year-old with a serum egg-specific IgE 42 kU/L who developed redness at the injection site 24 hours after vaccination.

A total of 38 separate lots from 3 different companies were used for seasonal influenza (21 lots) or H1N1 (17 lots) vaccination. FluZone was the only vaccine approved for children under 4 years old before the start of the 2009 to 2010 influenza vaccine season, and 263 of the 292 vaccinations in this study used FluZone. Fourteen vaccinations used lot U3176AA, which was found by Waibel and Gomez[1] to contain 1.421 μg/mL ovalbumin. Up to 50% of the lots of FluZone may have contained more than 1.2 μg/mL ovalubumin.[1] This content is slightly higher than that deemed safe in patients with egg allergy by James et al.[5] None of

our subjects developed systemic reactions to this vaccine, suggesting that the threshold of ovalbumin tolerated by most patients with egg allergy may be higher than 1.2 μg/mL.

Our study suggests that most individuals with egg allergy can be safely vaccinated by a single dose of the influenza vaccine, even patients with severe egg allergy. As other studies have suggested,[3,4] our findings do not support the use of skin testing as a reliable predictor of which patients react to vaccination because all of our patients tolerated the vaccine. Prospective studies are ongoing to confirm our retrospective findings of the safety of single-dose vaccination of patients with egg allergy.

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References

1. Waibel KH, Gomez R. Ovalbumin content in 2009 to 2010 seasonal and H1N1 monovalent influenza vaccines. J Allergy Clin Immunol. 2010; 125:749–51. [PubMed: 20060576]
2. Li JT, Rank MA, Squillace DL, Kita H. Ovalbumin content of influenza vaccines. J Allergy Clin Immunol. 2010; 125:1412–3. [PubMed: 20451987]
3. Chung EY, Huang L, Schneider L. Safety of influenza vaccine administration in egg-allergic patients. Pediatrics. 2010; 125:1024–30.
4. Greenhawt MJ, Chernin AS, Howe L, Li JT, Sanders G. The safety of the H1N1 influenza A vaccine in egg allergic individuals. Ann Allergy Asthma Immunol. 2010; 105:387–93. [PubMed: 21055666]
5. James JM, Zeiger RS, Lester MR, Fasano MB, Gern JE, Masfield LE, et al. Safe administration of influenza vaccine to patients with egg allergy. J Pediatr. 1998; 133:624–8. [PubMed: 9821418]
6. Owens G, Macginnitie A. Higher-ovalbumin-content influenza vaccines are well tolerated in children with egg allergy. J Allergy Clin Immunol. 2011; 127:264–5. [PubMed: 21094520]
7. Gagnon R, Primeau MN, Des Roches A, Lemire C, Kagan R, Carr S, et al. Safe vaccination of patients with egg allergy with an adjuvanted pandemic H1N1 vaccine. J Allergy Clin Immunol. 2010; 126:317–23. [PubMed: 20579720]
8. Centers for Disease Control and Prevention (CDC). Estimates of deaths associated with seasonal influenza –- United States, 1976—2007. Morb Mortal Wkly Rep. 2010; 59:1057–62.
9. Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. J Allergy Clin Immunol. 2001; 107:891–6. [PubMed: 11344358]
10. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF, Bock A, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006; 117:391–7. [PubMed: 16461139]