

Letter to the Editor

Administration of influenza vaccine to pediatric patients with egg-induced anaphylaxis

To the Editor:

Administration of egg-containing influenza vaccine to subjects with egg allergy continues to generate discourse. From a public health perspective, vaccination offers clear benefits. However, the potential for egg-induced anaphylaxis remains a concern. For those with a history of a severe reaction to egg ingestion, there is understandable unease by both health care providers and patients' families regarding vaccination. Current Joint Task Force on Practice Parameter guidelines suggest that most patients with egg allergy can safely receive influenza vaccination.¹ Indeed, studies show a reaction rate to vaccination ranging from 0% to 6.2%²⁻⁸ in cohorts with egg allergy. However, these studies reported on relatively small numbers of patients with egg-induced anaphylaxis.

We thus performed a retrospective review of patients who received influenza vaccination at the Children's Hospital of Philadelphia allergy clinics between 2007 and 2009. H1N1 vaccinations were excluded. Each chart was reviewed for any record of an anaphylactic reaction to egg. Anaphylaxis was defined per the clinical criteria outlined by Sampson et al⁹ in 2006.

Patients were given influenza vaccine at current recommended doses: a 0.25-mL dose if less than 36 months of age and a 0.5-mL dose if 36 months of age or older. Patients first underwent skin prick tests (SPTs) with full-strength influenza vaccine, saline, and histamine by using a bifurcated needle. SPT responses were read at 15 minutes as maximal wheal-and-flare diameter. Those with a positive influenza vaccine SPT response (≥ 3 mm wheal) were to be given the vaccine in divided doses separated by 30 minutes. In the 2007 season, this consisted of 3 divided doses (0.05, 0.01, and 0.01 mL) or 4 divided doses (0.05, 0.1, 0.15, and 0.2 mL). In the 2008-2009 seasons, this consisted of one tenth of the final dose followed by the remaining nine tenths of the dose. Patients were observed for 30 minutes after vaccination for signs of an allergic reaction and told to contact us if any additional reactions occurred at home. Sanofi Pasteur (Lyon, France) manufactured the vaccine in all except 1 case, in which Novartis (Basel, Switzerland) vaccine was used. Nine lots were used, with 91% of vaccines coming from 4 Sanofi Pasteur lots.

In total, 119 vaccinations were performed on 56 patients with egg-induced anaphylaxis. A vaccination reaction occurred in 3 doses (2 patients); characteristics of these cases are compared with those of tolerated vaccine cases in Table I. Mean age at the time of vaccination was 4 years and 6 months (range, 7 months-13 years and 8 months). In all but 18 cases, the date of the most recent egg-induced anaphylactic episode was known. The most recent anaphylactic episode preceded the vaccination in 56 cases. Average time between egg anaphylaxis and vaccination was 26 months (range, 5 days-71 months). In 45 cases, although egg allergy was identified through SPT responses, history, or both before influenza vaccination, egg-induced anaphylaxis occurred after vaccine administration.

In all, 113 vaccinations were preceded by influenza vaccine SPTs. Table II shows SPT wheal size and subsequent single-dose versus multidose vaccination. Some subjects were given single-dose vaccination despite a nonnegative vaccine SPT response.

We speculate that this was because, with the exception of 3 cases without documentation, the subject previously tolerated flu vaccination either in a single dose if he or she had a negative influenza SPT response or a multidose if he or she had had a positive influenza SPT response.

Two patients had vaccine reactions, with 1 patient having 2 reactions. Patient A was a 2-year-old boy without asthma. At age 1 year, he experienced facial swelling after eating scrambled egg. During an egg oral food challenge at age 5 years, he experienced hives, cough, and rhinorrhea and received epinephrine and antihistamine. Before influenza vaccination, his egg and influenza SPT responses were both positive (10-mm wheal with a 20-mm flare and 4-mm wheal with a 5-mm flare, respectively). He had an eczema flare and hives on his wrists after 0.05 mL of vaccination. He received oral antihistamine and did not receive the remainder of the vaccine. The following year, the influenza SPT response was negative. He still received the vaccine in 2 doses. Six hours after the last dose of vaccine, facial swelling was reported, which was treated at home with oral antihistamine. A year later, his influenza SPT response consisted of a 2-mm wheal with a 3-mm flare. He had no reaction to the vaccine given in 2 doses.

Patient B was an 18-month-old boy with asthma. At 13 months, he experienced facial edema, hives, cough, and emesis 15 minutes after ingestion of scrambled egg. This was treated at home with albuterol. He had a positive influenza vaccine SPT response (4-mm wheal with a 12-mm flare). The most recent egg SPT response 2 months before was positive (6-mm wheal with a 22-mm flare). Hives developed behind the left ear 30 minutes after the final vaccine dose. Symptoms resolved with oral antihistamine. One month later, he tolerated a single-dose booster vaccine supplied from the same lot.

We report on the relative safety of influenza vaccination in subjects with a history of egg-induced anaphylaxis. Although practitioners should always be prepared to treat allergic reactions as they occur, here we demonstrate only mild reactions. In 119 vaccinations there were 3 cases of skin-limited reactions and no systemic reactions. In comparison, within our larger cohort of 520 children with egg allergy but without anaphylaxis in this same time period, there were 11 reactions, all of which were skin limited. Influenza SPTs were not helpful in predicting who would or would not react. Of note, 7 patients who had positive influenza SPT responses tolerated single-dose vaccination, suggesting that vaccination dose division might not be necessary.

A few studies comment on influenza vaccination outcomes in the population with egg-induced anaphylaxis. Howe et al⁵ reported on 14 children with egg-induced anaphylaxis who tolerated vaccination. Two children had positive influenza vaccine SPT responses, 9 had negative responses, and 3 did not have pre-testing. Greenhawt et al⁴ identified 25 patients with egg-induced anaphylaxis all of whom tolerated vaccination; 13 received graded challenges for positive vaccine SPT responses, whereas 12 received a single dose for a negative SPT response. James et al⁶ reported on 27 children with egg-induced anaphylaxis who tolerated the vaccination in 2 divided doses. In all but 1 of 34 patients with a history of egg-induced anaphylaxis studied by Webb et al,⁷ vaccination was tolerated. The exception case had a negative influenza vaccine SPT response and a mild local reaction after single-dose vaccine administration. Gagnon et al³

TABLE I. Comparison of patients with egg-induced anaphylaxis by reaction to influenza vaccination

Clinical factors	Tolerated influenza vaccine (%)	Reacted to influenza vaccine (%)
No. of patients	54 (96)	2 (4)
Male sex	40 (74)	2
Asthma	39 (72)	1 (50)
No. of influenza vaccine administrations	116 (97)	3 (3 of total)
Average egg SPT (mm [range])*	8 (0-15)†	8 (6-10)
Influenza vaccine SPT response (mm)		
0	81 (70)	1 (33)
1	4 (3)	0
2	12 (10)	0
≥3	13 (11)	2 (67)
Not done	6 (5)	0
Influenza vaccine reactions		
Localized	NA	3 (100)
Multisystem	NA	0

NA, Not applicable.

*Egg SPTs were done on the same visit date immediately before flu vaccination in 97 cases. The remaining cases had egg SPTs an average of 4 months prior (range, 1-8 months).

†The egg SPT response was 0 mm in 1 patient immediately preceding flu vaccine. However, egg SPT responses in the previous year were positive.

reported on high-risk patients with egg allergy, as defined by history of an egg-induced allergic reaction involving the cardiorespiratory system or a history of uncontrolled asthma in comparison with other patients with egg allergy. Seventy-two (9%) high-risk subjects were identified. Adverse event frequency was similar between high-risk and not high-risk patients. There were no cases of vaccine-mediated anaphylaxis.

Additionally, our results support findings by Owens and MacGinnitie⁸ that higher vaccine ovalbumin content does not increase the risk of a reaction. Although we did not measure ovalbumin content in our vaccines, independent assay of the 2009-2010 vaccines demonstrated that the Sanofi Pasteur formulation had a median ovalbumin concentration higher than those of comparable brands¹⁰ used in other studies.^{3,4,6}

A limiting factor in our study is possible natural selection bias in our patient population. Although no patients in our cohort refused the vaccine, there are likely patients with egg-induced anaphylaxis who do not present to the clinic for vaccination for fear of an adverse event. Nonetheless, our study adds to growing data that influenza SPTs and division of vaccination doses might be unneeded practices.

TABLE II. Influenza vaccination SPT wheal size and single-dose versus multidose influenza vaccination

Influenza vaccine SPT wheal size (mm)	No. of subjects given single-dose vaccine	No. of subjects given multidose vaccine
0	82	0
1	4	0
2	5	7
≥3*	7	8

*In total, these 15 cases represented 14 subjects.

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