Letters to the Editor

Use of Live Attenuated Influenza Vaccine in Children With Egg Allergy and Asthma

To the Editor—I read with interest the recent publication by Haber et al regarding postlicensure surveillance of a trivalent live attenuated influenza vaccine (LAIV3) and was reassured that their “review of reports to VAERS [Vaccine Adverse Event Reporting System] after LAIV3 vaccination in children aged 2–18 years during 7 influenza seasons did not identify any new or unexpected safety concerns” [1].

However, the authors go on to say that they “did identify [adverse event] reports in persons for whom LAIV is contraindicated (ie, children with egg allergy or asthma, administration to pregnant teenagers), demonstrating the need for greater efforts to educate vaccine providers and administrators on the proper indications for LAIV.” The implication is that had LAIV not been given to patients with these conditions, these adverse events (AEs) would not have occurred. A closer look at the details of these AEs makes such a conclusion highly unlikely.

The 1 report of anaphylaxis in a patient with egg allergy stated that he had ingested eggs before receiving FluMist and had a reaction (diffuse urticarial rash, wheezing, and dyspnea) 5 hours later. If this reaction was related to egg allergy, it would almost certainly have been caused by the ingestion of eggs and almost certainly not by the minuscule amount of egg protein (ovalbumin, <0.24 μg/dose) in the vaccine [2]. The 3 additional serious AEs in the 10 VAERS reports of children with egg allergy were ataxia, pneumonia and reactive airway disease, and headache with bilateral foot pain; these reactions are not consistent with egg allergy and, thus, are coincidental.

In a recent study, Des Roches et al [3] described the administration of LAIV to 68 children (median age, 6.5 years) with egg allergy, defined as an allergic reaction within 1 hour of egg ingestion and a positive skin test or specific IgE antibody to egg protein. They also administered the vaccine to 55 control children without a history of egg allergy. All of the patients received LAIV in the usual manner and were kept under observation for 1 hour, during which time no allergic reactions were observed. A follow-up telephone call 24 hours later revealed a somewhat higher rate of nonspecific adverse reactions in the egg-allergic subjects than in the controls, but none was suggestive of an allergic reaction. Although this is the only published study to date on the safety of LAIV in egg-allergic recipients, the results are consistent with those of the multitude of published studies in which thousands of egg-allergic patients have uneventfully received injected inactivated influenza vaccine containing even more egg protein than does the LAIV [4].

Haber et al also reported that 95 AE reports involved patients with asthma, but only 10 described asthma exacerbations [1]. An additional 24 VAERS reports were apparently filed to indicate only that a child with asthma had inadvertently received LAIV but not to report any reaction. One of the fatalities reported was of a 13-year-old boy whose cause of death was “status asthmaticus due to lymphocytic bronchitis,” with onset 13 days after vaccination; the results of viral studies performed at the Centers for Disease Control and Prevention were negative for influenza A and B, which makes it exceedingly unlikely that LAIV contributed to his death. Thus, the vast majority of children with asthma who have received LAIV did not have an asthma exacerbation. Some previous studies, but not others, have shown an increased rate of wheezing episodes after receipt of LAIV in children younger than 3 years [5]. On the basis of these data, the Advisory Committee on Immunization Practices recommends that LAIV, which is otherwise approved for healthy persons aged 2–49 years, not be administered to children aged 2–4 years with a diagnosis of asthma or a history of wheezing [6]. Studies have not demonstrated any increase in asthma episodes after the receipt of LAIV in recipients aged 5 years or older, although most studies excluded patients with severe asthma; thus, in this age group, asthma is considered a precaution rather than a contraindication for LAIV [6]. In the Des Roches et al study [3], 40 (59%) of the 68 children with egg allergy who uneventfully received LAIV also had mild asthma, but none suffered an asthma exacerbation.

It is appropriate to continue conducting surveillance for AEs after immunization with LAIV and other vaccines. However, LAIV is now preferred over inactivated influenza vaccine for children aged 2–8 years because of its superior efficacy [6]. This clear-cut benefit should be weighed against the apparently non-existent risk of administering LAIV.
to children with egg allergy and in those older than 5 years with asthma.

John M. Kelso
Division of Allergy, Asthma and Immunology, Scripps Clinic, San Diego, California

References

Corresponding Author: John M. Kelso, MD, Division of Allergy, Asthma and Immunology, 3811 Valley Centre Dr, Scripps Clinic, San Diego, CA 92124. E-mail: kelso.john@scrippshealth.org. Journal of the Pediatric Infectious Diseases Society, Vol. 4, No. 1, pp. 81–2, 2015 © The Author 2014. Published by Oxford University Press on behalf of the Pediatric Infectious Diseases Society. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.

DOI:10.1093/jpids/piu116 Electronically published December 26, 2014


Reply to Letters to the Editor—We thank Dr Kelso for his thorough review of our article, thoughtful comments, and concise presentation of the evidence regarding the safety of live-attenuated influenza vaccine (LAIV) in children. Dr Kelso raises many important points about the safety of LAIV in special populations that we have traditionally considered potentially “high risk” for adverse events (AEs) after LAIV.

The purpose of our study was to describe the safety of LAIV in children aged 2 to 18 years on the basis of a descriptive review of AE reports in the Vaccine Adverse Event Reporting System (VAERS). These AEs occurred in temporal association with the receipt of LAIV.

In response to our statement about AEs after LAIV administration in patients with contraindications, Dr Kelso states, “The implication is that had LAIV not been given to patients with these conditions that these adverse events (AEs) would not have occurred.” We regret that Dr Kelso interpreted our findings this way. As we mentioned in the discussion of our article, the VAERS and other passive surveillance systems are subject to many limitations, including their inability to determine whether a vaccine caused a given AE [2]. Our primary objective was to describe instances of LAIV administration to individuals in whom the vaccine was not indicated; we did not attempt to confirm or rule out a causal association with the vaccine. We based this determination on the published recommendations and indications for LAIV during the study period [1]. In fact, we did not assess the causality of any AEs; such an evaluation requires systematic collection of medical records, a thorough review of all available information by clinical experts, and the application of a detailed causality algorithm [3, 4].

We appreciate Dr Kelso’s summary of the research literature on the use of LAIV among patients with a history of egg allergy and/or asthma. The Advisory Committee on Immunization Practices (ACIP) issues its recommendations on the basis of rigorous evidence-based assessments of the available data [5, 6]. We believe that it is important to describe AE reports in the context of precautions and contraindications, as stated in the current ACIP recommendations. Dr Kelso correctly points out that for the 2014–2015 influenza season, the ACIP identifies asthma in children aged 5 years and older as a precaution rather than a contraindication for LAIV [7]. However, during the study period, the ACIP recommended against the use of LAIV among persons with asthma [1].

Penina Haber,1 Pedro L. Moro,1 Maria Cano,1 Claudia Vellozzi,1 Paige Lewis,1 Emily Jane Woo,2 and Karen Broder1

1Immunization Safety Office, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia
2Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research, US Food and Drug Administration, Rockville, Maryland