epinephrine being delivered intramuscularly, the concern is that it might. Needle lengths of EAI's have already been cited as potentially inadequate to reliably deliver epinephrine to the muscle bed. Any amount of unexpected recoil that occurs while using a real EAI during an emergency might further reduce the likelihood of successful intramuscular administration. On the basis of this pilot study, it might be prudent for practitioners to inform patients that there are indeed differences with regard to how much force is required to activate different brands of EAI's, as well as differences in recoil generated. This might be of particular importance for those patients or providers who have been using one brand of EAI exclusively and then switch to a different brand of EAI. Encouraging patients to practice with real expired EAI's on tissue simulants, such as an orange, might also be beneficial. Regardless of the brand of EAI used, providers should instruct patients to firmly grasp the device and to continually depress the EAI into the thigh after activation occurs. This compression might also help displace subcutaneous fat and reduce the distance to muscle in some patients, potentially increasing the likelihood of intramuscular administration of epinephrine.  

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Ryan C. Jacobsen, MD*  
Trent M. Guess, PhD*  
A. Wesley Burks, MD*

From *the Department of Emergency Medicine at Truman Medical Center, University of Missouri–Kansas City School of Medicine, Division of Emergency Medical Services at Children’s Mercy Hospitals and Clinics, Kansas City, Mo; †the Department of Mechanical Engineering, University of Missouri–Kansas City, Kansas City, Mo; and ‡the Division of Pediatric Allergy and Immunology, Duke University Medical Center, Durham, NC. E-mail: ryan.jacobsen@tmcmd.org.

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REFERENCES


positive SPT response (>1 mm) in the immunization clinic and was currently avoiding the food in question. A recent history was defined as less than 1 month before the clinic food challenge for egg (because egg allergy can resolve rapidly in infancy) or 2 months for peanut and sesame. Only 11 infants were excluded from egg challenge and 5 from peanut challenge based on these criteria (<2% of sensitized infants were excluded). No infants were excluded from sesame challenge. Food challenge involved gradually increasing doses on day 1 in the hospital and continued ingestion of the maximum day 1 dose (1 teaspoon of peanut butter or tahini paste or 1 whole raw egg white) on days 2 through 7.

HealthNuts standardized cessation criteria for a positive OFC result were any of the following signs occurring within 2 hours of ingestion:

- 3 or more concurrent noncontact urticaria persisting for at least 5 minutes;
- perioral or periorbital angioedema;
- vomiting (excluding gag reflex); and
- evidence of circulatory or respiratory compromise (anaphylaxis7; eg, persistent cough, wheeze, change in voice, stridor, difficulty breathing, and collapse).

The food challenge result was also considered positive if any of the above reactions occurred within 2 hours of ingestion of the food on days 2 to 7 of the challenge at home.

Allergic reactions meeting the HealthNuts food challenge criteria occurred in 121 (33%) of 370 peanut challenges, 385 (65%) of 594 raw egg challenges, and 29 (30%) of 97 sesame challenges. Of the 130 subjects with raw egg allergy who completed a challenge to baked egg, 84% tolerated an egg-containing muffin.

Fig 1 shows the occurrence and overlap of each of the different signs included in the HealthNuts cessation criteria for each food allergen for those infants who reacted on day 1 during the in-hospital challenge. Anaphylaxis occurred less often in subjects with positive egg challenge results (1.6%) compared with both peanut (4.3%, \( P = .09 \)) and sesame (6.3%, \( P = .07 \)) challenges. Of the 13 episodes of anaphylaxis, all were treated with intramuscular adrenaline, and 9 of these subjects also received albuterol (Ventolin; GlaxoSmithKline, London, United Kingdom). No biphasic reactions were observed.

Overall, 1.6% of the infants who underwent OFCs did not react on day 1 of the challenge but subsequently had symptoms meeting the criteria for a positive OFC result on days 2 or 3 of the challenge at home: 3.6% for raw egg challenges, 1.3% for peanut challenges, and 0% for sesame and baked egg challenges. None of the reactions occurring at home required treatment with adrenaline.

Transient urticaria and cases with only 1-2 urticarial wheals were common during challenges in infants who did not have any other signs of a positive reaction, occurring as the only sign of a reaction in 16% of peanut challenges, 20% of sesame challenges, and 29% of egg challenges. Less than 1% of infants with no urticaria during food challenges had a reaction meeting the HealthNuts criteria on continuing the challenge at home. In comparison, 10.6% and 5.0% of infants with some urticaria on day 1 (not meeting the HealthNuts criteria for a positive challenge result) had a reaction at home to egg and peanut, respectively (Table I).

We have reported the largest series of OFCs ever undertaken in a single age group (1-year-old infants). We found that our predefined challenge criteria could be applied safely in 12-month-old infants with a low prevalence of anaphylaxis during challenge and no episodes of anaphylaxis occurring in those continuing the challenge at home, despite challenges being performed in all children with a detectable SPT wheal response irrespective of wheal size or a previous history of less than recent reaction. Furthermore, few of those (<2%) who completed day
1 of the challenge without a reaction subsequently had immediate reactions on days 2 to 7 of the challenge at home.

Although we found that infants with transient urticaria (insufficient to meet our cessation criteria on day 1) were more likely to have positive challenge criteria on subsequent days of the challenge than those with no transient urticaria, decreasing the threshold criteria to include transient urticaria would increase the false-positive rate of food challenges significantly.

Although our criteria appear appropriate for 1-year-old patients, alternate criteria might be required for older children, and further studies are required to address this.

Development of a standardized set of criteria to define a positive challenge result has the potential not just to inform clinical practice but also to allow direct comparison across studies of prevalence and risk factors for the development of food allergy, including genotype/phenotype correlations. Such criteria will also enable direct comparison of the effectiveness of novel therapeutics, such as oral immunotherapy and peptide vaccines, that are currently in development. We have shown that our clearly defined inclusion/exclusion and predetermined cessation criteria can be safely applied to OFCs in infants. Development of challenge cessation criteria that can be applied across different age groups is urgently required to improve food challenge standardization.

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Jennifer J. Koplin, PhD, Mimi L. K. Tang, MMBS, PhD, FRACP, FRCPA, FAAAP, Pamela E. Martin, BBiomedSc (Hons), Nicholas J. Osborne, PhD, Adrian J. Lowe, PhD, Anne-Louise Ponsonby, MMBS, PhD, FAFPHM, FRACP, Marnie N. Robinson, MMBS, FRACP, Dean Tey, MMBS, FRACP, Leone Thielle, RN, RM, MNSw, David J. Hill, MMBS, FRACP, Lyle C. Gurrin, PhD, Melissa Wake, MMBS, MD, FRACP, for the HealthNuts investigators

From the Murdoch Childrens Research Institute; the Department of Paediatrics, University of Melbourne; the Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, University of Melbourne; the Centre for Community Child Health, Royal Children's Hospital; the Department of Allergy and Immunology, Royal Children’s Hospital, Parkville, Victoria, Australia, and the European Centre for Environment and Human Health, Peninsula College of Medicine and Dentistry, University of Exeter, Truro, United Kingdom. E-mail: katie.allen@rch.org.au.

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REFERENCES