

Getting to the Root of the Food Allergy “Epidemic”



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Over the past 3 decades, the increase in food allergy, as measured by hospitalizations and self-report, can only be described as explosive. For example, in one survey, peanut allergy more than tripled between 1997 and 2008,¹ whereas food allergy–related emergency visits nearly tripled in a 4-year period in a U.S. study,² and hospitalizations nearly doubled over 16 years in Australia³ and quintupled in the UK over a 14-year period.⁴ Is such an increase in a noninfectious disease biologically plausible, or must it be due to changes in recognition?

This question is critically important because if food allergy prevalence has indeed increased so quickly, it is essential that we find the cause and intervene. The fact that even now we are still not sure whether increases are due to changes in recognition or other environmental influences is due to the inherent difficulty in determining food allergy prevalence in populations. Definitive classification of food allergy requires oral food challenge, which is difficult to perform on a population level. The alternative, self-reporting, is notoriously imperfect.

Sensitization to foods, although not a perfect surrogate for clinical food allergy, is a possible objective alternative that can be measured on a population level. Although many more people are sensitized than clinically allergic, the presence of food-specific IgE, whether measured in blood or by skin prick test, is a prerequisite for IgE-mediated food allergy. Trends in sensitization should correlate with those of clinical food allergy. Yet, very few studies of trends in sensitization levels have been performed. Our group recently compared food-specific IgE among children in a large nationally representative survey, the National Health and Nutrition Examination Survey (NHANES), from 1988–1994 to 2005–2006 and found no increases in milk, egg, or peanut IgE sensitization despite large apparent changes in food allergy prevalence in the United States over the same period.⁵

In this issue of *JACI-In Practice*, Peters et al⁶ further explore this question by comparing rates of sensitization between 2 cohorts recruited in the same area of Australia and born in 1991–1994 and

2006–2010. The earlier cohort, the Melbourne Atopy Cohort Study, was a high-risk cohort recruited from allergic families, and the second cohort was the population-based HealthNuts cohort. Because of these differences in underlying risk factors, the authors employed statistical methods to create adjusted prevalence in the HealthNuts study, essentially creating 2 high-risk cohorts that could be compared. Peters et al found no differences in overall or high-level food sensitization between the 2 groups. Because the authors focused on high-risk infants, they cannot exclude the possibility that changes in lower risk children or in the composition of the high-risk group could still be compatible with changes in sensitization in the population overall.

When combined with data from NHANES, and data from a series of birth cohorts in the Isle of Wight from 1989 and 2001 that similarly did not show changes in peanut allergy prevalence over time,⁷ it is reasonable to conclude that sensitization has not increased substantially over the period of time when perceived and diagnosed food allergy has exploded. If this is true, then there are 2 possible explanations that are not mutually exclusive: (1) the apparent increase in food allergy is due to changes in recognition or (2) there has been some change in the relationship between sensitization and clinical allergy over time.

There is no question that awareness of food allergy has increased over the past several decades. Laws mandating labeling, educational initiatives, and prevention campaigns have all contributed to a growing awareness of food allergy among patients and providers. Not only will increased awareness lead more people to attribute many symptoms to food allergy without seeking confirmation, but it is also likely to lead to the increased use of IgE testing, with inevitable false-positive results.

In addition, we may now be increasingly recognizing mild, and potentially transient, yet real, reactions to foods and attributing these symptoms to food allergy. Recent studies hint that comprehensive screening and challenge finds many children who have true food allergy that might never be recognized. For example, HealthNuts, one of the very few studies where young children were comprehensively screened for food allergy, found a very high rate of challenge-proved food allergy; 10.4% were allergic to egg, peanut, or sesame.⁸ Recognition of milder food allergy will increase the apparent incidence of food allergy, and the act of recognition itself may alter the natural history of the disease and may lead to real increases in the prevalence of this condition. This is because identification of food allergy typically leads to implementation of avoidance diets instead of re-exposure. With avoidance, immunologic regulatory mechanisms may be lost, and the likelihood of clinically relevant and persistent disease may increase. Although increased recognition of potentially transient food allergy may change the rate of food allergy, it is unlikely to change the rate of sensitization, because sensitization is present even in these potentially transient cases.

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Delayed introduction of foods may similarly increase the rate of clinical food allergy while leaving the rate of sensitization largely unchanged. In the Learning Early About Peanut (LEAP) study where infants were randomized to early or delayed peanut introduction, rates of IgE sensitization were unchanged between the groups, despite the nearly 90% reduction in peanut allergy with early introduction.⁹ New guidelines to introduce allergenic foods earlier will hopefully reduce the rate of clinically significant food allergy, and may reverse trends seen over the past few decades. However, paradoxically, strategies to promote early introduction could lead to more identification of food allergy, including sub-clinical food allergy, if screening becomes more widespread.

It is possible that other factors, such as microbial exposure and dietary composition, may also modify the relationship between food sensitization and clinical disease. As much of the epidemiologic work on factors contributing to food allergy has focused on sensitization, more research needs to be conducted to understand those environmental exposures that may lead to, or away from, the clinical expression of this sensitization.

We still have too little data about trends in food sensitization over time, but the limited information we have, which now includes Peters et al's work reported in this issue, suggests that increased self-report of and health care utilization for food allergy has not been accompanied by commensurate increases in sensitization. It is essential that we understand why this is the case.

REFERENCES

1. Sicherer SH, Munoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *J Allergy Clin Immunol* 2010;125:1322-6.
2. Dyer AA, Lau CH, Smith TL, Smith BM, Gupta RS. Pediatric emergency department visits and hospitalizations due to food-induced anaphylaxis in Illinois. *Ann Allergy Asthma Immunol* 2015;115:56-62.
3. Mullins RJ, Wainstein BK, Barnes EH, Liew WK, Campbell DE. Increases in anaphylaxis fatalities in Australia from 1997 to 2013. *Clin Exp Allergy* 2016;46:1099-110.
4. Turner PJ, Gowland MH, Sharma V, Ierodiakonou D, Harper N, Garcez T, et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: an analysis of United Kingdom national anaphylaxis data, 1992-2012. *J Allergy Clin Immunol* 2015;135:956-963.e1.
5. McGowan EC, Peng RD, Salo PM, Zeldin DC, Keet CA. Changes in food-specific IgE over time in the National Health and Nutrition Examination Survey (NHANES). *J Allergy Clin Immunol Pract* 2016;4:713-20.
6. Peters RL, Koplin JJ, Allen KJ, Lowe AJ, Lodge CJ, Tang MLK, et al. The prevalence of food sensitization appears not to have changed between 2 Melbourne cohorts of high-risk infants recruited 15 years apart. *J Allergy Clin Immunol Pract* 2018;6:440-8.
7. Venter C, Maslin K, Patil V, Kurukulaaratchy R, Grundy J, Glasbey G, et al. The prevalence, natural history and time trends of peanut allergy over the first 10 years of life in two cohorts born in the same geographical location 12 years apart. *Pediatr Allergy Immunol* 2016;27:804-11.
8. Osborne NJ, Koplin JJ, Martin PE, Gurrin LC, Lowe AJ, Matheson MC, et al. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. *J Allergy Clin Immunol* 2011;127:668-676.e1-2.
9. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med* 2015;372:803-13.

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