

Peanut allergy: Overestimated in epidemiology or underdiagnosed in primary care?

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Key words: Peanut, peanut allergy, food allergy, epidemiology

Peanut allergy is one of the most common and severe food allergies and is usually lifelong.¹ Recent systematic reviews of the literature on the prevalence of food allergies have reported considerable heterogeneity between different studies^{2,3} and confirmed that the prevalence estimates based on self-reported symptoms tend to be higher than those based on objective assessments.³ In this issue of the Journal, Kotz and Sheikh⁴ report the data on incidence, prevalence and trends of diagnosis of peanut allergy recorded by primary care physicians (general practitioners) in England between 2001 and 2005. The authors used a large health database in which they interrogated information on almost 3 million patients registered with 422 general practices.⁴ The results add to the debate on what is the true prevalence of peanut allergy and raise important questions on time trends and risk factors. An estimated 25,700 people were found to have a recorded diagnosis of peanut allergy in England.⁴ The results suggest that the crude lifetime prevalence rate of general practitioner-recorded diagnosis of peanut allergy was 0.049%, with the highest rates found in boys 5 to 9 years old (0.25%). The observed prevalence rates are markedly lower than the estimates derived from other reports from England. In the most recent report, we confirmed peanut allergy by using oral peanut challenge and estimated the prevalence to be ~2% in school-age children.⁵ Similarly, studies from the Isle of Wight,⁶ London,⁷ and Southampton/Manchester⁸ estimated the prevalence of peanut allergy to be >10-fold higher than that reported by Kotz and Sheikh.⁴

How can we explain such marked differences in the estimates of prevalence of peanut allergy? Is this study⁴ underestimating the true prevalence of peanut allergy, or have the methods used in previous studies resulted in an overestimation? It is well recognized that it is difficult to compare the results of studies that have used different methodologies. Kotz and Sheikh⁴ correctly point out that most of the estimates to date have been based on data from cross-sectional surveys.⁶⁻⁸ Although such studies allow more detailed assessment and relatively accurate diagnosis, selection bias consequent to increased proportion of participants with peanut

allergy taking part in these surveys may result in overestimates of prevalence (eg, subjects without food allergy may be less likely to respond to a questionnaire than those suspecting that they may have food allergy). Furthermore, the inconsistency in diagnostic criteria⁹ and the wide CIs around prevalence estimates consequent to relatively small sample sizes are among factors that might have contributed to overestimation of the prevalence of peanut allergy. Despite these limitations, a recent meta-analysis reported little heterogeneity between studies that used objective measures (peanut sensitization or food challenge) in children ages 0 to 4 years and 5 to 16 years, with the estimates of prevalence of peanut allergy based on oral challenge ranging from 0.2% to 1.6% in different countries.² In several subsequent studies that used objective outcomes, the estimates of prevalence of peanut allergy appeared remarkably similar.^{5,10}

In the study by Kotz and Sheikh,⁴ the definition of peanut allergy was based on a computer-recorded diagnosis in the electronic health records from primary care. These data were routinely collected by primary care physicians and may not be an accurate indicator of true peanut allergy. The authors point out that this may substantially underestimate the prevalence of peanut allergy but argue that the large number of participants allows a more reliable estimation of frequency measures than previous studies involving smaller samples.⁴ There is no doubt that the large sample size resulted in small CIs around the estimate of frequency of the main outcome in the studied population⁴; however, the question remains whether the definition of main outcome measure accurately reflected clinical allergy to peanuts. Thus, bigger sample size might not necessarily result in a better estimate of the true prevalence of peanut allergy (or at least, a very large sample size alone might not be good enough, because the phenotypic precision might be lost in a study of this size). Taking methodologic considerations into account, the authors assume that the true estimate of peanut allergy is likely to lie somewhere between the estimates provided in this and previous studies.⁴

We have recently attempted to overcome methodologic problems by investigating prevalence of peanut allergy in a population-based birth cohort representative of the general population, with a high follow-up rate (>90%). By corroborating history with detailed objective assessment (skin tests, specific IgE, and oral peanut challenge), we estimated the prevalence of peanut allergy among 8-year-old children to be 1.9% (95% CI, 1.3% to 3.0%). Of note, this estimate is similar to other data from the United Kingdom,⁶⁻⁸ the United States,¹¹ Canada,¹⁰ and Australia,¹² suggesting that true prevalence of peanut allergy in school-age children in England may be closer to 2% than 0.2%.

Taken together, the result of previous studies⁵⁻⁸ and the report in this issue of the Journal⁴ suggest a worrying possibility that a considerable proportion of children with peanut allergy are not diagnosed (and appropriately treated) by their primary care physicians. This alarming suggestion underpins the urgent need to

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Disclosure of potential conflict of interest: A. Custovic receives research support from the Medical Research Council and the Moulton Charitable Trust. N. Nicolaou has declared that he has no conflict of interest.

Received for publication January 4, 2011; accepted for publication January 4, 2011.

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J Allergy Clin Immunol 2011;127:631-2.

0091-6749/\$36.00

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doi:10.1016/j.jaci.2011.01.026

tackle this problem. Our current knowledge on the epidemiology of food allergies resembles that of respiratory allergies before the conduct of large standardized international studies (the International Study of Asthma and Allergies in Childhood and the European Community Respiratory Health Survey). The pressing need to address this issue is further emphasized by evidence suggesting that the prevalence of peanut allergy may be increasing. In the United States, Sicherer et al¹¹ demonstrated in 3 nationwide telephone surveys that the prevalence of self-reported peanut allergy in children in 2008 was 1.4%, compared with 0.8% in 2002 and 0.4% in 1997. In the United Kingdom, Venter et al⁶ reported rates of peanut allergy of 0.5%, 1.4%, and 1.2% in 3 cohorts children 3 to 5 years old born in 1989, from 1994 to 1996, and from 2001 to 2002 in the same geographic area. Kotz and Sheikh⁴ report no recent increase in the incidence of peanut allergy for the period 2001 to 2005, although the prevalence rate almost doubled from 0.024% in 2001 to 0.051% in 2005.⁴ On the basis of these data, the prevalence appears to have increased in 1990s and seems to have stabilized more recently. Unfortunately, the data to provide accurate estimates on time trends of peanut allergy are lacking, and we have to fill this knowledge gap as a matter of urgency.

Kotz and Sheikh⁴ suggest that one way to overcome problems arising from methodologic issues would be to carry out large-scale representative national birth cohort studies, but they argue that the costs and logistics of such projects are likely to prove prohibitive.⁴ One such effort, which aims to characterize the patterns and prevalence of food allergies across Europe, is already under way: EuroPrevall is a multidisciplinary research project funded by the European Union with a budget of over €14 million.¹³ As a part of the project, a multicenter birth cohort study recruited more than 12,000 newborns in 9 European countries between 2005 and 2009,¹³ and all children with suspected food allergy were evaluated, including double-blind placebo-controlled food challenge tests. It would be important for similar endeavors using standardized methodology and accurate phenotyping to follow across the United States, because an increasing body of evidence suggests that peanut allergy represents a significant health concern for the country.¹¹ This is indirectly confirmed in a recent report from the European Community Respiratory Health Survey on the prevalence of sensitization to foods in a multicountry sample of young adults from Western Europe, the United States, and Australia, reporting that prevalence of sensitization to peanut was highest in the US center in Portland, Ore (9.3%).¹⁴

To facilitate future studies, it would be useful to develop simple tests that discriminate subjects with peanut allergy from peanut-tolerant subjects without the need to perform oral peanut

challenge. We have identified IgE to peanut component Ara h 2 as a predictor of peanut allergy among schoolchildren in England.^{5,15} If similar markers could be identified and validated in other populations, age groups, and geographic areas, then big multinational studies to provide accurate data on epidemiology and time trends of peanut allergy would be easier to conduct.

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