Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy

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Background: Despite guidelines recommending avoidance of peanuts during infancy in the United Kingdom (UK), Australia, and, until recently, North America, peanut allergy (PA) continues to increase in these countries.

Objective: We sought to determine the prevalence of PA among Israeli and UK Jewish children and evaluate the relationship of PA to infant and maternal peanut consumption.

Methods: A clinically validated questionnaire determined the prevalence of PA among Jewish schoolchildren (5171 in the UK and 5615 in Israel). A second validated questionnaire assessed peanut consumption and weaning in Jewish infants (77 in the UK and 99 in Israel).

Results: The prevalence of PA in the UK was 1.85%, and the prevalence in Israel was 0.17% ($P < .001$). Despite accounting for atopy, the adjusted risk ratio for PA between countries was 9.8 (95% CI, 3.1-30.5) in primary school children. Peanut is introduced earlier and is eaten more frequently and in larger quantities in Israel than in the UK. The median monthly consumption of peanut in Israeli infants aged 8 to 14 months is 7.1 g of peanut protein, and it is 0 g in the UK ($P < .001$). The median number of times peanut is eaten per month was 8 in Israel and 0 in the UK ($P < .0001$).

Conclusions: We demonstrate that Jewish children in the UK have a prevalence of PA that is 10-fold higher than that of Jewish children in Israel. This difference is not accounted for by differences in atopy, social class, genetic background, or peanut allergenicity. Israeli infants consume peanut in high quantities in the first year of life, whereas UK infants avoid peanuts. These findings raise the question of whether early introduction of peanut during infancy, rather than avoidance, will prevent the development of PA. (J Allergy Clin Immunol 2008;122:984-91.)

Key words: *Allergy, children, food allergy, peanut allergy, prevalence, allergy prevention, oral tolerance, weaning, peanut consumption*

The prevalence of peanut allergy (PA) in children in the United Kingdom (UK) and North America has doubled in 10 years and approximates 1.8% and 1.2%, respectively.[1,2] PA presents during early childhood, is infrequently outgrown, and can cause anaphylaxis.[3-7] Dietary avoidance of peanut during pregnancy, breastfeeding, and early life has been recommended in the UK and Australia and, until recently, also in the United States.[8-11] Studies eliminating food allergens during pregnancy, lactation, and infancy have consistently failed to prevent IgE-mediated food allergy.[12-14]

There are 2 hypothetical explanations for the failure of these studies. First, sensitization does not occur through oral exposure but through other routes. Second, early oral exposure might be required to induce tolerance.[15]

Allergic sensitization can occur through the skin. The risk of food allergies increases with the severity of eczema in infancy.[16,17] Moreover, application of topical preparations containing peanut oil on infants with eczema was associated with a high risk of PA (odds ratio, 6.8).[16] However, not all countries with an increased prevalence of PA use such preparations. In those countries cutaneous exposure to other peanut products could lead to

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Abbreviations used
FAQ: Food Allergy Questionnaire
FFQ: Food Frequency Questionnaire
PA: Peanut Allergy
RR: Relative risk
SA: Sesame allergy
TNA: Tree nut allergy
UK: United Kingdom

sensitization. Environmental exposure to peanut is 10-fold higher during the first year of life in infants with PA compared with that seen in atopic infants without PA.[18] Indeed, peanut allergen is detectable in significant quantities in saliva and on hands after exposure to peanut products.[19,20] Other foods (egg, milk, and fish) have also been detected in house dust.[21,22]

There is also evidence to support the second explanation. Oral tolerance is well recognized in murine models. Numerous studies demonstrate that early high-dose oral exposure confers both immunologic and clinical tolerance to food allergens. A single oral dose of allergen (β-lactoglobulin, ovalbumin, or peanut) is sufficient to achieve tolerance and prevent subsequent allergic sensitization.[23-25] In human subjects cutaneous exposure to nickel during childhood leads to sensitization and nickel allergy, but oral exposure to nickel through orthodontic braces before ear piercing protects against nickel allergy.[26,27] Similarly, subjects exposed to pancreatic extract by means of inhalation or contact have IgE-mediated allergic reactions, whereas subjects exposed orally do not.[28] Furthermore, in a large observational cohort of children, Poole et al[29] demonstrate that delaying the initial exposure to cereal grains until after 6 months might increase the risk of IgE-mediated wheat allergy.

Importantly, in the Middle East, Southeast Asia, and Africa, where peanut is consumed in high amounts during infancy, PA is reportedly rare.[30-32] However, different rates of food allergies in the UK compared with those in Asia and Africa might be due to genetic differences or the generally lower rates of atopic disease in developing countries, possibly resulting from differences in microbial exposure.[33,34]

We therefore compared Jewish children (who have a similar genetic background) in the UK and Israel. The UK and Israel are industrialized countries with high levels of atopy.[35] The aim of this study was to determine the PA prevalence among Israeli and UK Jewish children and evaluate the relationship of PA to infant and maternal peanut consumption.

METHODS

Questionnaires

Two validated questionnaires were used. Questionnaires recorded categorical answers only.

The Food Allergy Questionnaire. The Food Allergy Questionnaire (FAQ) was distributed in schools in the UK and Israel. In the UK eligible Jewish schools in the greater London region were identified from the UK Jewish Board of Deputies. In Israel schools were identified by the Israel Ministry of Education and were located within the Mehoz Merkaz Region of Tel Aviv. This region was selected because it was thought to represent comparable residential environments (ie, both urban and suburban) to those found in North London. Schools with more than 100 pupils were targeted. It asked about allergies to cow's milk, hen's egg, sesame, peanut, and tree nuts (including the nature and timing of symptoms after exposure to these foods); asthma; hay fever; and eczema. Parental occupation was used as a surrogate for social class (by using the Standard Occupational Classification System, UK Office of National Statistics, 2000). The questionnaire was completed by high school pupils and by parents on behalf of primary school pupils. Repeat sampling was performed by means of postal reminders or telephone. The FAQ was validated against rigorous clinically confirmed diagnostic criteria for the diagnosis of allergy or tolerance to peanut.

The Food Frequency Questionnaire. The Food Frequency Questionnaire (FFQ) is a validated consumption questionnaire that was distributed to mothers of Jewish infants aged 4 to 24 months.[36] The infants and mothers were chosen by consecutive registration (Tipat Halav clinics in Israel and general practitioner clinics in the UK). An information sheet was handed out to all parents attending the clinic. We explained in the information sheet that we wanted dietary history from Jewish children. The information was obtained by researchers (GZH in Israel and HF in the UK) from mothers in the waiting room. The FFQ made a detailed determination of peanut, sesame, and other solid-food consumption during the child's first year and through the mother (during pregnancy and lactation). The FFQ included a comprehensive list of peanut products available in both countries. Additional questions concerned breast-feeding, infant formula, weaning, and introduction of other solid foods. Consumption was compared between countries for infants aged 8 to 14 months. In both countries infants were identified in nurseries and well-baby clinics. Questionnaires were completed over the period March 2004 to 2005.

Definition of PA and other allergic disease

By using the FAQ, individual food allergies were defined as a history of at least 1 of the following within 2 hours of eating the food: itchy rash, wheezing, vomiting, diarrhea, and swelling.

The following questionnaire-based definitions for allergic disease were used: (1) physician-diagnosed asthma and use of short-acting β_2-agonist and use of an inhaled corticosteroid; (2) physician-diagnosed eczema and use of corticosteroid applications or use of topical calcineurin inhibitor preparations; and (3) physician-diagnosed hay fever and use of antihistamines or an intranasal corticosteroid.

Validation of the FAQ-based diagnosis of PA

All children with a questionnaire-based diagnosis of PA were invited for allergy testing. PA was confirmed if allergy test results (skin prick tests, specific IgE measurements, or both) were greater than 95% positive predictive values[37-39] or if children had a positive oral peanut challenge result.[37]

Comparison of the protein content and allergenicity of peanut-containing foods

Total protein content of the foods was determined by using LECO nitrogen analysis (LECO Corp, St Joseph, Mich). Anti-peanut ELISA assays were used to determine the percentage of peanut protein in each product. The products were all normalized according to peanut protein content and subjected to SDS-PAGE, Western blotting, and slot-blot analysis with anti-peanut and anti-Ara h 1, 2, and 3 antibodies and pooled sera from individuals with PA.

Statistical analysis

Statistical Analysis was performed with Stata statistical software (release 8.0; StataCorp, College Station, Tex). For food allergy comparison, formal comparisons were made for all children and for primary school children. Risk ratios and 95% CIs of food allergy in the UK compared with those in Israel were calculated and stratified on confounding factors by using Mantel-Haenszel procedures. We further investigated the effects of socioeconomic class on food allergy in a nested case-control study. Kaplan-Meier estimates of weaning patterns and the age at introduction of particular food types in the 2 countries were calculated and compared by using the log-rank test. Peanut and