

Specific immunoglobulin E to peanut, hazelnut and brazil nut in 731 patients: similar patterns found at all ages

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Summary

Background Previous studies have reported reactions to an increasing range of nuts as patients with nut allergy grow older. Most patients with symptoms suggesting nut allergy have specific IgE to more than one nut. Furthermore, fatal reactions have followed eating nuts different from any causing the deceased's previous reactions.

Objective To explore the pattern of specific IgE to three distantly related nuts in patients of all ages with nut allergy.

Methods This study includes all patients referred to our laboratory for nut allergy testing from January 1994 to August 1998 who were tested for peanut, hazelnut and brazil nut, and had specific IgE to at least one of these nuts. All tests were performed using the Pharmacia Unicap system.

Results Seven hundred and thirty-one patients (age 7 months to 65 years, median 6.6 years) had specific IgE > 0.35 kU_A/L to at least one of these three nuts: 282 had IgE to one nut, 130 to two nuts, and 319 to all three nuts. When analysed by gender and age quartile, very similar patterns were found in all subgroups though significant age trends and age interactions were found for IgE to individual nuts and combinations of nuts.

Conclusions The probability of a patient with nut allergy having specific IgE to a particular combination of peanut, hazelnut and brazil nut is similar, whatever their age or sex. The apparent increase in multiple nut reactivity with increasing age may therefore be due to exposure of previously unchallenged sensitivity. The frequency of multiple-nut specificity is sufficiently high that patients should always be tested for allergy to a range on nuts if they have a history of reacting to any nut.

Keywords: anaphylaxis, atopy, immunoglobulin E, peanut, tree nut

Clinical and Experimental Allergy, Vol. 29, pp. 1256–1259. Submitted 27 August 1998; revised 23 November 1998; accepted 18 January 1999.

Introduction

The need to investigate patients for possible multiple-nut allergy was highlighted by the histories of patients dying from nut anaphylaxis. In some cases, fatal reactions have been caused by a species of nut different from any causing the deceased's previous reactions [1]. We have therefore routinely tested all patients with a history of acute allergic reactions of nuts to a range of nuts, including peanut, almond, hazelnut, walnut, brazil nut, pistachio and cashew.

Peanuts are in the family Leguminosae (Fabaceae) and so not regarded as nuts by some [2]. However, almonds are Rosaceae, pistachio and cashew are Anacardiaceae, macadamia nuts are Protaceae, walnuts are Juglandaceae, hazelnuts are Corylaceae and brazil nuts are Lecithidaceae. In as far as the term 'nut' has a strict botanical meaning (a dry indehiscent fruit, the product of more than one carpel [3]), it describes the structure of the fruit but not the relationship of plants bearing nuts. The relationship between the great variety of plant families is not completely defined and many different schemes have been proposed. Some classifications [4] hold that peanuts and almonds are related in the order Rosidae, hazelnuts, walnuts and Spanish chestnut in

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the order Hamamelididae, and brazil nuts are placed in the order Dileniidae.

There is little information about the pattern of sensitization to the different nut species [2,5]. We have chosen to analyse here one nut species commonly eaten in the UK from each of three orders – Rosidae (peanut), Hamamelididae (hazelnut) and Dileniidae (brazil nut) to explore the frequency and pattern of specific immunoglobulin (Ig) E to combinations of nut species.

Methods

Patients

The study was carried out in the Regional Immunology Service Laboratories, St Mary's Hospital, Manchester, between January 1994 and August 1998. Seven hundred and thirty-one consecutive patients with a history suggestive of nut allergy and a positive serum IgE to one of the three allergens (peanut, hazelnut and brazil nut) had their serum analysed for all three allergens. All tests have been performed using the Unicap system (Pharmacia, Uppsala, Sweden). Some patients had been tested more than once in that time; in every case, the most recent result was used for analysis. The age of the patients is taken as the age at the time of testing, not the time of their allergic reaction.

In analysing the results, three different cut-offs were used to identify a level of specific IgE to be regarded as positive: $>0.35 \text{ kU}_A/\text{L}$, $>3.5 \text{ kU}_A/\text{L}$ and $>17.5 \text{ kU}_A/\text{L}$ corresponding with grades 1, 3 and 4. Patients were then assigned to one of seven groups according to the combination of nut species against which they have positive IgE antibodies.

Statistical analysis

The distribution of ages of the subjects included in this study was found to be positively skewed and approximated very closely to log-normal. To enable the use of parametric statistical methods, the ages were converted to natural logarithms for analysis. Analyses of variance were used to estimate the individual and combined (statistical) influences of age, gender and allergen on IgE positivity. Age was analysed as a continuous variable, but was separated into quartiles to provide a simplified summary of the study findings.

Results

Venn diagrams of the specific IgE relationships in male and female subjects, and for the four age quartiles are presented in Figs 1 and 2. Statistical results for the three cut-off levels for specific IgE were as follows:

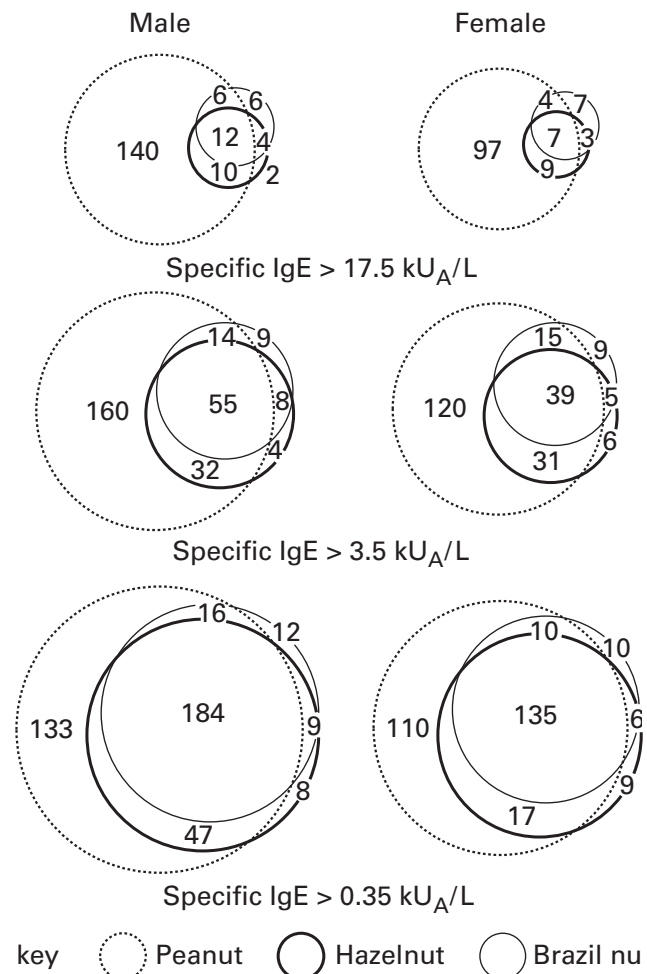


Fig. 1. Venn diagrams showing overlap between peanut, hazelnut and brazil nut specific IgE antibody activity in males ($n = 409$) and females ($n = 322$). The patterns of IgE specificity are similar for either gender. The areas of circles are proportional, and the areas of intersections approximately proportional, to the number of patients in each group.

Specific IgE $>0.35 \text{ kU}_A/\text{L}$

There was a borderline age trend for peanuts ($P = 0.067$) with higher incidence of peanut positive in young patients and an age interaction between hazelnuts and brazil nuts ($P = 0.002$) with more young patients being either positive for both or negative for both.

Specific IgE $>3.5 \text{ kU}_A/\text{L}$

There was an age trend for peanuts ($P = 0.025$) and an age interaction between hazelnut and brazil nut ($P = 0.019$), the trends being the same as the previous group.

be a cohort effect, reflecting an increasing incidence of peanut allergy in recent years as previously reported [4].

The presence of specific IgE antibodies measurable by the Pharmacia Unicap system does not necessarily mean that that nut will cause allergic symptoms. The population studied here had several examples of high levels not associated with acute allergic reactions, mostly in patients with eczema. We have identified patients who failed to react to one nut but on accidental exposure to another nut against which they had a lower level of specific IgE, did react, sometimes severely. Nor does absence of specific IgE preclude the possibility of nut allergy, though the proportion of patients with a history of probable nut allergy, negative specific IgE and positive skin prick tests (SPT) is low (1% for peanut, 4% for brazil nut, our unpublished findings). From a practical point of view, it is generally best to advise avoidance of all nuts if there is allergy to any, as one nut may commonly be substituted for another in preparation of food.

A recent study [6] suggested that resolution of nut allergy could be established by open challenge testing. The high frequency of sensitivity to multiple nuts, and impossibility of predicting the severity of reaction from specific IgE levels or skin prick tests, indicates that such challenge testing should include a range of nut species if the patient is to be confident that nut-sensitivity has truly been lost. If only one nut is tested, the patient should be warned of the possibility of reactions to other nuts.

In conclusion, the probability of a patient with nut allergy having specific IgE to a particular combination of peanut,

hazelnut and brazil nut is similar, whatever their age or sex. The apparent increase in multiple nut reactivity with increasing age may therefore be due to exposure of previously unchallenged sensitivity. The frequency of multiple-nut specificity is sufficiently high that patients should always be tested for allergy to a range of nuts if they have a history of reacting to any nut.

Acknowledgements

We would like to thank Janet Fairfield and other staff in the Regional Immunology Service Laboratories, St Mary's Hospital for measurement of the specific IgE levels.

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