

Clinical characteristics of peanut allergy

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Summary

Background Current clinical advice regarding peanut allergy is based on small series of patients.

Objective To determine, in a large group of peanut allergic subjects, the patterns of clinical severity, symptom progression and availability and use of rescue medications.

Methods Questionnaire study of 622 self-reported allergic subjects.

Results A total of 406 patients (66%) reported symptoms on contact with peanut. Only 121 (19%) had been knowingly exposed to peanut before the first documented reaction, implying a high frequency of occult sensitization. Severe symptoms were more common in adults. Abdominal symptoms were significantly associated with collapse. Fifty per cent reported reactions in the previous year. Only 82 (13%) had been admitted to hospital because of a reaction. Adrenaline was carried in some form by 65% though only 78 subjects (12.5%) had ever received injected adrenaline. Only 18/43 subjects (41%) who collapsed were given adrenaline. Skin-prick test weal size correlated weakly with severity but there were large overlaps between the groups. Peanut-specific IgE peaked in the teenage group, but did not correlate with severity.

Conclusions Peanut allergy is characterized by more severe symptoms than other food allergies and by high rates of symptoms on minimal contact. Skin-prick testing and peanut-specific IgE levels do not predict clinical severity. Avoidance of peanut is difficult. Many people suffering severe reactions are inadequately treated. Sufferers need education and training in the use of rescue medication.

Keywords: peanut allergy, symptom progression, severity, rescue medication

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Introduction

Increased medical awareness of peanut allergy in Britain over the last 3 or 4 years was generated by a burst of publicity regarding deaths due to peanut allergy in 1990 [1] and 1993 [2]. It has become clear that existing information regarding peanut allergy has been based on studies of small series of patients [3]. Advice based on these series may not reflect accurately some of the problems peanut allergies have in Britain. It is only recently that Ewan has published results of an audit of a year of her practice in Cambridge [2]. These are the first British data that have been gathered

prospectively. However, the numbers remain small with only 47 cases of peanut allergy.

Many peanut allergic people and particularly the parents of peanut allergic children, remain concerned about the lack of information regarding peanut allergy. They ask about, among other things, the nature of the allergy and its origins, the chances of remission [3], risks of repeated exposures, particularly to hidden peanut and to peanut oil, and the availability of rescue medication at home and especially at school.

In 1994 the University Department of Child Health in Southampton set up a study to investigate issues regarding peanut allergy in Britain. Data regarding family background, route of sensitization (via breast milk or *in utero*), age of onset of peanut allergy and the presence or absence of other atopic manifestations in the proband have been published elsewhere [4]. This report deals with questions

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regarding symptomatology, progression of severity of successive reactions and the use of rescue medication or attendance at hospital.

Methods

Details of the questionnaire with which these data were collected have been described elsewhere [4]. The questionnaire, sent to a total of 833 individuals, was validated in a group of 50 peanut allergic children whose parents answered the questions in a face to face interview with a doctor experienced in the diagnosis and treatment of allergic disorders. This subgroup, who were all skin-prick tested (SPT) with peanut, revealed a false positive rate for questionnaire-based diagnosis of peanut allergy in children of 14% [4]. Other subjects answered an identical postal questionnaire. A further subgroup of 69 adults who returned the questionnaire by post were later involved in a challenge study of peanut oil (in press). They were also challenged with peanut; 60 out of 69 subjects were proven by SPT and peanut challenge to be peanut allergic. This group revealed a 13% false positive rate for questionnaire-based diagnosis of peanut allergy in adults.

Reported reactions were considered mild if they involved urticaria, pruritus, moderate if facial swelling, throat tightness or breathing difficulty (other than wheeze) were reported and severe if subjects reported wheeze, cyanosis or collapse/faint. Overall severity was assigned on the basis of the most severe reaction reported.

Total IgE was measured using the Immucap system (Pharmacia, Milton Keynes, UK). The assays limits of detection were ≥ 2 to ≤ 2000 KU/mL. Peanut specific IgE

Table 1. Reported symptoms

Symptom	First reaction (%)	Most recent reaction (%)
Facial swelling	444 (72)	365 (60)
Rash	399 (65)	311 (51)
Itch	342 (55)	319 (52)
Wheeze	239 (38)	248 (40)
Vomiting	240 (38)	214 (35)
Breathing difficulty	229 (37)	236 (38)
Abdo pain/cramp	133 (21)	133 (21)
Cyanosis	88 (14)	54 (9)
Collapse/faint	42 (7)	46 (7)

was measured on serum samples of 346 individuals using the specific IgE Immucap system (Pharmacia) according to manufacturer's instructions. The detection rate for the peanut-specific IgE assay was ≥ 0.35 to ≤ 100 KU/mL.

McNemars χ^2 test with one degree of freedom was used to compare rates of categorical data in discordant pairs. Kruskal–Wallis one-way ANOVA was used to correlate non-parametric categorical data. Two-tailed *P*-values and 95% confidence intervals (CI) were used throughout the analysis.

Results

Some 622 valid replies were received [4]. Age and sex distributions of respondents are shown in Fig. 1. Only 121 (19%) of subjects reported having been exposed to peanut before the exposure that caused the first documented reaction. 569 (90%) of subjects reported reacting after eating less than one nut. 298 (50%) reacted to touching a peanut. 273 subjects (52% of subjects with more than one reaction to peanut) reported immediate symptoms on exposure to peanut; 467 (76%) reported reactions with 5 min; and 573 (93%) within 30 min. Only 15 subjects (3%) reported a delay of onset of symptoms of more than 1 h after the most recent exposure to peanut. Of these 15 slow reactors, eight had mild reactions, one had a moderately severe reaction and six had a severe reaction. The questionnaire may not have distinguished slowly evolving severe reactions that started with minor symptoms.

The symptoms reported on first and most recent reactions are shown in Table 1. Mild symptoms were more common in children and severe symptoms more common in adults (Kruskal–Wallis one-way ANOVA, $P = 0.0002$) see Fig. 2. The most severe symptoms, collapse and cyanosis, were reported by only 42 subjects (7%) on first exposure and 46 (7%) subjects on most recent reaction. Comparison of severity of first and most recent reactions is shown in

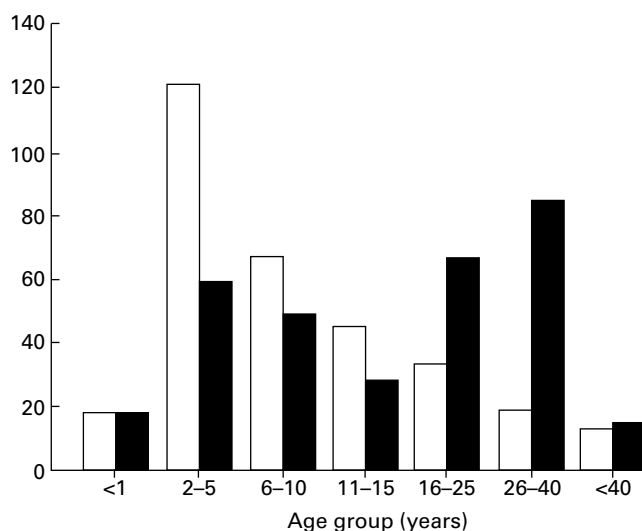


Fig. 1. Age and sex of 622 peanut allergic subjects (314 males). □, Male; ■, Female.

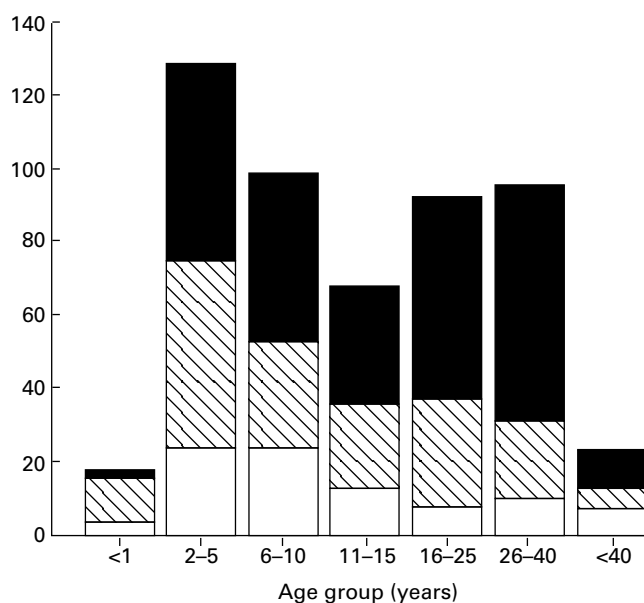


Fig. 2. Severity of reaction according to age category. ■, Severe; ▨, Moderate; □, Mild.

Table 2. Wheeze was the most common severe symptom, reported by $\approx 40\%$ of subjects on both first and last reaction. Subjects who reported a history of asthma were more likely to suffer severe reactions ($\chi^2 = 17.9$, $P = 0.00013$).

There was a significant association between reported abdominal pain and severe symptoms such as wheeze, cyanosis and collapse ($P < 0.001$). There was no association between abdominal symptoms and more minor symptoms such as itch or rash. Other severe symptoms correlated strongly with each other but less so with minor symptoms (see Table 3). The most severe symptoms (cyanosis and collapse) were never reported in the absence of other symptoms.

Excluding 85 subjects who had only one reaction to peanuts, 33 (6%) had an allergic reaction to peanuts in the previous month; 51 (9%) had not had a reaction to peanut for more than 5 years (see Table 4); 266 (50%) felt their

Table 2. Comparison of first and most recent reactions in 527 subjects

First reaction	Mild	Moderate	Severe	Total
Mild	44	29	34	107
Moderate	27	111	59	197
Severe	21	29	173	223
Total	92	169	266	527*

* Data missing on 10 subjects, 85 subjects one reaction only.

Table 3. Association of symptoms

	Throat	Wheeze	Cyanosis	Collapse
Throat	—	<0.0001*	<0.001*	0.001*
Wheeze	<0.001*	—	0.001*	<0.0001*
Cyanosis	<0.001*	<0.001*	—	<0.0001*
Collapse	<0.0001*	<0.0001*	<0.001*	—
Vomiting	0.0001*	0.04*	0.017*	0.16
Abdominal pain	<0.0001*	0.0001*	0.002*	<0.0001*
Rash	0.91	0.006*	0.04*	0.97
Itch	0.10	0.025*	0.11	0.31
Oedema	<0.0001*	<0.001*	<0.0001*	0.04*

* = $P < 0.05$.

reactions were of stable severity, and 201 (38%) felt they were suffering worse reactions on each exposure. Only 13 (2.5%) felt the reactions to peanut were successively improving. Exercise was felt to exacerbate reactions by 18 subjects (2.9%) and to ameliorate symptoms by five subjects (0.8%).

Some 232 (37%) had never attended hospital because of a reaction to peanuts and only 82 (35% of hospital attenders, 13% of entire group) had been admitted overnight. Only two subjects (0.3%) had ever been admitted to an intensive care unit. The presence of severe symptoms (wheeze, cyanosis or collapse) on most recent reaction correlated strongly with both hospital admission ($\chi^2 = 2.03$, $P < 0.01$, odds ratio [OR] 3.7) and the administration of injected adrenaline ($\chi^2 = 21.36$, $P < 0.0001$, OR 2.87); 78 subjects (15%) received or self-administered injected adrenaline to treat the most recent reaction. These subjects had varying combinations of minor and major symptoms. Adrenaline was administered to 60 of 247 subjects with wheeze (24%), 28 of 54 subjects with cyanosis (52%) and 18 of 43 (41%) of subjects with collapse. Of the 78 adrenaline injections administered, 68 (82%) were given within 1 h and 72 (92%) within 2 h.

The most common medications used to treat any reactions to peanut were antihistamines (359 subjects — 57%), followed by adrenaline injection (110—18%) and adrenaline inhaler (45—7.3%). Rescue medications carried by peanut allergic subjects are shown in Table 5.

Skin-prick testing was undertaken on 62 children [4], and 69 adults (Hourihane *et al.* in press). Mean weal diameter (mm) correlated with severity (Kruskal–Wallis one-way ANOVA, $P = 0.04$, Fig. 3) but there was substantial overlap between the groups. Total IgE was measured in 360 subjects and peanut-specific IgE in 346 subjects. Mean total IgE increased with age to 11 years and declined thereafter (Kruskal–Wallis one-way ANOVA, $P < 0.001$, Fig. 4a). Mean peanut-specific IgE, however, peaked in the older age group

Table 4. Time since last reaction to peanut

	≤5 years old (cumulative %)	≥6 years old (cumulative %)	Total cumulative (%)
< 1 month	4 (3)	29 (8)	33 (6)
1–2 months	6 (7)	20 (13)	26 (11)
3–5 months	26 (25)	46 (25)	72 (25)
6–12 months	63 (68)	68 (43)	131 (50)
1–5 years	47 (100)	162 (86)	209 (92)
> 5 years	–	51 (100)	51 (100)
Total	146	376	522*

* Excludes 85 with one reaction and 15 missing data.

of 12–16 year olds (Kruskal–Wallis one-way ANOVA, $P=0.008$, Fig. 5), but did not correlate with clinical severity (data not shown).

Discussion

Peanut allergy has become an issue that involves doctors, regulatory authorities, educational authorities and particularly the food and catering industries. In the past knowledge about peanut allergy has suffered from a relative lack of medical attention and scientifically collected data on adequately sized representative groups. With such a lack of information many misconceptions have persisted regarding peanut allergy, in much the same way as previous worries regarding bee and wasp sting anaphylaxis have been refuted by more comprehensive studies of larger groups of patients.

Our group of peanut allergic subjects is the largest ever collected. The false-positive rate (13%) for questionnaire-based acceptance of the diagnosis of peanut allergy determined in the two subgroups that were skin-prick tested is unlikely to have affected the results in such a large group, though the effects in smaller groups may be considerable. In fact the often atypical reactions reported by the adults who were challenge-negative to peanut may have actually

skewed figures such as speed of onset further from the norm for the cohort in general.

There is a predictable male preponderance in the younger age groups. The apparent female predominance in adults may be due to a selection bias, caused by the advertisement of the study in a university press release which received a lot of publicity in women's magazines. However, asthma has a similar age specific difference in gender ratios.

Our study shows that, despite a large proportion of affected individuals reacting to very small doses of peanut (such as can be absorbed on contact with intact skin or oral mucosa), half the group felt their reactions were stable and only a third felt reactions were worsening. The association between abdominal symptoms and both airway compromise and collapse is noteworthy. Abdominal pain is a symptom that is often overlooked, especially in the light of more dramatic, but much less significant cutaneous symptoms. Its

Table 5. Availability of rescue medication (adrenaline)

	Number	%
None	154	26
Inhaled adrenaline only	69	11
Injectable adrenaline only	279	46
Inhaled and injectable adrenaline	103	17
Total	605	100

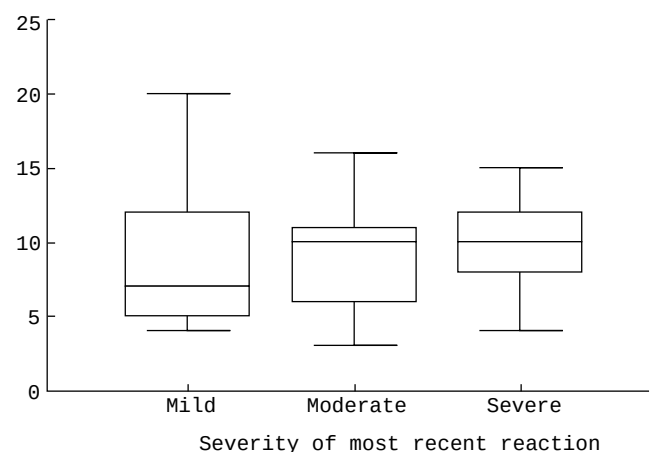


Fig. 3. Skin-prick test weal size vs severity of most recent reaction. Kruskal–Wallis 1-way ANOVA, $P = 0.04$.

association with severe symptoms warrants closer medical attention when evaluating subjects reacting to peanut.

Nearly 40% of subjects have wheeze even on their first reaction. Wheezing is a severe symptom and this finding is in keeping with findings of other groups that peanut allergy is probably the worst of the food allergies with which to be afflicted [5,6].

The increasing proportion of severe reactors with increasing age could be interpreted as showing either that severity increases with age (and, by extrapolation, with successive reactions) or that children with mild reactions grow out of the allergy, leaving severe reactors in childhood to remain severe reactors in adulthood.

The peak of peanut-specific IgE in the teen years is interesting because this is the age group in which fatal and near fatal reactions often occur. Parents and doctors have suggested to us that this may be due to teenage denial of the allergy and non-compliance with peanut avoidance and rescue medication regimens. Parents of teenagers who have died have also commented that previous reactions had not been severe. It may be speculated that previous reactions (before the peak of peanut-specific IgE) were less severe but the peak of peanut-specific IgE in the teen years made the subjects who died more vulnerable to a severe reaction. However, the lack of correlation between symptom severity and peanut specific IgE does not support this theory.

The typically rapid onset of reaction and typical clinical symptoms mean that people with unusual timing of symptoms, such as reactions that start more than 1 h after exposure to peanut, or symptoms which are more vague such as headache or lassitude, may actually be intolerant rather than allergic to peanut. This would certainly support our clinical impression on reviewing many of these patients in our clinical practice. It may be that up to 13% of adults who report peanut allergy are actually not allergic.

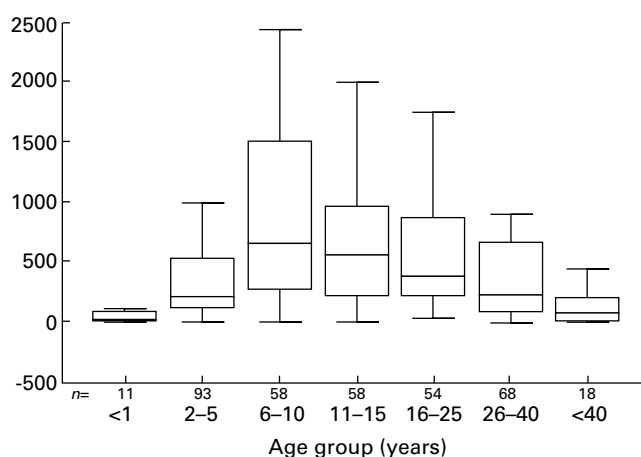


Fig. 4. Total IgE according to age category. Kruskal–Wallis 1-way ANOVA, $P < 0.0001$.

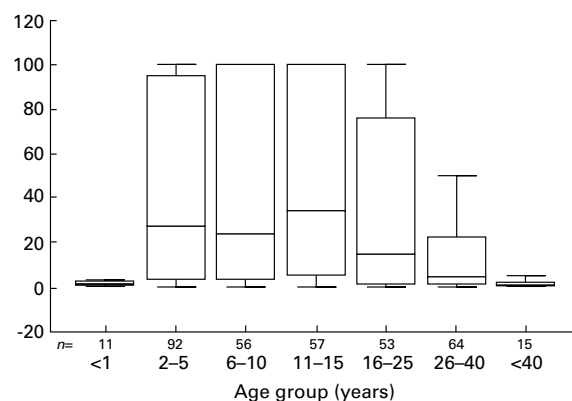


Fig. 5. Peanut-specific IgE according to age category. Kruskal–Wallis 1-way ANOVA, $P = 0.008$.

The high frequency of inadvertent exposure and reaction to peanuts supports the findings of other studies [3]. It is surprising that even in a well characterized group who have been aware of the recent focus on peanut allergy in Britain that reactions are so frequent with 6% having had a reaction in the previous month and 50% within the last year. It is however, reassuring that the phenomenon of exercise-induced anaphylaxis is unusual in this group with a severe food allergy.

Not all peanut allergics may be at risk of anaphylaxis [7]. The use of adrenaline appears to increase with increasing severity of reaction but alarming proportions of collapsed and cyanotic subjects did not receive adrenaline at all. It is clearly vital to raise awareness of the serious nature of peanut allergy and to ensure that sufferers are equipped with and trained in the use of adrenaline rescue therapy.

Sixty-five per cent of subjects in this study carry some form of adrenaline although the actual percentage who carry both inhaled and injected forms is rather lower. The fact that only 37% had ever attended hospital after a reaction emphasizes that the approach to peanut allergy must be community-based, ensuring the empowerment of sufferers, their families and responsible authorities to treat reactions appropriately. Medical evaluation of symptoms usually downgrades severity and the relative lack of hospital admissions despite the reported severity of reactions may reflect either over-reporting of symptoms by subjects or under-estimation of severity by attending medical staff.

This simple questionnaire survey of self-identified peanut allergics supports data generated by smaller studies and can form the basis for more accurate information to be given to peanut allergic individuals in Britain.

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