

General paediatricians and the case of resolving peanut allergy

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Children with peanut allergy are almost always advised to avoid nuts for life. There have been recent reports from academic centres that in some cases the allergy might resolve and thus these dietary restrictions can be lifted. To evaluate resolution of peanut allergy in a selected group of children in a general paediatric setting. Children 4–16 yr old with a clear history of an allergic reaction to peanuts who had not had any reaction in the previous 2 yr were eligible. Specific immunoglobulin E (IgE) or skin prick test (SPT) at the time of diagnosis was sought. A SPT and specific IgE was then done and if this was ≤ 8 mm and ≤ 17.5 kU[A]/l respectively, a double-blind placebo-controlled food challenge was undertaken. A negative challenge consisted of tolerance to a cumulative dose of 15.8 g peanuts followed by an open challenge. From the 82 case notes reviewed 54 children were eligible to participate. Twenty-nine agreed to participate and underwent SPT (29) and specific IgE (28). Of these children eight were eligible for food challenge. Four challenges were negative and four positive. Peanut allergy may resolve in approximately 15% of selected children attending an allergy clinic run by general paediatricians in a district general hospital. Food challenge constitutes the appropriate way of removing the burden that comes with a diagnosis of peanut allergy and enables dietary restriction to cease.

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Children diagnosed with peanut allergy (1) are advised to avoid nut-containing products and are often prescribed adrenaline. This dietary restriction is usually advised for life. A diagnosis of peanut allergy thus has major implications (2) including causing considerable patient and parental anxiety and problems with supervision at school or nursery (3). The initial diagnosis should be determined with great care because of its implications for the child and the family. Carrying adrenaline injections may also cause a personal and professional anxiety (4).

The widespread notion that peanut allergy is for life has recently been challenged in studies from academic centres with experience of allergy investigation and management (5–8). Therefore, review and confirmation or otherwise of the initial diagnosis is justified (9). This is important,

as after a negative food challenge dietary restriction and adrenaline carriage may be discontinued in most cases. General Paediatricians in the United Kingdom have often not had the training or resources to offer food challenges on a routine basis. It is, therefore, likely that some children diagnosed with peanut allergy in infancy may have grown out of their condition but have not been reviewed or challenged to investigate this. We sought to establish if resolution of peanut allergy could be identified in a general paediatric setting.

Methods

Children 4–16 yr old with a clear history of an allergic reaction to peanuts who had not had any reaction in the previous 2 yr were eligible. Specific

immunoglobulin E (IgE) or skin prick test (SPT) at the time of diagnosis was sought. They were identified from medical and dietetic records. Children were excluded if, on step 3 or higher of the British Thoracic Society (BTS) Guidelines (10) on management of asthma; life-threatening anaphylaxis to nuts at anytime previously; severe anaphylactic reaction to other antigens necessitating usage of adrenaline in the last 2 yr.

The Local Research and Ethics Committee approved the protocol. Written information about the study was sent to parents and informed consent obtained prior to participation. SPT (11–13) was carried out by nurses trained in SPT programme, using standard reagents (ALK Abello, Reading, UK). After supporting the child's arm, it was performed on the internal aspect of the forearm 5 cm above wrist and 3 cm below the elbow flexor. A numbered tape was applied to test site and drops of the allergens (peanut, walnut, hazelnut, almond and brazilnut) followed by negative and positive controls were placed at prescribed intervals. A sterile lancet, one for each allergen, was introduced through the centre of each droplet at an angle of 90° and gentle but firm pressure was used. Controls are read 5–10 min and allergens, 15–20 min after the test. Reactions were noted by measuring the diameter of the weal. Specific IgE (Pharmacia CAP; Pharmacia Diagnostics UK, Milton Keynes, UK) for peanuts, walnut, hazelnut, almond and brazilnut were performed.

Children with an 8 mm weal or less on SPT with peanut (14, 15) or other nut and specific IgE against peanut (16, 17) or other nut <17.5 kU[A]/l were eligible for food challenge. A double-blind, placebo-controlled food challenge was performed in accordance with standard practice (18–20), by a doctor and nurse trained in resuscitation techniques and emergency drugs calculated and readily available. The food was at first rubbed five to six times over the lower lip. Providing there was no reaction to this, it was followed by oral challenge. The initial dose was 100 mg, which was doubled every 15–20 min to a maximum of 8 g in the active challenge. For severe symptoms (21), the challenge was discontinued and unblinded. If the symptoms were minor (21) and resolved without medication (itching, soreness in the lips or mouth, lip swelling, urticaria, or abdominal pain), 1 h after resolution of these symptoms, the challenge with the second ingredient was commenced and unblinding was carried out only after completion of both arms of the challenge. The double-blind challenge was complete when a single dose of 8 g of peanut (total cumulative dose = 15.8 g) was

reached. If there was no reaction to the double-blind challenge an open challenge with peanuts was given 1 h later.

Results

Eighty-two children with peanut allergy were identified from medical and dietetic records (Fig. 1). All case notes were reviewed. Fifty-four children met the inclusion criteria and 28 children were excluded. The reasons for exclusion were recent reactions within 2 yr (22), previous life-threatening reactions to nuts (5) and moved away (1).

Twenty-nine families were willing to participate whilst 25 did not reply or declined. Reviewing the case notes of those who were willing to participate and those who declined, there were no differences in the early history and presentation between the two groups. Of those who gave reasons for not participating (16), the majority wanted to consider this in the future, but felt that they were not ready now (11), some suggested anxiety of undergoing a food challenge (4) and one family expressed unhappiness with hospitals since they had a delay at diagnosis. All 29 children had SPT and 28 children had specific IgE levels. Eight children had SPT of 8 mm or less and a specific IgE of 17.5 kU[A]/l or less and were eligible for food challenge. All eight eligible children underwent food challenge of whom four

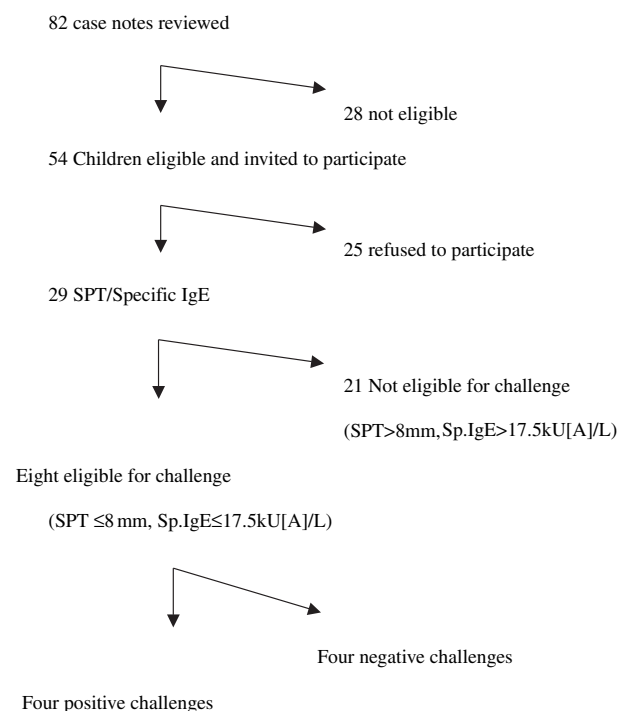


Fig. 1. Summary flow chart of the pathway to peanut challenge.

had a negative reaction and four a positive reaction. None of them had a local reaction to rubbing peanut on their lips. Of those who reacted, two children had facial swelling and itchiness and two children vomited profusely. Three children reacted within the first hour of the food challenge. All the children who reacted received antihistamine and were closely observed. None required adrenaline.

The SPTs and specific IgE at diagnosis were sought. In 16 children the initial SPT results were available. When this was compared with the recent SPT result, 10 children had a rise in the reaction, three had a fall and three were unchanged. Initial specific IgE were available in 15 children. When this was compared with the recent specific IgE result, 11 children had a similar result and four had a fall.

Table 1 shows the history of allergy in food challenged children (criteria: 8 mm wheal or less on SPT and specific IgE <17.5 kU[A]/l). In children who reacted the median SPT at challenge was 6.5 (range: 5–8) and median specific IgE was 1.97 kU[A]/l (range: 1.35–13.7). In non-reactors, the median SPT at challenge was 4 mm (range: 0–7) and specific IgE was 0.39 kU[A]/l (range: 0–7.86).

Table 1. Comparison of children with positive food challenge (reactors) and children with negative food challenge (non-reactors) of the food challenge

	Positive food challenge (n = 4)	Negative food challenge (n = 4)
Age at presentation*	3.5 yr (2–5 yr)	8.5 months (8 months to 3 yr)
Age at challenge*	8.5 yr (5–12 yr)	7.5 yr (6–12 yr)
SPT at challenge*	6.5 mm (5–8)	4 mm (0–7)
Specific IgE at challenge*	1.97 kU[A]/l (1.35–13.7)	0.39 kU[A]/l (0–7.86)
History of asthma	3	2
History of eczema	0	1
History of other allergies	2	3

*Median values (range).

SPT, skin prick test; IgE, immunoglobulin E.

Details of children who underwent food challenge is shown in Table 2.

Discussion

Peanut allergy can be life-threatening. Because of its potentially serious manifestations in some individuals the current standard advice is to avoid tree nuts because of the possibility of contamination by peanuts or co-existing allergy to other tree nuts in peanut allergic individuals. Marked restriction in the child's diet and activities are justification for review and confirmation or otherwise of the resolution of peanut allergy. It cannot be over emphasized that a careful diagnosis of peanut allergy is important for the same reasons. It was previously thought that peanut allergy was lifelong, however, this has recently been challenged. A case-control study of peanut allergy resolution showed that preschool children with a history of moderate allergic reaction to peanut had a 20% chance of resolution (22). Skolnick et al. have also demonstrated similar results with 26 of 103 children outgrowing their peanut allergy (8, 23). It is possible, however, that a small number of children may re-sensitize to peanuts, and thus it seems prudent to maintain access to emergency medications for patients with resolved peanut allergy until peanuts are routinely tolerated in relevant quantities for 1–2 yr (1).

Peanut allergy has become a more common general paediatric problem and it is likely that most peanut allergic children in Britain do not regularly attend specialist clinics. Their care is undertaken by general paediatricians who may, or may not, have a particular interest in allergic disease or involve adult allergists. An increasing number of children are being diagnosed with peanut allergy and it is important that general paediatricians dealing with them are increasingly familiar with food challenge and diagnostic tests.

Table 2. Details of children underwent food challenge

Case number	1	2	3	4	5	6	7	8
Food challenge outcome	+	+	+	+	–	–	–	–
Age at presentation	3 yr	4 yr	2 yr	5 yr	9 months	8 months	3 yr	10 months
History of asthma	Yes	No	Yes	Yes	No	No	Yes	Yes
History of eczema	No	No	No	No	No	Yes	No	No
History of other allergies	No	No	Yes	Yes	No	Yes	Yes	Yes
Age at challenge	8 yr	9 yr	5 yr	12 yr	6 yr	7 yr	8 yr	12 yr
SPT at diagnosis (mm)	8	5	NA	NA	NA	7	4	NA
SPT at challenge (mm)	8	6	5	7	0	4	4	7
Specific IgE at diagnosis*	NA	NA	Grade 4	Grade 2	Grade 3	Grade 0	NA	Grade 2
Specific IgE at challenge*	Grade 2	Grade 2	Grade 3	Grade 2	Grade 3	Grade 0	Grade 0	Grade 2

*Grade 0, <0.35 kU/l; grade 1, 0.35–0.7 kU/l; grade 2, 0.7–3.5 kU/l; grade 3, 3.5–17.5 kU/l; grade 4, 17.5–52.5 kU/l; grade 5, 52.5–100 kU/l; grade 6, >100 kU/l.

Diagnosis of resolution of symptoms by performance of food challenge should become more common in the general paediatric settings and no longer be exclusive to specialized centres. The general paediatrician should ensure that such challenge takes place in a safe environment with the necessary resuscitation equipment and drugs (18–20), and performed by staff trained in paediatric resuscitation skills (21). There should be access to paediatric intensive care. Performing a double-blind placebo-controlled food challenge may need the expertise of a specialist paediatric dietician (18, 20).

We set out to evaluate if peanut allergy can resolve. In our small study, we found that in the selected group of children there was a high chance of resolution (four of eight). Thus, overall there was an approximately 15% chance of peanut allergy resolution in children who have not had any recent reaction and no major allergic reactions. Our conservative choice on SPT result of <8 mm and specific IgE <17.5 kU[A]/l was based on previous studies (14–17). We were especially cautious in the case of children with associated asthma because of the higher risk of such children so that we excluded any child on treatment at or above step 3 of BTS guidelines.

While we demonstrated that in a small number of children, peanut allergy resolved, it is interesting to see that in the majority of repeat SPTs, reactions increase in size. It is probably good practice to repeat SPTs every 2–3 yr in children who have had no reactions in order to determine their current allergenicity status – either to reinforce the fact that they are still allergic and not to relax their diet restriction or to determine if they are fit to undergo a food challenge, provided the reaction is <8 mm and other criteria are fulfilled.

Our conservative inclusion criteria may mean that our resolution rate may be an underestimate as, for example, some asthmatics may have outgrown peanut allergy. It is difficult to predict those children in similar selected groups who will tolerate peanuts. There was no significant difference in their associated allergies, eczema or asthma. Presence of asthma is shown to be a high risk for severe reaction (22) but it may not mean that presence of asthma of any severity is associated with non-resolution of peanut allergy. There was overlap of the SPTs and specific IgE values between reactors and non-reactors thus the only way to identify resolution in similar selected groups appears to be a food challenge.

The immunological mechanism of resolution is uncertain and larger prospective studies will be needed. The removal of the diagnosis of peanut

allergy for a proportion of patients is a therapeutic result worth striving for, even if most peanut allergic patients should anticipate persistence of peanut allergy.

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