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Should children with a history of anaphylaxis to foods undergo challenge testing?

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Clinical and Experimental Allergy

Summary

Background Data on the frequency of resolution of anaphylaxis to foods are not available, but such resolution is generally assumed to be rare.

Objective To determine whether the frequency of negative challenge tests in children with a history of anaphylaxis to foods is frequent enough to warrant challenge testing to re-evaluate the diagnosis of anaphylaxis, and to document the safety of this procedure.

Methods All children ($n = 441$) who underwent a double-blind, placebo-controlled food challenge (DBPCFC) between January 2003 and March 2007 were screened for symptoms of anaphylaxis to food by history. Anaphylaxis was defined as symptoms and signs of cardiovascular instability, occurring within 2 h after ingestion of the suspected food.

Results Twenty-one children were enrolled (median age 6.1 years, range 0.8–14.4). The median time interval between the most recent anaphylactic reaction and the DBPCFC was 4.25 years, range 0.3–12.8. Twenty-one DBPCFCs were performed in 21 children. Eighteen of 21 children were sensitized to the food in question. Six DBPCFCs were negative (29%): three for cows milk, one for egg, one for peanut, and one for wheat. In the positive DBPCFCs, no severe reactions occurred, and epinephrine administration was not required.

Conclusions This is the first study using DBPCFCs in a consecutive series of children with a history of anaphylaxis to foods, and no indications in dietary history that the food allergy had been resolved. Our study shows that in such children having specific IgE levels below established cut-off levels reported in other studies predicting positive challenge outcomes, re-evaluation of clinical reactivity to food by DBPCFC should be considered, even when there are no indications in history that anaphylaxis has resolved. DBPCFCs can be performed safely in these children, although there is a potential risk for severe reactions.

Keywords anaphylaxis, double-blind, food allergy, food challenge, placebo-controlled food challenge, resolution

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Introduction

Food allergy may present with a variety of symptoms, of which anaphylactic symptoms are the most severe. Anaphylaxis to food may be life threatening or even fatal [1, 2]. Because food allergy may be misdiagnosed and true food allergy may resolve in some patients [3–6], the diagnosis of food allergy generally needs to be confirmed by challenge tests [7]. However, in general, challenge testing to establish the diagnosis in patients with a clear-cut history of anaphylaxis to foods is considered unne-

cessary, unsafe, and undesirable, particularly if there is IgE sensitization to the food in question [8, 9], unless the patient is believed to have outgrown the food allergy [9, 10]. According to these guidelines, patients with a clear-cut history of anaphylaxis to a clearly identified food are often excluded from food challenge testing [11, 12].

To date, little is known about long-term sequelae following food anaphylaxis. Although no data are available on the frequency of non-recurrence or resolution of anaphylaxis to food, it has been reported in some studies in individual patients [13–16]. To date, no studies have

been performed in consecutive series of patients with a history of anaphylaxis to food to estimate the prevalence of resolution or persistence of the food allergy. Therefore, the aims of this study were first to determine whether the non-recurrence or resolution of anaphylaxis in children with histories of clear-cut anaphylaxis to food is sufficiently frequent to warrant challenge testing to re-evaluate the diagnosis of anaphylaxis and, second, to document the safety of this procedure in these patients.

Methods

Study population and sensitization

All children ($n = 441$) who underwent a double-blind, placebo-controlled food challenge (DBPCFC) between January 2003 and March 2007 were screened for symptoms of anaphylaxis to food by history. Anaphylaxis was defined as cardiovascular symptoms and signs, such as anaphylactic shock with objective hypotension, collapse, syncope, hypotonic reactions, or decreased level of consciousness, occurring within 2 h after ingestion of the suspected food. Anaphylactic symptoms were verified in the medical records and with the parents. All children were on a diet restricted in the suspected food, as was verified by a dietician. Children in whom there were indications by history that tolerance to the food may have occurred were excluded from the study. Some patients of our study population reported that adverse reactions to foods had occurred, but in these cases, the culprit ingredient remained unclear.

The study was exempt from medical ethical approval, as DBPCFCs in children were performed as a routine diagnostic test, as is usual at our institution despite recent discussions of this topic [17]. The physician thoroughly discussed the potential risk of severe reactions during challenge testing with the parents. All parents of the children included in this study preferred to have certainty about the diagnosis of anaphylaxis to food, or wanted to have the diagnosis updated.

The children underwent DBPCFCs in our clinic between January 2003 and March 2007.

Sensitization to the allergenic food in question was determined by ImmunoCap RAST (Phadia AB, Uppsala, Sweden) and skin prick tests (SPTs) with commercially available extracts (ALK-Abelló, Hørsholm, Denmark) within 6 months before the DBPCFC. SPTs were expressed as histamine equivalent prick (HEP) [18]. This index is computed by dividing the size of the weal of the SPT of the food tested by the weal of histamine. RAST results of ≥ 0.35 kU/L and SPT scores ≥ 0.3 were considered positive. Children showing either a positive SPT or a specific IgE or both to the food tested were considered as sensitized to the food in question.

Previous determination of specific IgE in all children was investigated by searching their medical records and questioning their general practitioners.

Symptoms during the most recent anaphylactic episode, as well as the time intervals between the most recent episode of anaphylaxis and the DBPCFCs were determined.

Food challenges

Placebo and active challenges were randomly administered on separate days with at least a 2-week interval in between. For the active challenge, the suspected allergenic food was disguised in a food matrix to which the patient was tolerant. Validation of adequate blinding of the test materials was achieved by sensory testing in a dedicated food laboratory [19]. The challenge doses were administered according to incremental scales for the allergenic food (active food) as described previously [20], preceded by a labial challenge with the test food. For safety reasons, the challenges started at very low doses, such as 0.05 mL of milk (1 drop), or 6 mg of peanut, which is a very small crumb. The subsequent doses were administered at time intervals of at least $\frac{1}{2}$ h. The challenge was discontinued when objective allergic symptoms occurred, when subjective allergic symptoms occurred twice on two successive administrations of the same dose of the challenge material.

Symptoms and signs during challenges were categorized as follows: 1, anaphylaxis (cardiovascular symptoms and signs); 2, dermal symptoms; 3, gastro-intestinal symptoms; 4, local and upper airway symptoms; 5, lower airway symptoms; and 6, 'other' symptoms, such as pallor and cyanosis [20].

Immediate symptoms were defined as symptoms occurring during the challenge or within 2 h after the last challenge dose. The patient was discharged when symptoms had resolved. Late-onset symptoms were defined as symptoms occurring between 2 and 48 h after the last challenge dose. Two days after each challenge session, late-onset reactions were recorded by telephone questionnaire. In this phone questionnaire, the occurrence and type of symptoms was questioned in detail. Forty-eight hours after the second challenge session, the code was broken and the outcome of the DBPCFC was assessed according to a protocol as described previously [20]. Patients with a positive DBPCFC were advised to continue the avoidance of the challenged food. Negative challenges were followed by an open food challenge or were advised to introduce the challenged food at home. Patients received written instructions explaining how to introduce the food at home, using incrementing amounts of allergenic food (or in equivalent amounts in their usual household forms, such as peanut butter or chocolate spread with hazelnut), and ranging from less than the maximum challenge dose to normal daily food servings. Results of introduction at home were evaluated by telephone 1 month after the DBPCFC.

Statistics

Because of the small numbers, median results of patient characteristics and test results are presented. Spearman's ρ was used to calculate correlations between the cumulative eliciting doses (reactive dose in mg food) in DBPCFCs (not normally distributed) and specific IgE or SPT. Between children with positive and negative DBPCFCs, the following statistical tests were used to analyse differences: the Mann–Whitney test (two sided) for differences in age, specific IgE, SPTs, and time intervals between the anaphylactic reactions and the DBPCFCs, and the χ^2 test for the number of non-sensitized children and the presence of asthma.

Results

Study population and sensitization

Twenty-one children were enrolled (13 males, 8 females, median age 6.1 years, range 0.8–14.4 years). At the time of challenge, 17 children had symptoms of atopic eczema (81%), 14 had asthma (67%), and 11 had rhinitis (52%). All but one (Table 1; patient no. 3) had at least one of these atopic symptoms. The remaining patient characteristics are presented in Table 1.

Median specific IgE ($n = 21$) was 5.99 kU/L (range <0.35 to >100) and median HEP ($n = 19$) was 0.9 (range 0.00–2.0). Data on previously determined specific IgE levels were incomplete.

History of anaphylaxis

Children were not always referred immediately to our clinic following their anaphylactic reactions and in some cases only after several years. The median time interval between the most recent anaphylactic reaction and the DBPCFC was 4.25 years, range 0.3–12.8 years.

Details of the most recent anaphylactic reaction to food are presented in Table 1. All children had reacted with cardiovascular symptoms and at least two or more concomitant allergic symptoms. All anaphylactic reactions occurred within 10 min following ingestion of the suspected food.

Results of double-blind, placebo-controlled food challenges

The results of the DBPCFCs are shown in Table 1. Twenty-one DBPCFCs were performed in 21 children with cow's milk (nine challenges), egg (two challenges), peanut (six challenges), hazelnut (two challenges), and wheat (two challenges).

Fifteen DBPCFCs were positive (71%): six for cow's milk, one for egg, five for peanut, two for hazelnut, and one for wheat. Six DBPCFCs were negative (29%): three for cow's milk, one for egg, one for peanut, and one for wheat.

In positive DBPCFCs, a variety of symptoms occurred, such as dermal symptoms (nine cases), gastro-intestinal symptoms (nine cases), local symptoms (nine cases), and 'other symptoms' (three cases). No severe reactions occurred: we observed no immediate lower airway symptoms (except for coughing in patient no 12; Table 1), no stridor, and no hypotension. No epinephrine was administered. An intramuscular antihistamine was administered in one patient, and oral antihistamine in four patients.

In all positive challenges, symptoms occurred immediately (either alone or in combination with late-onset symptoms), except in one patient (Table 1; patient no. 3): this child reacted with late-onset gastro-intestinal symptoms to wheat. In 13/15 positive challenges, children showed objective symptoms, whereas two children reported repeated subjective symptoms only, which resulted in termination of the challenges.

In four children, placebo events occurred (patient nos. 11, 14, 15, and 18). Patient nos. 11 and 14 reported vague feelings of a tight and sore throat during the placebo challenge. Because of clearly more convincing reactions during the active food challenge session, these challenges were assessed as positive. Patient no. 15 reported late-onset symptoms of cramp and diarrhoea following both the active food challenge session and the placebo challenge. This challenge was assessed as negative. Patient no. 18 reported late-onset cramps on the placebo day, but no symptoms on the active food challenge. This challenge was assessed as negative.

In Fig. 1, the cumulative eliciting doses (expressed in mg food) of the positive DBPCFCs are shown. The highest eliciting amounts were found for egg and wheat, whereas the lowest eliciting amounts were found for cow's milk and peanut.

Statistical analysis showed no correlation between the eliciting amount of food in positive food challenges and specific IgE or SPT. All children with a negative DBPCFC introduced the food successfully into their diets. The shortest time interval between anaphylaxis and negative DBPCFC was 1.0 year (patient no.15; Table 1).

Characteristics of negative vs. positive double-blind, placebo-controlled food challenges

We compared several characteristics of children with positive and negative DBPCFCs as predictors for the outcome of food challenge tests (Table 2). Non-sensitized children were found in both groups (NS). In the negative group, three out of six patients were not sensitized, and in the positive food challenge group, two out of 15 patients were not. The latter children reacted to dose 6 (highest challenge dose). Also, the other characteristics presented in Table 2, such as size of SPT (HEP), age, time interval between anaphylaxis and DBPCFC, or the presence of asthma, did not differ significantly between both groups. Only specific IgE to the food in

Table 1. Characteristics of patients, anaphylactic reaction in dietary history, and results of double-blind, placebo-controlled food challenges (DBPCFCs)

Patient No.	Sex	Age (years, months) at time of DBPCFC	Food	Symptoms during anaphylaxis (categories 1–6) [†]	SPT (mm) (HEP)	Specific IgE (KU/L)	Time interval (years)*	Results of DBPCFC (positive/negative, cumulative amount of food)	Valid symptoms during active challenge sessions (categories 1–6) [†]	
									Immediate	Late onset
1	M	6.4	Cow's milk	1. Hy 2. U, gi, ad 3. N, vo	5 (0.9)	1.44	6.3	Positive Dose 3 0.4 mL	2. U	3. Cr, d
2	M	6.0	Peanut	1. Co 2. U, gi, ad 3. N, vo 4. Oas, lo 5. Co, wh 6. A	7 (1.4)	78	3.5	Positive Dose 5 547 mg	2. Gi, o 4. Rhi 6. A	–
3	F	3.2	Wheat	1. Dlc 3. cr, d	0 (0.0)	<0.35	2.7	Positive Dose 6 21.9 g	–	3. Cr, d
4	M	6.1	Peanut	1. Dlc 2. U, o 3. Cr, n, vo, d 4. Oas, lo 5. Dys	8 (1.2)	>100	3.1	Positive Dose 5 787 mg	2. U 3. N, vo	–
5	F	13.6	Peanut	1. Syn 2. U, gi, o 3. Ab 4. Oas, lo, ts 5. Dys 6. Tach, a	4 (0.7)	0.41	12.1	Positive Labial challenge Trace/0.6 mg	4. Ls	–
6	M	5.8	Hazelnut	1. Dlc 2. R 3. N, vo 4. Oas, ls, ts 5. Dys, wh	5 (0.8)	23.5	2.7	Positive Dose 6 2724 mg	2. R 3. Cr	2. Ad 3. Cr 6. Dr
7	M	3.10	Hazelnut	1. Syn 2. U, gi, o 3. N, vo 4. Oas, lo, ts stri	4 (0.9)	5.99	1.9	Positive Dose 3 137 mg	4. Tt, ie	–
8	M	6.1	Egg	1. Co 2. O 6. Dr, leth	7 (1.3)	3.79	4.3	Negative	–	–
9	F	1.8	Cow's milk	1. Syn 2. U, gi, o 3. Cr, ab 4. lo, ts 6. Tach	–	8.78	1.1	Positive Dose 5 12.5 mL	2. U, gi 3. Cr	–

10	M	0.8	Cow's milk	1. Hy 2. R 3. N, vo 5. Dys 6. Cy	8 (2)	> 100	0.3	Positive Dose 5 12.5 mL	2. U 3. Vo	-
11	F	11.9	Egg	1. Dlc 2. U, o, ad 3. Cr, n, vo, d 4. Oas, ts	0 (0.0)	< 0.35	8.9	Positive Dose 6 16.8 g	2. U, gi, 4. Ie	6. Dr
12	M	5.8	Peanut	1. Syn 2. O 3. N, vo 4. Oas, lo	5 (0.9)	> 100	3.3	Positive Dose 4 307 mg	2. O	3. D 4. Sne 5. Co
13	F	9.4	Cow's milk	1. Dlc 2. R, o 6. Ieth	-	> 100	6.8	Positive Dose 4 2.5 mL	2. R 3. N, vo, cr 4. Rhi	-
14	M	7.3	Cow's milk	1. Co 2. O 3. N, vo 3. Oas, lo 5. Dys 6. Pa	6 (1.3)	19.4	5.8	Positive Dose 5 12.5 mL	3. Cr 4. Ls, st	-
15	F	4.2	Cow's milk	1. Dlc 2. U, gi, 3. N, vo, cr, d	0 (0.0)	< 0.35	1.0	Negative	-	-
16	M	4.9	Peanut	1. Syn 2. U, o	2 (0.6)	< 0.35	4.3	Negative	-	-
17	F	10.3	Peanut	1. Dlc 2. O 4. Oas 5. Dys	6 (1.3)	1.19	9.3	Positive Dose 1 6 mg	4. Oas	-
18	M	3.2	Cow's milk	1. Syn, hy 3. N, vo, cr, d 6. Ta	2 (0.3)	< 0.35	2.6	Negative	-	-
19	F	13.2	Wheat	1. Dlc 2. R, u, gi, o, ad 3. N, vo, ab 4. Oas 6. Pa	4 (0.9)	6.85	10.3	Negative	-	-
20	M	12.2	Cow's Milk	1. Syn 2. R, u, gi, O, 3. N, vo, cr, d, 5. Dys 4. lo, ts 6. Pa	7 (1.2)	> 100	11.8	Positive Labial challenge Trace/0.005 mL	4. Ls, tt	4. rhi

Table 1. continued

Patient No.	Sex	Age (years, months) at time of DBPCFC	Food	Symptoms during anaphylaxis (categories 1–6) [†]	SPT (mm) (HEP)	Specific IgE (KU/L)	Time interval (years)*	Results of DBPCFC (positive/negative, cumulative amount of food)	Valid symptoms during active challenge sessions (categories 1–6) [‡]	
									Immediate	Late onset
21	M	13.3	Cow's milk	1. As 2. R, u, gi, o 3. N, vo, cr, d 5. Dys 6 Pa	5 (0.8)	0.62	12.8	Negative	–	–

*Time interval since most recent anaphylaxis to the food in question.

[†]Category 1: Cardiovascular symptoms: As, anaphylactic shock (objectified hypotension); co, collapse; syn, syncope; hy, hypotonic reactions; dlc, decreased level of consciousness.

Category 2: Dermal symptoms: r, rash/exanthema; u, urticaria; gi, generalized itch; o, (quincke's) oedema; ad, exacerbation of atopic dermatitis.

Category 3: Gastro-intestinal symptoms: n, nausea; vo, vomiting; cr, cramp; d, diarrhoea.

Category 4: Local and upper airway symptoms: oas, oral allergy symptoms; lo, laryngeal oedema; ls, lip swelling; ts, tongue swelling; rhi, rhinitis/conjunctivitis; stri, stridor; tt, tight throat/itchy throat; ie, itchy ears; sne, sneezing; st, sore throat.

Category 5: Lower airway symptoms: dys, dyspnoea; co, coughing; wh, wheezing.

Category 6: Other symptoms: a, anxiety; ta, tachycardia; dr, drowsiness; leth, lethargic; cy, cyanosis; pa, pallor.

HEP, histamine equivalent prick.

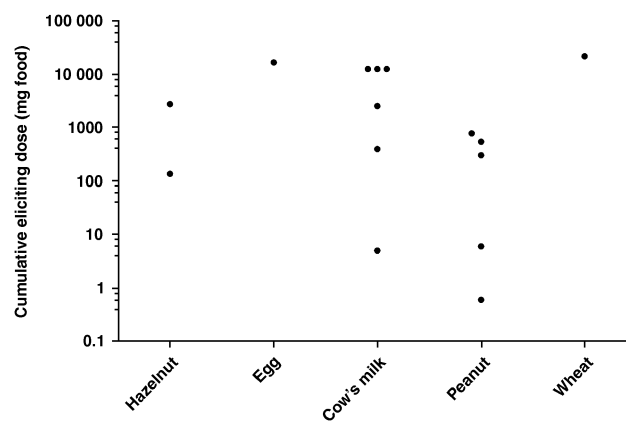


Fig. 1. Cumulative eliciting dose in positive double-blind, placebo-controlled food challenges in mg of food ($n = 15$).

question was significantly higher in the positive food challenge group ($P = 0.029$) (Table 2).

Discussion

To our knowledge, this is the first study using DBPCFCs in a consecutive series of children with a history of anaphylaxis to foods, and no indications in dietary history that tolerance to these foods might have supervened. Previous studies have reported the resolution of anaphylaxis to foods in individual patients [13–16]. In a study by Bock [15], serial food challenges were performed in a selected series of nine children with severe reactions to foods in their first year of life. Of these children, only three had experienced cardiovascular symptoms as part of their allergic reactions. One of these three children became tolerant to the food in question. The culprit foods in this study were cow's milk, egg, and soy, and no children with peanut or nut allergy were reported. Spergel and Fiedler [21] found no development of tolerance to peanut by open food challenges in five children with a history of anaphylaxis, but in a subsequent report, one patient was re-challenged and was found to be tolerant [16]. While these studies demonstrate that resolution of anaphylaxis to foods can occur, it is difficult to estimate how frequent this may be the case. Our results show that 29% (six cases) of consecutively referred children did not react to the foods in question at the time of the challenges. Additionally, two (non-sensitized) patients reacted to the highest challenge dose (Table 1; patient nos. 3 and 11), and it is possible that they were in the process of outgrowing their food allergy [22]. Thus, in children with a history of anaphylaxis to food, re-evaluation of the clinical reactivity to food by challenge testing should be considered by the physician, even when there are no indications in dietary history that they have outgrown their anaphylaxis. Without this re-evaluation, patients may be unnecessarily diagnosed as being severely food allergic for

Table 2. Characteristics of positive vs. negative double-blind, placebo-controlled food challenges (DBPCFCs)

	Positive DBPCFCs	Negative DBPCFCs
Sensitized (<i>n</i>)	13/15 (cow's milk, peanut, hazelnut)	3/6 (cow's milk, egg, wheat)
Non-sensitized (<i>n</i>)	2/15 (wheat, egg) (dose 6)	3/6 (cow's milk 2×, peanut)
Decreasing specific IgE	0/9	2/5
Increasing/unchanged specific IgE	9/0	3/5
Median specific IgE (kU/L)	19.40* (<0.35 to >100)	0.46* (<0.35 to 6.85)
Median HEP	0.90 (0.0–2.0)	0.70 (0.0–1.3)
Median age (years)	6.1 (0.8–13.6)	5.5 (3.2–14.4)
Median time interval (years)	3.6 (0.3–12.1)	4.3 (1.0–12.8)
Asthma	11	3

**P* = 0.029.

HEP, histamine equivalent prick.

prolonged periods of time. This may also have been the case in our study, as the duration between anaphylaxis and DBPCFC was up to 12.8 years.

An important limitation of this study is that we had very few children who had experienced their anaphylactic reaction to foods relatively shortly (i.e. weeks to months) before being tested. It therefore cannot be excluded that the frequency of negative test outcomes could be much lower in such cases. Further studies are needed to define minimum time intervals following anaphylaxis at which food challenges may be useful.

There are two possible explanations for the negative test results in six patients of the study population. Because the differential diagnosis of anaphylaxis is extensive, and initial food challenges were not performed to establish the diagnosis, it cannot be excluded that some of these children had another diagnosis initially. However, the same is true for other studies describing resolution of anaphylaxis to food in individual patients [13–16], as only one of these studies [15] utilized initial DBPCFCs. The other possibility is that previous anaphylactic reactions to foods have gone into spontaneous remission, as has been described for other systemic reactions to foods [3–6]. Several observations favour the latter explanation. The first is the short time interval between consumption of the food and the onset of anaphylaxis (all within 10 min). Secondly, in all children the causative food or ingredient could be determined precisely by the parents. Thirdly, no recurrent episodes of anaphylaxis were reported by the children after the culprit food was eliminated from the diet. Thus, we think these children had true anaphylaxis to foods initially that resolved over time.

Children with negative DBPCFCs were able to relinquish their epinephrine self-administration devices. This is important, because, while the availability of an epinephrine self-administration device during anaphylactic reactions is of unquestioned value, concerns have recently been raised about over-prescription of this medication [23]. These concerns seem warranted given, the negative effects of carrying such a device on quality of life [24].

We looked for predictors of the outcome of the DBPCFCs. In our analysis, only the levels of specific IgE were predictive. These were significantly higher in those with a positive than in those with a negative DBPCFC. This is in agreement with studies that have shown that the probability of clinical reactivity to food increases with increasing specific IgE levels [25]. As we found no negative challenge results in the 43% of children who had specific IgE values for cow's milk, egg, and peanut beyond which 95% of the patients react [25], undertaking DBPCFCs may not be necessary in children with sensitization levels beyond these decision points.

It has been reported that decrease in sensitization may predict development of tolerance of food allergy over time [22]. We carefully investigated previous determination of specific IgE in all children by searching their medical records and inquiring their general practitioners. We found that these data were incomplete. In 7/21 children, we did not find any data on previous specific IgE levels. In 14/21 children, previous data on specific IgE were available. In only six of these children, specific IgE was determined at the time of anaphylaxis. The data on previous specific IgE in positive and negative challenges are presented in Table 2. No children (0/9) with a positive challenge test and only 2/5 children with a negative challenge test showed a decline in specific IgE to the food in question (Table 2). However, in the other three children with a negative challenge, specific IgE was determined at the time of anaphylaxis in only one child, and it cannot be excluded that in the other two children with a negative test, specific IgE may have been higher at the time of anaphylaxis.

DBPCFCs may be performed safely in children with a history of anaphylaxis, although there always remains a potential risk of severe reactions. We observed no severe reactions, and no epinephrine was required in the treatment of reactions during challenge testing. Other studies also conclude that food challenges may be performed safely [12, 26]. Elements of the challenge protocol that we feel contribute to the safety of the procedure are very low starting doses (in the 1.75 mg of protein range), a time

interval between doses of at least $\frac{1}{2}$ h, and a gradual increase of the amount of allergenic food (initially doubling, later fivefold increases). Also, food challenge sessions were terminated when repeated subjective symptoms were reported by the patients or when mild objective symptoms were observed, and the avoidance of higher doses in these situations may have prevented severe reactions from occurring. Although the numbers of our study population are small, to date, in more than 500 DBPCFCs performed in our centre, including more than 180 with peanut, no severe or life-threatening reactions have occurred.

In conclusion, in children with a history of anaphylaxis to foods and specific IgE levels below established decision points, resolution or non-recurrence of anaphylaxis is not uncommon, and re-evaluation of clinical reactivity to food by DBPCFC should be considered, even when there are no indications of tolerance to the food in question. Such challenge testing may not be necessary in children with sensitization above well-established decision points. As determination of food-specific IgE levels over time may be able to predict the development of tolerance, periodic determination of specific IgE as well as SPTs may be useful to assess the probability of tolerance development and consequent usefulness of challenge testing in individual patients. In our study, these data were too incomplete to allow for any conclusions. DBPCFCs can be performed safely in these children, allowing a substantial number of these children to return to a normal diet and to relinquish their epinephrine self-administration devices. The value of challenge testing in children with recent anaphylactic reactions is presently unknown.

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