

Egg and milk allergy in adults

Diagnosis and characterization

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Nineteen adult patients representing a total of 24 medical histories of immediate adverse reactions to egg or cows' milk underwent 1) standardized questioning about signs/symptoms occurring less than 2 h after ingestion of egg or milk, 2) skin prick test, RAST and histamine release test, and 3) titrated, oral, double-blind, placebo-controlled challenge (DBPCFC) with fresh egg or milk. Eleven medical histories (46%) were confirmed by DBPCFC in 10 patients (53%). All DBPCFC-positive patients experienced gastrointestinal symptoms, and in 80% of the patients, gastrointestinal symptoms were accompanied by respiratory or skin symptoms. Threshold doses varied between 50 mg and 250 g, with 4 patients presenting objective signs following 5 g or less. DBPCFC-positive patients reported significantly more symptoms and had a significantly higher number of positive tests than had DBPCFC-negative patients. None of the tests were in significant concordance with DBPCFC, although RAST showed a sensitivity of 100%. Thus, DBPCFC cannot be substituted in the diagnosis of milk and egg allergy in adults. The use of titrated, fresh foods in DBPCFC proved to be a safe and well-controlled procedure.

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Less than 60% of suspected adverse reactions to food can be confirmed in double-blind, placebo-controlled food challenges (DBPCFC) (9), presently the gold standard for diagnosing food allergy (5, 6, 8, 9, 19, 28, 29). DBPCFC with different foods has now been performed in a great number of children (8, 19, 20, 30), allowing evaluation of symptoms, challenge procedures, and diagnostic tests, such as skin prick test (SPT), RAST and histamine release (HR). Egg and milk are among the foods most frequently causing adverse reactions in children (20, 28), and several studies have investigated egg and milk allergy in children (5, 13–17). Recently, DBPCFC has been applied in the diagnosis of adverse reactions to different foods in adults (3, 6, 11, 26). The purpose of this study was to identify a group of adults with immediate egg and/or milk allergy, using DBPCFC with fresh foods, to describe symptoms, thresholds and timing of reactions during challenges, and to estimate the diagnostic value of SPT, RAST and HR in these patients.

Material and methods

Nineteen adult patients (14 women, 5 men) referred to the Food Allergy Unit for evaluation of immediate allergic reaction to hen's egg and/or cows' milk were included in the study. The patients reported a total of 24 cases of immediate allergic reactions to

milk or egg: 8 patients reported symptoms to egg only, 6 to milk only, and 5 to both egg and milk. Inclusion criteria were the following: a medical history of allergic signs/symptoms occurring within 2 h after ingestion of the suspected food item on at least 2 separate occasions. All patients were questioned about the following signs/symptoms: asthma, rhinitis, conjunctivitis, rhinoconjunctivitis, nausea, vomiting, diarrhoea, pruritus/erythema, urticaria, angioedema and fainting/anaphylaxis. Moreover, the patients were encouraged to report any other symptoms experienced within 2 h after ingestion. Oropharyngeal itching/swelling (OPIS) was spontaneously reported in 11/24 cases. Two patients reported abdominal pain. Five patients reported exacerbation of atopic eczema 8–24 h after ingestion, but this symptom was not included in the study. Reported number of symptoms per medical history was between 1 and 7 (mean: 2.3). Symptoms reported are listed in Table 1. Median age was 27 years (range: 16–44). Four patients reported age at onset of symptoms to be between 0 and 5 years of age, and 15 patients stated approximately 17 years of age. None of the patients deliberately ingested the offending food item, and the time interval from the last reaction is not known. Sixteen of the included patients were also allergic to one or more (mean 2.8) common inhalant allergens as estimated by asthma or rhinitis following exposure, in combination with a positive SPT or RAST. All food challenges were, however, per-

Table 1a. Patients suspected of egg allergy

Pt	DBPCFC	History	SPT	HR	RAST	IgE
01	+	A, RC, N, V, U, AE	-	+	4	471*
02	+	A, N, V, D	+	ic	4	636
03	+	A, RC, N, V, AP, U, AE	+	+	3	1213*
04	+	N, V	+	+	2	360
05	+	OPIS, P, AS	+	-	2	5055*
06	+	OPIS, P	-	-	1	1938*
07	+	OPIS, P	+	+	4	6060*
08	-	P	+	-	2	3020*
09	-	OPIS, N,	+	-	1	25*
10	-	OPIS	+	+	4	8805*
11	-	OPIS, N, V	-	+	3	475
12	-	OPIS, AE	-	-	0	721
13	-	P	+	+	4	13000*

OPIS: oropharyngeal itching/swelling, A: asthma, RC: rhinoconjunctivitis, N: nausea, V: vomiting, AP: abdominal pain, D: diarrhoea, P: pruritus, U: urticaria, AE: angioedema (other site than oropharynx), AS: anaphylactic shock. ic: inconclusive. Total IgE given in kIU/l, normal range 0–150 kIU/l. n.d.: not done.

* Atopic dermatitis.

Table 1b. Patients suspected of milk allergy

Pt	DBPCFC	History	SPT	HR	RAST	IgE
02	+	OPIS, A	+	-	2	636
14	+	OPIS, P	+	+	4	500*
15	+	OPIS, U	+	+	3	273*
19	+	A, AP, D	-	+	2	731
03	-	A, P	-	-	0	1213*
07	-	P	+	-	2	6060*
09	-	P	-	-	0	25*
11	-	N	-	-	0	475
16	-	OPIS, RC, AE	+	+	4	8054*
17	-	N, D	+	ic	0	n.d.
18	-	R	-	-	0	5

Abbreviations: see Table 1a.

formed out of peak season for the relevant inhalant allergens. Eleven suffered from atopic dermatitis (AD). Total serum IgE was elevated in 17 (Table 1). No connection was reported between exercise, food ingestion and symptoms. Lactase deficiency was excluded in patients reporting gastrointestinal (GI) symptoms after ingestion of milk. All patients gave their informed consent to participation. The study protocol was reviewed and approved by the local ethics committee.

Skin prick test with egg and milk extract was performed by the same nurse in all patients according to the recommendations made by the European Academy of Allergology and Clinical Immunology (12). Glycerinated whole hen's egg 1:100 w/v and cows' milk 1:20 w/v, histamine hydrochloride 10 mg/ml, and diluent/negative control were supplied by ALK Laboratories, Hørsholm, Denmark. The wheal size was measured by the formula: $(D + d)/2$, D being

the maximum diameter and d its perpendicular diameter. A net wheal diameter 3 mm larger than the negative control wheal was considered positive. Prior to testing, the patients discontinued medication with oral antihistamines for 5–7 days (astemizole for 8 weeks), systemic steroid for 2 weeks and topical steroid on the SPT area for 72 h.

Histamine release test was performed as previously described (22, 25). Briefly, 25 µl of whole blood was applied to allergen-coated microtitre wells. Allergenic extracts were identical to those used in SPT. Each allergen was tested at six 3.5-fold dilutions, starting with 1:10 of the stock solution. After incubation for 1 h at 37°C the plates were rinsed, and protein residues were enzymatically removed (21). Histamine bound to the microfibrils was measured spectrofluorometrically with a Gilson fluorimeter. A histamine release of more than 15 ng/ml was considered positive. The results from patients with non-responding basophils, i.e. basophils releasing less than 15 ng/ml of histamine following anti-IgE challenge, were considered inconclusive.

All patient sera were tested with Phadebas-RAST (Pharmacia Diagnostics AB, Uppsala, Sweden) for cows' milk and hen's egg white and scored in RAST classes 0–4 according to the Phadebas-RAST scoring system. RAST class 1 or more was considered positive. Total serum IgE was measured by the commercially available PRIST kit (Pharmacia, Uppsala, Sweden). The results are given in kIU/l.

All challenges were performed in a double-blind, placebo-controlled fashion. The patients were challenged only when free of symptoms; or, in case of atopic dermatitis, only during periods of minimal activity.

Challenge constituents comprised fresh hen's egg and fresh whole-fat, homogenized and pasteurized cow's milk bought locally. Active challenges with egg contained between 0.45 mg and 5 g of whole, fresh hen's egg diluted in saline (0.9%) or 50 g of whole hen's egg. The egg was concealed in a vehicle of Vivonex Elemental Diet and blackcurrant juice. Doses ranging from 0.45 mg to 5 g of egg were easily concealed in 100 ml of the vehicle, whereas 50 g required 500 ml. In the placebo challenges, diluted hen's egg was substituted by equal volumes of pure saline (0.9%). Challenges with milk were prepared in essentially the same manner. Doses ranging from 0.45 mg to 50 g were easily concealed. Since a few patients only reported symptoms to larger doses of milk, a dose of 250 g was prepared with milk partly substituting the water required for preparation of Vivonex.

The blinding was tested by 6 volunteers. No difference was found between active and placebo in the egg doses between 0.45 mg and 5 g, and the milk doses between 0.45 mg and 50 g. However, 2 vol-

unteers reported a slight difference in texture (though not in taste) between active and placebo in the 250 g dose of milk and the 50 g dose of egg, and it therefore cannot be excluded that the presence of egg or milk in these doses may have been detected by some patients.

All challenge doses were served chilled, in identical opaque plastic cups with lid and straw. All challenge doses were prepared and coded by the same dietician. The order of active and placebo days was randomized by the dietician, whereas the nursing staff serving the challenge doses, and the physician evaluating the reactions did not know the constituents.

None of the patients deliberately ingested the offending food item. However, in order to avoid any accidental intake, all patients were instructed by the dietician to keep a strict elimination diet (egg and/or milk free) for 2 weeks prior to and during the whole challenge period.

A safe challenge procedure and determination of the threshold (smallest dose of antigen eliciting symptoms) was essential. For this purpose 3 challenge phases were designed.

Phase A included 2 separate challenge procedures on separate days, one active (A) and one placebo (A-pl). A comprised 6 doses: dose 0 = placebo vehicle (baseline recording of parameters), dose 1 = 0.45 mg followed by a 10-fold increase until a cumulated dose of 5 g was attained. A-pl comprised 6 doses containing the placebo vehicle in volumes identical to the A doses.

Phase B comprised 2 separate challenge procedures on separate days, one active (B) and one placebo (B-pl). B comprised 4 doses: 0, 0.5 g, 5 g, 50 g, B-pl comprised 4 doses containing the placebo vehicle in volumes identical to the B doses.

Phase C was applied for milk challenges only and comprised a minimum of 3 active doses of 250 g and 3 placebo doses (randomized order) given on 6 separate days. Patients reporting symptoms elicited by very small doses and/or severe reactions (including pharyngeal swelling) started with *Phase A*. If no reaction to a cumulated dose of 5 g was seen, patients proceeded to *Phase B*. Patients reporting milder symptoms such as pruritus started directly with *Phase B*. Patients tolerating small doses of milk (butter, milk in e.g. sauces) but experiencing mild symptoms from larger amounts (a glass of milk) started directly in *Phase C* milk challenges. All challenge days and phases were separated by a wash-out period of 48 h.

Prior to challenge the patients discontinued medication: antihistamine for 5–7 days (astemizole for 8 weeks); systemic steroid for 2 weeks, topical beta₂-agonist for 12 h.

If discontinuation of topical beta₂-agonist caused

asthma, half-dose medication was allowed since the patients had to be free of symptoms before the challenge. Medication scheme was identical on all challenge days.

All challenges were performed at the Food Allergy Unit, where appropriate medication and resuscitation equipment were directly available. The patients were examined as to the presence of symptoms, and pulse, blood pressure and FEV₁ were measured. The patients were challenged only if free of symptoms. An intravenous line was established in all challenges except in *Phase C* milk challenges, in which patients reported mild symptoms only to larger amounts, and no evidence of specific IgE was found. Subjective symptoms, objective signs and measurements were recorded in a standard record by the patients and the nursing staff. Starting dose was chosen as described above, and if no reaction was seen within 30 min (or longer if indicated by history), the dose was 10-fold increased. When objective signs appeared, the challenge was stopped and treatment was given, if required.

When interpreting challenge results a positive reaction was defined as objective signs to an active challenge without any symptoms to the corresponding placebo challenge. In the case of symptoms to a placebo challenge or purely subjective symptoms, the patient was re-challenged, and if he correctly identified the 3 active challenges among 6 randomized challenges, the reaction was scored as positive. Asthma was defined as dyspnoea accompanied by a decrease in FEV₁ > 20%. Asthma, rhinoconjunctivitis, vomiting, diarrhoea, urticaria, and angioedema were objectively visible, whereas nausea, pruritus and often OPIS were subjective. The patient was considered clinically tolerant to the food if a dose of 55 g of egg or 250 g of milk produced no symptoms during challenge.

Statistics

A 2-sample rank sum test (Mann-Whitney) was used for comparison of test results and symptoms in the DBPCFC-positive and -negative group. Sensitivity (SE) was calculated as the proportion of DBPCFC-positive individuals correctly identified by a positive test result. Specificity (SP) was calculated as the proportion of DBPCFC-negative individuals correctly identified by a negative test result. Concordance between test results and the results of DBPCFC was calculated by sign test or Fisher's exact test with Yates' correction for a small sample size. Calculations were made with the SPSS PC statistical software.

Results

Challenge results

Totally, 11/24 cases (46%) of immediate allergic reaction (7/13 to egg and 4/11 to milk) were confirmed by DBPCFC in 10/19 patients (53%) (Table 1). Nineteen patients were included in the study. According to their medical histories, 8 patients were challenged with egg only, 5 with both egg and milk, and 5 with milk only. Prior to this study one patient (No. 14; milk only) had been challenged in another double-blind, placebo-controlled protocol and had developed a severe, anaphylactic reaction. It was considered unethical to re-challenge this person, and he was included in the study as challenge-positive. Eighteen patients representing 23 case histories were tested by titrated, oral DBPCFC. In the following, the 23 cases will be referred to as 23 patients.

DBPCFC was performed on 94 occasions (mean: 4.1; range 2–12) including a total of 283 administered single challenge doses; 121 active and 162 placebo. The patients were given a mean of 12.3 single challenge doses, 57% being placebo. Results of the 283 single food challenges are shown in Fig. 1. Two patients, who were scored as DBPCFC-negative, had experienced subjective symptoms to an active

case	phase		DBPCFC score
	A	B	
01	closed	closed	pos
02	closed	open	pos
03	closed	open	pos
04	open	closed	pos
05	open	closed	pos
06	open	closed	pos
07	open	closed	pos
08	open	open	neg
09	open	open	neg
10	open	open	neg
11	open	open	neg
12	open	open	neg
13	open	open	neg

Fig. 1a. Course and results of the egg challenges. Closed bars: positive reaction during challenge phase. Open bars: no reaction during challenge phase.

case	phase			DBPCFC score
	A	B	C	
02			closed	pos
03			open	neg
07	open	open	open	neg
09			open	neg
11	open	open	open	neg
14 ¹⁾				pos
15	open	closed		pos
16	open	open	2)	neg
17	open	open	3)	neg
18			open	neg
19	open	closed		pos

Fig. 1b. Course and results of the milk challenges. Closed bars: positive reaction during challenge phase. Open bars: no reaction during challenge phase. 1) challenged outside study; 2) not available for further challenges; 3) started daily ingestion of milk without symptoms.

challenge. However, at repeated challenges, this could not be reproduced. Positive reactions were seen in 2/162 placebo challenges, both demonstrating a 20% decrease in FEV₁ not accompanied by any other symptoms. In both patients (1 DBPCFC-positive and 1 DBPCFC-negative) challenge procedures were repeated, and no reactions were seen at the placebo challenges. The DBPCFC-positive patient also showed more allergic signs during the positive food challenge.

DBPCFC-positive patients

The 11 DBPCFC-positive patients (7 patients to egg and 4 to milk) are listed in Table 2 together with symptoms following challenge and threshold dose.

Objective signs were observed in 10 patients. In one patient the symptoms were purely subjective, but reproducible during repeated, randomized DBPCFC. Patient 14 was challenged outside the study and is not considered in the following. The most frequent single symptom on challenge was OPIS (7/10 patients), followed by asthma (5/10) and nausea (5/10). If occurring, OPIS was always the first symptom to occur, and in 3 patients (Nos 01, 03, 15)

Table 2. DBPCFC positive patients

Pt	Age/Sex	Food	Dose (g) eliciting reaction	Symptoms following challenge
03	28/F	egg	0.005 0.05 0.250	OPIS (mild) OPIS, C A, RC, N, V, AP, AE
02	39/M	egg	0.05	A, N, D
01	24/F	egg	0.5 5.0	OPIS, A OPIS, A, RC, N, U, AE
04	16/F	egg	2.5	OPIS, N
05	37/F	egg	50	OPIS, N, AE
06	27/F	egg	50	OPIS, R, P
07	22/F	egg	50	A, AP
14*	36/M	milk	—	anaphylaxis
15	29/F	milk	5 50	OPIS (mild) OPIS, U
19	44/F	milk	50	AP, D
02	39/M	milk	250	OPIS, A

* Challenged outside study.

OPIS: oropharyngeal itching/swelling, A: asthma, C: conjunctivitis, R: rhinitis, RC: rhinoconjunctivitis, N: nausea, D: diarrhoea, P: pruritus, AE: angioedema (other site than oropharynx), U: urticaria, AP: abdominal pain.

OPIS completely disappeared within 20 min. When the challenge dose was increased, OPIS reappeared together with objective signs. Respiratory symptoms (asthma, rhinitis, rhinoconjunctivitis) were seen in 6/10, skin symptoms, (pruritus, angioedema, urticaria) in 5/10, and GI symptoms (OPIS, nausea, vomiting, abdominal pain, diarrhoea) were seen in all patients (10/10). In 8 patients the GI symptoms were accompanied by respiratory or skin symptoms, and 2 patients had GI symptoms only.

Threshold doses varied between 50 mg and 250 g (fresh, liquid egg/milk). Four/11 patients showed objective signs following 5 g or less. All these patients were allergic to egg. The lowest dose seen to elicit an objective reaction was 50 mg of egg. This dose caused a moderately severe asthma (40% decrease in FEV₁), nausea and diarrhoea within 15 min after ingestion (Patient 02). Patient 03 experienced subjective OPIS after ingestion of 5 mg, whereas a dose of 250 mg was needed to elicit the reported objective signs. The highest dose needed to elicit objective signs was seen in Patient 02 (milk), in whom 250 g caused OPIS immediately and asthma within 30–40 min.

All reactions occurred within 10–40 min after ingestion. Symptoms were generally self-limiting and disappeared within 3 h, except in Patient 01, who was given antihistamine, beta₂-agonist and steroid intravenously due to rapid systemic reaction.

Reported symptoms

All DBPCFC-positive patients reported GI symptoms, and 90% reported respiratory and/or skin

symptoms. This distribution correlated well with the one seen during challenge, and a comparison between Tables 1 and 2 shows that generally the DBPCFC-positive patients reproduced the reported single symptoms. However, vomiting was only reproducible in 1/4 patients and in Patients 05 and 07 the clinical pattern during challenge differed from the one reported by the patients. Only 54% of the DBPCFC-negative patients reported GI symptoms, and 15% reported a combination of GI with respiratory and/or skin symptoms. DBPCFC-positive patients had a mean of 3.2 reported symptoms/patient (range: 2–7), whereas DBPCFC-negative patients reported a mean of 1.6 symptoms/patient (range: 1–3). This difference was significant ($p < 0.01$).

SPT, RAST and HR

The results of SPT, RAST and HR are listed in Table 1. SPT was positive in 8/11 (73%), RAST in 11/11 (100%) and HR in 7/11 (63%) of the DBPCFC-positive patients. RAST was the most sensitive test (SE = 1.00), but also had a low specificity together with SPT (SP = 0.46 in both), whereas HR were slightly more specific (SP = 0.61). There was no significant concordance between either SPT, RAST, or HR and DBPCFC ($p > 0.05$). DBPCFC-positive patients had a significantly higher number of positive tests (mean: 2.4, range: 2–3) than DBPCFC-negative patients (mean: 1.3; range: 0–3) ($p < 0.05$).

Discussion

Diagnostic procedures

The purpose of the study was to identify and to characterize a group of adults with a clinically manifest allergy to egg or milk. As inclusion criteria for the medical history were chosen symptoms observed during challenge in previous studies (9, 11, 13, 14, 30), i.e. asthma, rhinitis, rhinoconjunctivitis, nausea, vomiting, diarrhoea, pruritus/erythema, urticaria, angioedema and anaphylaxis. Moreover, the time limit for immediate reactions was set at 2 h (4, 7, 11, 30). The study population was thus highly selected with regard to immediate, objective, allergic signs.

By means of titrated, oral DBPCFC 11/24 (46%) medical histories were confirmed in 10/19 (53%) patients. These results are comparable with those of previous studies, in which 39–60% of children suspected of adverse reactions to food (7, 19, 28), and in particular 50% of children suspected of egg or milk allergy, have been found to react during challenge (13, 15). In adults this proportion has been reported to be between 30 and 43% (4, 6, 11, 26) and 55% in a recent study in children and adults in

which 72% of the DBPCFC-positive patients were allergic to egg/milk (23). Our results confirm the general conclusion of these studies that a convincing medical history cannot exclude DBPCFC in the diagnosis of clinical food allergy, even though DBPCFC-positive patients reported significantly more symptoms than DBPCFC-negative patients, and more often GI symptoms in combination with symptoms from other organs. For identification of DBPCFC-positive patients, SPT showed a SE of 0.73, and a SP of 0.46 which is in accordance with other findings (8, 30, 31). Bernstein (6) found a SE of HR of only 0.15, as compared with DBPCFC, but in our study HR showed a SE of 0.63 and a SP of 0.54. This seems to confirm the findings of some authors (10, 27) that HR may be a tool for identifying food-allergic patients. However, this test needs further development, e.g. of the allergen extracts used (unpublished observations). The diagnostic value of RAST in food allergy has been strongly debated. Some authors have found it very sensitive, though dependent on the single food allergen (1, 32), whereas others have found that in children with AD, SPT was of greater value (30, 31), and Bernstein reported a correlation of only 7.6% between RAST and DBPCFC in adults (6). Daul found a good correlation between high symptom score (immediate allergic symptoms) and RAST activity (11). In our study, RAST was the most sensitive test (SE = 1.00; SP: 0.46) when a RAST class of 1 or more was considered positive. Considering the risk of nonspecific binding due to the high IgE levels, we examined SE and SP at a cut-off of 2, as suggested by some authors (1, 32). SE then decreased to 0.91, and at a cut-off 3, as suggested by Sampson (30), SE decreased to 0.55 and SP was only improved to 0.69. The high cut-off level has been found necessary when testing children with AD. In an adult population presenting a positive medical history, RAST could be used as a further means of selecting patients for DBPCFC. A high sensitivity (low cut-off) would then be most important, since it is essential not to miss any potential DBPCFC-positive patients. Further, a low cut-off is necessary if not all patients suffer from AD, as in the present study. Since no significant concordance between SPT, RAST, or HR and DBPCFC was found, none of these tests could exclude the need of DBPCFC. The results of the diagnostic tests should therefore be combined with a positive medical history when selecting patients for challenge.

DBPCFC-positive patients

Positive DBPCFC was seen more frequently in patients suspected of egg allergy (54%) than in patients suspected of milk allergy (36%), a finding which is

in accordance with that of Ford (13) in investigating children. Four patients had a threshold of 5 g or less; these 4 patients were all egg-allergic and were the ones reporting onset of symptoms before the age of 5 years. Only 4 patients were DBPCFC-positive to milk, and their thresholds were between 50 and 250 g. The total threshold range was 50 mg–250 g, which is comparable to the 5–100 g threshold range in adults found by Atkins (4). In children, thresholds of 25–100 mg of dried whole egg have been observed (8), which theoretically equals 100 mg–1.2 g of fresh liquid egg (9). Since in our study 4/12 patients reacted to 5 g or less, and no patients reacted to the lowest dose in a titration phase, we consider titration to be a necessity and a starting dose in adults of 5 mg of fresh egg/milk to be safe, even in extremely sensitive patients. However, this low starting dose is probably only necessary in patients reporting reaction to minute amounts. In these sensitive patients a low dose increase, such as 2- or 5-fold might also be advisable, and perhaps also a longer time interval between the dose increases, since we observed strong reactions following the 10-fold dose increase in 2 such patients. The use of diluted fresh/liquid foods in this study facilitated a controlled dose administration and timing in sensitive subjects. Moreover, it allowed the occurrence of OPIS, which is not the case if encapsulated, dried foods are used (9). Although blinding of diluted doses of milk and egg presented no problem, complete blinding of the maximum doses (50 g of egg and 250 g of milk) was not achieved. OPIS was the first symptom experienced by 70% of the DBPCFC-positive patients during challenge. This symptom, referred to by some authors as the oral allergy syndrome (OAS), is often seen in pollen/fruit-sensitive patients (2, 24) but has also been described in 78% of patients with different food allergies (32), in 80% of DBPCFC-positive adults (4) and in "most subjects with a positive challenge" (11).

As was to be expected from the inclusion criteria, the symptoms observed during challenge were qualitatively similar to those observed in previous reports (4, 11, 14, 30) and generally identical to those reported by the patient. GI symptoms were seen in 100% DBPCFC-positive patients (70%, if excluding OPIS), skin symptoms in 50%, and respiratory symptoms in 50%, which is in agreement with the findings of Bock (8) in children older than 3 years, in whom GI symptoms were observed in 93%, skin symptoms in 62.5%, and respiratory symptoms in 56%. Our findings also agree with those of Atkins (4) in adults, of whom 80% showed GI symptoms (40%, if excluding OPIS), and 60% showed respiratory symptoms. However, our data could not confirm the high proportion of skin symptoms (80%, primarily urticaria) found in this study. A predom-

inance of skin symptoms, 79–94%, has also been observed in children with AD (18, 28, 31) in whom GI symptoms were seen in 23–43% and respiratory symptoms in 5–28%.

In conclusion, we confirmed 46% of the medical histories of immediate, allergic reaction to egg and milk in a group of 19 adults. Symptoms reported and observed during challenge were suggestive of IgE-mediated allergy, and specific IgE against the suspected food item was demonstrated in all DBPCFC-positive patients. However, medical history or diagnostic tests alone or in combination could not diagnose clinical food allergy, and should rather be used for selecting patients for DBPCFC. We consider a titrated administration of fresh/liquid egg or milk a necessary and safe challenge procedure, provided that sensitive subjects are challenged in a sufficiently safe protocol.

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