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Maize food allergy: a double-blind placebo-controlled study

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Clinical and
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Allergy

Summary

Background Maize allergy is not very common especially in Europe. The number of studies that address IgE mediated maize allergy is all too few.**Objective** Evaluate subjects with a history of maize allergy by double-blind, placebo-controlled food challenge; identify the spectrum of symptoms manifested during challenge; determine the lowest provocation dose (PD) during challenge; determine the performance characteristics of maize skin prick test and specific IgE.**Methods** Twenty-seven patients with a history of maize allergy were enrolled to be evaluated by skin test, specific IgE and double-blind placebo-controlled maize challenge.**Results** Forty-eight percent of the patients were challenge positive. PD range was 0.1–25 g. Fifty-four percent of the maize allergic subjects had a PD that was ≤ 2.5 g; two subjects reacted to 100 mg of maize. Comparison of maize specific IgE levels and skin test results to the challenge results revealed the following (specific IgE level/skin testing): sensitivity 1.00/0.846, specificity 0.077/0.384, positive predictive value 0.520/0.579, and negative predictive value 1.00/0.714.**Conclusion** Maize is a cause of IgE-mediated allergic reactions to foods in adults and children. Nearly half of the subjects recruited were confirmed by challenge to be allergic to maize.

Twenty-three percent of the positive challenge patients manifested symptoms that involved two organ systems, thus fulfilling the criteria for maize induced anaphylaxis. Maize is allergenic and can pose a risk for symptomatic food allergy at a dose of 100 mg.

Keywords allergy symptoms, anaphylaxis, corn allergy, double-blind, food allergy, hypersensitivity, maize allergy, performance characteristics, placebo-controlled food challenge, provocation dose

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Introduction

The first reports of allergic reactions to maize concerned anaphylaxis attributed to maize starch in surgical glove powder [1–3]. Maize has also been reported as a cause of “baker’s asthma” [4]; these subjects, however, virtually never have problems with ingested cereal grains. Despite its wide consumption, maize has been described only recently as a cause of food allergy. In the literature we can find single case reports of reactions of variable severity, considered as sporadic and accidental events. A few cases of maize food allergy in children were reported by Bock et al [5]. A study by Jones et al. evaluated 145 children with atopic dermatitis and positive skin prick test (SPT) results to one or more cereal extracts (wheat, rice, rye, barley, oat, maize); oral challenge confirmed maize

allergy in five of 45 subjects tested [6]. The first report of a maize-induced anaphylactic reaction dates back to 1984 [7]. More recently, two cases of anaphylaxis to maize confirmed by oral challenge performed in a controlled setting were reported [8, 9]. Reports of oral allergy syndrome (OAS), urticaria and anaphylaxis to maize come in particular from Italy, where maize is consumed mainly as polenta. It is noteworthy that polenta is cooked maize flour and the allergenicity of maize has been demonstrated to be resistant to cooking also for long periods of time [10]. The higher frequency of reactions to maize in the Italian population is probably due to the old tradition of eating polenta. Maize allergy also has received greater attention after genetically modified maize that was originally intended for animal feed was found in human food supply [11].

A key point in the diagnosis of maize allergy is the difficulty in discriminating a clinically apparent sensitization from an asymptomatic sensitization. SPTs and serum-specific IgE measurement are frequently positive in asymptomatic subjects, due to a high degree of cross-reactivity among cereals and grasses. It has been reported that only 21% of patients with a positive SPT to one or more cereals have symptomatic sensitization to cereals, as demonstrated by specific food challenge [12]. Recently Weichel et al. [13] have reported significant homology between wheat and maize thioredoxins as well as significant cross-reactivity between thioredoxins in cereals and grass. Moreover *in vitro* studies on wheat allergens have shown that there is significant homology between wheat and maize lipid transfer protein (LTP), thus further contributing to cross-reactivity among cereals [14], however this cross-reactivity has not been reported *in vivo*.

The IgE antibodies of patients with symptomatic sensitization to maize will react specifically with the allergenic proteins of maize. The major allergen of maize has been identified as a 9 kd LTP, which also has been recognized in patients with severe systemic reactions to maize [15]. This allergen has been shown to be very similar to the LTP that is found in peach, thus explaining the high rate of clinical cross-reactivity between peach and maize allergy. This protein is resistant to high temperatures and is present in the water-soluble fraction as well as the total protein fraction of maize. Sensitization to this protein, which occurs especially in the Mediterranean area, may explain the greater prevalence of allergic reactions to maize in the Italian population. Moreover, the lack of sensitization to maize LTP could explain why some countries with a large consumption of maize rarely have allergic reactions to this food item, as compared with Italy.

The aim of this study is to evaluate the clinical reactivity after maize provocation; identify the range and severity of symptoms that are manifested during maize double blind placebo-controlled food challenge (DBPCFC); determine the lowest provocation dose (PD) during DBPCFC; determine the performance characteristics of maize SPT and maize specific IgE as compared with DBPCFC; identify subjects with real maize allergy and obtain sera for potential immunoblotting studies.

Methods

The term maize will be used herein to identify the species *Zea mays*, the term *corn* has not been used because it is used to identify maize typically in the United States.

Study

The study was an international research project supported by the European Union. The frequency of maize allergy was investigated in three European countries: Denmark, Switzerland and Italy.

Patients

During the period March 2002–April 2004 out-patients from four allergy Units in Europe were used to identify subjects with presumed maize allergy: Niguarda Cà Granda Hospital (Milan, Italy), Milan University Hospital (Milan, Italy), the Swiss University Hospital Zürich (Zürich, Switzerland), and the Allergy Center, Department of Dermatology, Odense University Hospital, Odense, Denmark. Approval for the study was obtained by the Ethics Committees of all four Hospitals.

Patients were selected on the basis of suspected maize allergy and not on the basis of allergy to pollen or positive skin test or specific IgE for maize. All of the patients selected reported a clinical history of symptoms shortly after the ingestion of maize or products that contained maize as an ingredient. All the subjects had eliminated maize from their diet. Patients with a history of severe symptoms such as anaphylaxis or severe asthma following maize ingestion were not recruited. Treatment with antihistamines and glucocorticoids was suspended at least 10 days before the challenge. The patient was asymptomatic on the day of the challenge. In case of atopic dermatitis the patient obtained the best possible skin condition before undergoing challenge. Subjects with a history of anaphylaxis to maize were not enrolled in this study inasmuch as patients with a clear-cut case history of anaphylaxis (or a severe systemic reaction) to one or more specific food items should not be challenged [16]. Patients with a clear history of maize anaphylaxis were recruited for the employment of the sera for subsequent maize allergen characterization.

Skin testing

All the subjects underwent SPT with commercial maize extract (Stallergenes, Antony Cedex, France) as well as extracts for grass, birch, mugwort, parietaria and ragweed (Stallergenes). Skin testing was carried out on the volar aspect of the forearm with a monodentate lancet; histamine (10%) was used as positive control and saline as negative control. Tests were considered positive if the weal produced had a mean diameter of at least 3 mm [17].

Specific immunoglobulin E

All patients were tested for maize specific IgE antibodies (CAP FEIA, Pharmacia, Upjohn, Uppsala, Sweden).

Challenge testing

Maize was eliminated from the diet at least 1 week before the challenge. The patients were given the test meals as in-patient on separate days after an overnight fast. The physician and patient were both blinded to the protocol.

The test meal was developed by the dieticians of the Niguarda Cà Granda Hospital [18]. The ingredients used for the preparation of active meal were maize flour, potato starch, bitter cocoa powder, sugar, water, lemon syrup, and saffron. The same ingredients were used for the placebo meal, partially cooked minced rice was used instead of maize. Allergies to the masking ingredients were excluded before submitting the patient to the challenge. Pre-challenge analysis of the maize flour by PCR amplification (Agnesi Spa, Imperia, Italy) did not reveal transgenic contamination.

The triangle test was used in a group of maize tolerant subjects to evaluate for sensory difference between the active and placebo tests [19]. DBPCFC with up to 25 g of maize flour was performed on all the patients enrolled.

Challenge procedure. Informed Consent was obtained from all the patients; consent was obtained by the parents of minors (i.e. under 18 years). Precautions were taken for possible systemic reactions. Intravenous access was obtained for all the patients.

Before administering the test meal the oral cavity and skin were carefully inspected for pre-existing lesion; blood pressure and forced expiratory volume in 1 s (FEV₁) were measured on all the patients before the challenge; pediatric patients that could not properly perform spirometry underwent peak expiratory flow (PEF) measurement. Spirometry was performed before each subsequent dose if there was a history of asthma and whenever respiratory symptoms were reported during the challenge. A positive reaction for asthma was defined as a decrease in FEV₁ of at least 15% as compared with baseline.

Only 'immediate' skin reactions were recorded as positive in patients with a history of atopic dermatitis. Immediate skin reaction were defined as erythema, and/or pruritus and/or wheal-papule, in an area known to be subject to eczema, observed throughout the challenge period.

Double-blind, placebo-controlled food challenge. Active and placebo test meals were administered on separate days. Doses were delivered at 20 min intervals. A minimum starting dose of 100 mg of raw maize flour was administered; subsequently the following doses were administered (cumulative dose is shown in parentheses): 500 mg (600 mg), 1 g (1.6 g), 1.5 g (3.1 g), 3.5 g (6.6 g), 6.4 g (13 g), 12 g (25 g). The total cumulative dose administered was 25 g of raw maize flour. All the doses were administered unless convincing symptoms appeared. Cooked maize flour was used for challenging 4 children for better taste compliance with the challenge meal.

Open challenge. As indicated by European guidelines [16] patients with negative maize DBPCFC underwent open

challenge with 25 g of cooked maize flour (polenta). However open challenge was given as a graded challenge and not as a single dose as a precaution in case of false negative DBPCFC. Provided that no symptoms occurred each subject ate 1 g of polenta, this amount was doubled every 20 min until completion of the test meal. Open challenge was performed soon after the negative DBPCFC (7–21 days).

Data analysis

Sensitivity (SE), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) for maize skin test and specific IgE were calculated according to the method of Goldman [20].

We defined the above statistics as:

P (prevalence) = Positive oral provocations/Total patients tested

TP (true positive): patients with positive oral provocation and positive SPT and/or specific IgE

FP (false positive): patients with negative oral provocation and positive SPT and/or specific IgE

TN (true negative): patients with negative oral provocation and negative SPT and/or specific IgE

FN (false negative): patients with positive oral provocation and negative SPT and/or specific IgE

$$SE = TP / (TP + FN)$$

$$SP = TN / (TN + FP)$$

$$PPV = (TP \times P) / [(TP \times P) + FP(1 - P)]$$

$$NPV = TN(1 - P) / [TN(1 - P) + FN \times P]$$

Results

Only Italy and Switzerland recruited maize allergic patients. Maize allergy was not detected in the Danish centre throughout the entire study period.

Patients

A total of 27 patients (24 Italian and 3 Swiss) with suspected maize allergy were selected for the study. Clinical histories for maize food allergy were in keeping with IgE mediated symptoms. Patient characteristics were distributed as follows for sex and age: 23 adults, 4 children; 20 F, 7 M; age 4–68 years, mean 30.2. Table 1 lists demographic data, SPT and specific IgE, clinical history and sensitizing pollens. All of the subjects had positive skin test and/or specific IgE for maize. The majority of the patients selected were grass pollen positive, 19/27 (70.4%).

The patients studied also had a high rate of sensitivity to other fruits and vegetables: apple (pts. 3–7, 15, 18, 23, 24),

Table 1. Demographic data, clinical history for maize, maize skin test and specific IgE values, pollen sensitization

N	Sex	Age (year)	History	Maize			N	Sex	Age (year)	History	Maize			Pollen	N	Sex	Age (year)	History	Maize			Pollen
				SPT	Maize CAP (kU/L)	Maize SPT					Maize CAP (kU/L)	Maize SPT	Maize CAP (kU/L)									
1	M	33	U	+++	2.8	+	10	F	12	V, GI	4.34	+	4.34	M	19	F	25	U	-	-	0.45	-
2	F	50	U, OAS, AE	+++	68.3	++	11	F	5	AD	28.6	++	28.6	G,B,M,R	20	M	21	OAS	+	+	7.53	G,B,M,P,R
3	F	35	AE	+++	7.51	+	12*	F	25	OAS	3.3	+	3.3	G,B	21	M	18	U	-	-	0.84	-
4	F	24	A, AD	++	63.4	++	13*	F	35	OAS	0.62	++	0.62	G,B	22	F	23	AE	-	-	2.49	-
5	F	25	OAS	-	5.59	-	14	F	48	GI	0.38	++	0.38	G,B,P,M	23	M	23	P	-	-	7.36	G
6	F	24	OAS, U	+++	2.54	++	15	F	31	AE	0.35	-	0.35	B,M	24	F	58	OAS	+	+	11.7	G,B
7	M	37	U, AE	-	0.42	-	16	F	38	E	1.15	++	1.15	G	25	F	29	OAS	-	-	0.46	G,B,M
8	F	24	OAS, U	++	1.36	++	17	F	28	OAS, AD	8.7	+	8.7	G,B,M	26	M	7	AD, E	++	++	2.73	G,B
9	M	4	A	+	1.44	+	18	F	60	P	0.37	+	0.37	G,B,M,P,R	27*	F	29	OAS, AE, D	++	++	2.65	G,B

*Swiss pts.

GI, abdominal colic/diarrhea; V, nausea/vomit; AD, atopic dermatitis; OAS, oral allergy syndrome; P, pruritus; E, erythema; U, urticaria; AE, angioedema; D, dyspnoea; A, asthma; G, grass; B, birch; P, parietaria; M, mugwort; R, ragweed.

apricot (pts. 2, 4, 5, 17, 23), banana (pts. 2, 5), barley (pts. 2, 5), carrot (pts. 2, 18, 24), beans (pts. 1, 2, 4), celery (pts. 2, 4, 18), cherry (pts. 2-4, 15, 17, 23), chestnut (pts. 2, 14, 18), fennel (pts. 2-5, 10, 14, 17, 18, 22, 23, 24), grape (pts. 2-4, 5, 18), hazelnut (pts. 1-5, 9, 11, 14, 17, 18, 20, 23, 24), kiwi (pts. 2, 18, 23, 24), melon (pts. 3, 18), orange (pts. 1, 2), parsley (pt. 1, 3-5, 14), peach (pts. 2-5, 15, 17, 19, 20, 22, 23), peanut (pts. 1-4, 6, 11, 12, 14, 19, 20, 22, 24-26), pear (pts. 3, 15, 18, 24), plum (pts. 2, 4, 5, 9, 17, 23), potato (pts. 1, 5, 18, 19), rice (pt. 1-5, 18), sesame seed (pts. 1, 16), soy (pts. 3, 4, 6, 11, 18, 20, 24, 26), strawberry (pts. 1, 4, 18), sunflower seed (pts. 1, 20), tomato (pts. 5, 14, 17, 19, 24), walnut (pts. 1-6, 10, 11, 17, 19, 20, 22, 23), wheat (pts. 1-4, 10, 15, 17, 23, 26). Food allergic symptoms to maize appeared in adulthood in all but 4 patients (pts. 9, 10, 11, 26).

Double blind placebo-controlled food challenge

A total of 27 patients underwent DBPCFC with maize (24 Italian, 3 Swiss). All the meals tested were well accepted by all the patients and no severe reaction was manifested during all 27 challenges. Table 2 shows the results of the positive challenges, the symptoms provoked and the lowest PD. Thirteen of the 27 (48%) patients had a positive DBPCFC with maize, 10 adults and 3 children.

Patients 14-27 were negative to DBPCFC: 2/14 patients were placebo-responders (pts. 15, 23) and 12/14 were non-responders. Nearly all of the non-responders reintroduced cooked maize flour openly (polenta, 25 g); patient 26 (age 7 years) failed to complete the open challenge because of poor taste compliance, however no symptoms were manifested after having eaten 5 g. Patients 16 and 19 complained 'drowsiness' after open challenge with maize.

Symptoms observed during positive double blind placebo-controlled food challenge

Nearly all the patients with positive challenge developed symptoms either during the challenge or immediately after test completion. The symptoms documented during the 13 positive maize DBPCFCs are reported in Table 2. Symptoms were subjective in seven patients, primarily OAS; generalized persistent erythema = 3, generalized pruritus = 2, generalized urticaria = 1, eczema flare = 1, angioedema = 2, abdominal pain/diarrhea = 3, nausea/vomit = 1, persistent cough = 1.

Patient 9 was a pediatric patient, who presented persistent cough during the challenge; the cough did not allow for proper spirometry or PEF measurement. However cough abated after inhalation of albuterol (100 mcg) via inhalation chamber. Patient 10 had OAS with gastrointestinal involvement thus it can be considered a level 2 severity of OAS [21].

Table 2. Detailed results of the positive maize DBPCFCs

N	DBPCFC		Symptoms	PD (g)	N	DBPCFC		Symptoms	PD (g)
	A	P				A	P		
1	+	—	U	10	8	+	—	OAS, AE	25
2	+	—	U, V	2.5	9	+	—	C	12.1
3	+	—	OAS	0.5	10	+	—	OAS, GI	0.1
4	+	—	E, AD, GI	1.6	11	+	—	Pr, GI	3.1
5	+	—	OAS	0.1	12	+	—	OAS	0.6
6	+	—	OAS	25	13	+	—	OAS	1.6
7	+	—	E, AE	25					

A, active; P, placebo; PD, provocation dose; OAS, oral allergy syndrome; Pr, pruritus; E, erythema; U, urticaria; AE, angioedema; GI, abdominal colic; V, nausea/vomit; AD, atopic dermatitis flare; C, cough; DBPCFC, double blind placebo-controlled food challenge.

A review of Table 2 shows that 23% of the positive patients (pts. 2, 4, 11) manifested symptoms that involved 2 or more organ systems; these patients did not require treatment with epinephrine.

Provocation dose

The range of PD for positive maize challenges was 0.1–25 g. Table 2 shows the lowest PD for all the positive challenges.

Four patients (30.8%) had a PD for maize that was <1 g: (pts. 3, 5, 10, 12); two of these patients (15.4%) reacted after 100 mg of maize. Four patients had a PD between 1.6 and 4.6 g (pts. 2, 4, 9, 11, 13). Five patients had a PD between 10 and 25 g. Only three of the 13 positive patients reacted to the total dose of 25 g (pts. 6, 7, 8). Only three patients showed maize induced anaphylaxis (i.e. symptoms in >2 organ systems); the PD was 1.6, 2.5 and 3.1 g, in pts. 4, 2 and 11, respectively.

Data analysis

Table 3 shows the results of SPT with commercial maize extract, and specific IgE for maize in patients with positive

Table 3. Results of SPT with commercial corn extract, and Specific IgE for corn in patients with positive and negative corn DBPCFC

TESTS	DBPCFC	
	+ve*	—ve†
Commercial SPT +ve	11	8
Commercial SPT —ve	2	5
IgE +ve (>0.35 kU/L)	13	12
IgE —ve (<0.35 kU/L)	0	1

*Active +ve, placebo —ve.

†Negative DBPCFC; 1 case active +ve and placebo +ve (pt. 23) was not considered.

DBPCFC, double blind placebo-controlled food challenge; SPT, skin prick test.

Table 4. Sensitivity (SE), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) values for corresponding results of skin prick test (SPT) with commercial maize extract and CAP for maize specific IgE in patients with positive and negative maize double blind placebo-controlled food challenge (DBPCFC)

Part A	SE	SP	PPV	NPV
Commercial SPT	0.846	0.384	0.579	0.714
CAP FEIA	1.00	0.077	0.520	1.00

and negative maize DBPCFC. Table 4 shows the performance characteristics of SPT with commercial maize extract and CAP for maize specific IgE in patients with positive and negative maize DBPCFC. We found no correlation between the specific IgE level and the PD ($r = 0.347$).

Discussion

This study demonstrates that symptomatic maize allergy takes place in Italy and Switzerland. This is the first report of suspected maize allergy confirmed by DBPCFC in a large group of patients. Nearly half of the patients tested (48%) were positive to DBPCFC. Twenty-three percent of the challenge-positive patients were children; this observation was most likely due to patient selection rather than a result of the general population. The fact that 48% of the patients tested were positive to maize DBPCFC confirms that maize is an important food allergen in southern Europe and should not be overlooked especially when the clinical history implicates this food as well as other food items.

In this study, 77% of challenge positive patients were grass pollen positive as compared with 64% in the challenge negative group. Thus, our study shows that there was little difference in grass pollen sensitization between the challenge positive and challenge negative groups. This was not the case in the wheat study carried out by our group [22], i.e. only 38% of the wheat

challenge positive patients were grass pollen positive as compared with 64% in the challenge negative group. Thus maize food allergy was more frequently associated to grass pollen sensitization.

In our study the symptoms observed during the challenge were in keeping with the symptoms of typical IgE-mediated food allergy; all of the symptoms were manifested either during the challenge or immediately after test completion. The fact that the symptoms reported in our study were observed during oral provocation and not simply those reported by the clinical history makes these maize induced symptoms evidence-based.

It is noteworthy that in this study 23% of the challenge-positive patients reported symptoms that involved two or more organ-systems, thus fulfilling the criteria for maize-induced anaphylaxis; none of the patients with maize induced anaphylaxis required emergency treatment with epinephrine.

The most severe manifestations observed were three cases of abdominal colic and one case of cough that subsided after use of albuterol (Italian patients).

Only one of the two patients with a clinical history of asthma after maize ingestion manifested respiratory symptoms after challenge (pt. 9, cough); the other patient with a clinical history of maize-induced asthma (pt. 4) probably did not present respiratory symptoms because the challenge was positive at a low PD, thus it is likely that greater doses of maize were necessary to induce asthma. Clinical history correlated well with challenge outcome in the remaining patients. Only five patients (three Italian, two Swiss) presented only OAS after maize challenge; all but one of these patients had a low PD (see Table 2). The two Swiss patients manifested only OAS symptoms during the challenge; the fact that we did not detect Swiss patients with maize anaphylaxis may be due to the absence of LTP sensitization in northern Europe.

It is interesting to note that those patients that reported only a history of maize-induced erythema or pruritus ended up having a negative challenge with maize (pts. 16, 18 and 23). Although only a small number of patients had pruritus this consideration may be of value when choosing patients for a diagnostic challenge with maize, because in our study the presence of erythema/pruritus alone was associated with a negative challenge outcome.

The fact that patients with severe food allergy can react to small amounts of hidden food has prompted many studies to evaluate the clinical reactivity by standardized challenge. In fact, the lowest provoking dose has been reported for some of the more commonly allergenic foods, i.e. wheat, peanut, soy, egg, milk [22–25], however there are no literature reports that verify the lowest provoking dose for maize under standardized DBPCFC conditions. Our study shows that in maize DBPCFCs symptoms were induced at a dose of 100 mg in two challenges (pts. 5 and 10); four patients developed objective symptoms with a

PD that was < 1 g (pts. 3, 5, 10 and 12). It is important to underline that the above provoking doses were observed in patients that did not present a history of very severe reactions. Present guidelines discourage the use of food challenges in patients with severe food allergy, thus one can never directly identify the threshold dose for an incriminated food in these exquisitely allergic patients. Sixty-two percent of the positive patients reacted to ≤ 3.1 g for maize. This percentage is much higher than the percentage observed for wheat allergic patients (46%) with the same PD cut-off [21]. When we considered the reactive dose limit ≤ 1.6 g of maize flour we found that 46% (6/13) of the patients reacted to such a low PD; 4/6 patients had OAS alone. Our study shows that nearly half of the maize allergic patients reacted to a dose that was ≤ 1.6 g.

The distribution of quantitative values for maize specific IgE was not comparable between the challenge-positive (pts. 1–13) and challenge-negative (pts. 14–27) groups (Table 1). In fact the mean CAP value for challenge positive group was 14.6 kU/L as compared with the 3.3 kU/L of the challenge negative group. Both positive and negative challenge groups presented both low and high values for maize specific IgE, thus a quantitative assessment of maize-specific IgE did not allow for the calculation of a cut-off via the use of a ROC curve. However, we found that the highest specific IgE value for negative challenge patients was 11 kU/L and that a value ≥ 11 kU/L was seen only in maize DBPCFC-positive patients. Nonetheless, we cannot conclude that CAP values below 11 kU/L do not correlate with positive maize challenge inasmuch as 10 of the 13 positive with positive maize challenge had maize specific IgE < 11 kU/L. Moreover, it is possible that challenge negative patients with a high CAP become reactive to maize only under certain conditions such as aspirin ingestion, infection, exercise etc.

We found that the performance characteristics of maize specific IgE (CAP System, Pharmacia) were superior to skin test as regards sensitivity (1.00 vs. 0.846); the SP, PPV were extensively disappointing for both tests; the NPV was 1.00 for maize specific IgE and 0.714 for SPT (see Table 4). Even if the CAP value did not allow us to discriminate all of the maize allergic subjects, comparison of the CAP results with the results of the challenge allowed us to detect that sensitivity and NPV were greater for specific IgE. Thus maize CAP System seems to be more useful than skin test when screening patients with suspected maize allergy; however both tests were poor predictors of disease when compared with DBPCFC.

In conclusion, our study is the first controlled study performed on a large group of maize allergic subjects from Italy and Switzerland. We have shown that maize food allergy does occur in adult and pediatric patients; in 38% of the maize allergic patients there was no grass pollen sensitization. Also, we have shown that the ingestion of

maize flour was able to provoke immediate symptoms in all the challenge-positive patients tested. In fact, we observed that 31% (4/13) of the adult patients with positive DBPCFC had symptoms that involved two or more organ-systems, thus a more appropriate classification of symptoms in these patients is maize anaphylaxis. Moreover, we have shown that in three patients a clinical history of only pruritus was associated with negative challenge outcome. Although only a small number of patients had pruritus this consideration may be of value when choosing patients for a diagnostic challenge with maize.

Lastly, all the patients included in this study were found to be maize allergic after purposely investigating the clinical histories for maize-induced symptoms. Therefore, it is important to always consider maize allergy in all food allergic subjects that report symptoms with this food item.

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