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Clinical relevance of sensitization to lupine in peanut-sensitized adults

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Original article

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Background: The use of lupine in food has been increasing during the last decade and allergic reactions to lupine have been reported, especially in peanut-allergic patients. The frequency and the degree of cross-reactivity to other legumes are not known. The aim of the study was to investigate the frequency of sensitization to lupine, and in addition to pea and soy, and its clinical relevance, in peanut-sensitized patients. Furthermore, to determine the eliciting dose (ED) for lupine using double-blind placebo-controlled food challenges (DBPCFC).
Methods: Thirty-nine unselected peanut-sensitized patients were evaluated by skin prick tests (SPT) and ImmunoCAP to lupine, pea, and soy. Clinical reactivity was measured by DBPCFC for lupine, and by history for pea and soy.
Results: Eighty-two percent of the study population was sensitized to lupine, 55% to pea, and 87% to soy. Clinically relevant sensitization to lupine, pea, or soy occurred in 35%, 29%, and 33% respectively of the study population. None of the patients was aware of the use of lupine in food. The lowest ED for lupine, inducing mild subjective symptoms, was 0.5 mg, and the no observed adverse effect level (NOAEL) was 0.1 mg. No predictive factors for lupine allergy were found.
Conclusion: In peanut-sensitized patients, clinically relevant sensitization to either lupine or to pea or soy occurs frequently. The ED for lupine is low (0.5 mg), which is only fivefold higher than for peanut. Patients are not aware of lupine allergy and the presence of lupine in food, indicating that education is important to build awareness.

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Key words: clinical relevance; double-blind placebo-controlled food challenge; lupine allergy; peanut; sensitization.

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Lupine (*Lupinus albus*), a member of the legume family, has been recognized as a novel food since 1996. The bran and flour of this legume have been supplied for food manufacturing, wherein it contributes to the fiber and protein contents, and also to some textural properties, particularly in bakery products (1). Lupine can be cultivated in all climates, making it an attractive crop.

The addition of lupine flour to foods was first permitted in countries like France and the UK (2). The inclusion of lupine in foods has increased notably in many European countries during the last decade. Reasons for this development are the import of bakery products from France and the use of lupine as replacement for potentially genetically modified soy.

The first published report of an allergic reaction to lupine appeared in 1994 (1), followed by 12 reports until 2006 based on a Pubmed search. Moreover, thermal processing appears to have no effect on the allergenicity of lupine (3–5). Therefore, the presence of lupine in processed food represents a potential risk for allergic consumers.

Lupine allergy may arise by cross-reactivity in people who are already allergic to another member of the Legume family, in particular peanut (1, 2, 4, 6), or by primary sensitization (7–9).

Serological cross-reactivity between members of the legume family occurs frequently, but is not always reflected by clinically relevant allergies (10–12). In 1994, Hefle et al. (1) investigated cross-reactivity between peanut and lupine. They showed that five out of seven (71%) peanut-allergic patients had a positive skin prick test (SPT) to lupine. The clinical relevance of this sensitization was not investigated. Moneret-Vautrin et al. (6) showed that 44% out of 24 peanut-allergic patients revealed a positive SPT response to both peanut and lupine, and five out of six patients tested, reacted to

Abbreviations: DBPCFC, double-blind placebo-controlled food challenge; ED, eliciting dose; NOAEL, no observed adverse effect level; PBS, phosphate buffered saline; SPT, skin prick test.

lupine as determined by double-blind placebo-controlled food challenge (DBPCFC). This suggests that the use of lupine is a risk especially for peanut-allergic patients.

In this study, we investigated the frequency of sensitization to lupine and its clinical relevance, and also to pea and soy, in peanut-sensitized patients. Furthermore, we determined the eliciting dose (ED) for lupine by DBPCFC.

Materials and methods

Patients

Ninety-two adult peanut-sensitized patients with or without symptoms to peanut, who visited the outpatient clinic of the Department of Dermatology/Allergology of the University Medical Center Utrecht between 2003 and 2006, were approached to participate via an invitation letter. The selection criteria were a SPT to peanut extract (ALK-Abelló, Nieuwegein, The Netherlands) with the area of the peanut wheal at least half of the area of the positive control [ratio ≥ 0.5, corresponding with SPT ≥ 2+ according to Aas et al. (13)], and/or specific IgE to peanut ≥ 0.7 kU/l (ImmunoCAP, Phadia, Uppsala, Sweden). These high cut-off levels were chosen to obtain a higher likelihood that sensitization would be associated with clinical allergy.

Pregnancy, significant concurrent disease, unstable asthma and oral medication with corticosteroids or β-blocking agents were the exclusion criteria.

Thirty-nine patients (42%) met these criteria, agreed to participate, and gave written informed consent before enrolment in the study. Detailed histories of allergies to peanut, green pea and soy, and atopy were obtained by using a standardized questionnaire.

Sixteen patients were unwilling to participate because of lack of interest ($n = 10$) or inability to discontinue antihistamines ($n = 6$). Thirty-seven patients (40%) did not respond.

This study was reviewed and approved by the Medical Ethical Committee of the University Medical Center Utrecht.

Skin prick tests and specific IgE measurements

All 39 patients included in the study were subsequently evaluated by SPT with commercial extracts of peanut, green pea, soy, grass pollen and birch pollen (ALK-Abelló, Nieuwegein, the Netherlands) and with lupine extract prepared in the following way: Lupine flour (20 g) was suspended in 200 ml phosphate-buffered saline (PBS, pH 7.4) containing 0.1% phenol, and was stirred overnight at 4°C. After clarifying the suspension by centrifugation (1800 ***g***, 30 min) and filtration, the supernatant solution was mixed with an equal volume of glycerol. The resulting solution in PBS-glycerol (50% v/v) was subsequently sterilized by filtration (0.22 μm pore size). The protein content of this extract was determined to be 10.2 mg/ml using the Bradford method (14). Ten healthy subjects were used as negative controls for SPT with lupine extract. Skin prick test responses in these control subjects were all negative.

Histamine dihydrochloride (10 mg/ml) and the glycerol diluent of the SPT extracts served as positive and negative controls, respectively (ALK-Abelló). The SPT were performed and recorded as described by Dreborg (15). Skin prick test were considered positive when the wheal reaction was 7 mm^2 (diameter 3 mm) and greater than the negative control. Skin prick test responses were expressed as the ratio of the wheal reaction in millimetres squared, evaluated by computer scanning (16) divided by the wheal reaction of the positive control to correct for the individual variance in reactivity (17). The use of computerized method is recommended to reduce the measurement error of traditional methods (18). Skin prick test ratios were regarded positive when the ratios were ≥0.25, i.e. when the wheal areas were at least 25% of the wheals induced by the positive control (corresponding with SPT 1+). As one patient had dermographism, the SPT results of this patient were not included in the analysis of SPT data.

Specific IgE levels to peanut, lupine, green pea, soy, grass pollen and birch pollen, were determined in all patients by the ImmunoCAP (Phadia). An IgE level of ≥ 0.35 kU/l was taken as a positive result.

Clinical reactivity

Clinical reactivity to lupine was investigated by DBPCFC in 30 of the 39 peanut-sensitized patients according to the threshold consensus protocol (19) with some modifications (20). Nine patients were unwilling to participate in this part of the study because of lack of time ($n = 4$), anxiety ($n = 2$), or lack of interest ($n = 3$). The lupine flour used was a commercially available mild white lupine flour (protein content 36.2% by Leco 2000 method, *L. albus*), obtained from Magenta Sales in England produced by CANA (Martigne-Ferchaud, France). The amounts of lupine flour were 0.01 mg, 0.1 mg, 0.5 mg, 1 mg, 10 mg, 100 mg, 300 mg, 1 g, and 3 g. To mask the lupine doses, 5 g of instant mashed potatoes were added. The validity of the binding was tested by experienced dieticians and by a team of 10 persons. No differences in flavor, texture, and smell were observed. The hospital pharmacy prepared the challenge materials. Four similarly prepared placebo doses of 5 g of instant mashed potatoes were randomly interspersed between the increasing lupine doses on the same day. The use of interspersed placebos was chosen because the procedure could be completed in 1 day. The doses were prepared with 15 ml warm water to a final dose of 20 g. The challenge was discontinued when objective symptoms occurred or when subjective symptoms lasted for more than 45 min. The ED was determined as the lowest dose eliciting a convincing subjective allergic reaction.

All of the challenges were conducted in a hospital setting, with careful monitoring of the patients. Full emergency treatment was readily available.

Statistics

Correlations were analyzed with the nonparametric Spearman's rank test. Differences in proportions between groups were tested by two-sided Fisher's exact test. Calculations were performed using SPSS (version 12, SPSS Inc., 2001, Chicago, IL, USA). *P*-values < 0.05 were considered statistically significant.

Results

Patient characteristics

Thirty-nine patients with sensitization to peanut entered the study. The mean age was 33 years (range, 17–57). Nineteen patients suffered from atopic eczema (49%), 17 from concomitant asthma (44%), and 36 patients reported pollinosis symptoms (92%). Sensitization to grass pollen was present in 79% of the study population and to birch pollen in 85%.

Table 1. Sensitization to legumes in peanut-sensitized patients with and without symptoms to peanut (number of patients, %)

	Peanut		Lupine		Green pea		Soy	
	CAP	SPT	CAP	SPT	CAP	SPT	CAP	SPT
Peanut-sensitized patients (n = 39)	36/39 (92)	33/38* (87)	21/39 (54)	26/37*† (70)	14/39 (36)	18/38* (47)	18/39 (46)	26/38* (68)
Peanut-allergic patients (n = 29)	27/29 (93)	25/29 (86)	18/29 (62)	21/28† (75)	11/29 (38)	14/29 (48)	15/29 (52)	19/29 (66)
Nonpeanut-allergic patients (n = 10)	9/10 (90)	8/9* (89)	3/10 (30)	5/9* (56)	3/10 (30)	4/9* (44)	3/10 (30)	7/9* (78)

Positive IgE: specific IgE ≥ 0.35 kU/l determined by the ImmunoCAP; positive SPT response: ratio ≥ 0.25.
*The SPT response of one peanut-sensitized patient without symptoms was not included, because of dermographism.
†One peanut-sensitized patient with symptoms was not tested by SPT with lupine.

Skin prick test responses to peanut were positive in 87% of the patients (n = 33), 92% had a positive CAP (n = 36), and 79% (n = 30) had both a positive SPT and CAP. Levels of IgE to peanut ranged from <0.35 to >100 kU/l (median 2.52 kU/l). Skin prick test responses to peanut ranged from a ratio of 0 to 18.4 when compared with the positive control. Twenty-nine of 39 patients (74%) reported symptoms to peanut by history. Three of these patients were previously challenged with peanut, which confirmed the diagnosis of peanut allergy.

Co-sensitization to lupine, pea and soy

To further characterize our study population, the grade of co-sensitization to different legumes was investigated. The majority (82%) was also sensitized to lupine as shown by CAP and/or SPT, whereas 55% was sensitized to pea, and 87% to soy.

The patients were further divided into two sub-groups, of patients that do have symptoms to peanut and those who have not, to determine whether clinically relevant peanut sensitization had an effect on the grade of co-sensitization to other legumes. Sensitization to legumes as measured by CAP and SPT in the whole peanut-sensitized group and in the two sub-groups is summarized in Table 1. In general, the sensitization frequency to lupine, green pea and soy was higher as measured by SPT than by CAP. The sensitization frequency to lupine, pea and soy as measured by CAP, and to lupine and pea as determined by SPT tended to be higher in peanut-allergic patients when compared with patients that were only sensitized, but this difference was not statistically significant.

The overlap of sensitization to lupine, pea, and soy with sensitization to peanut is demonstrated in Table 2. About half of peanut-sensitized patients (53%) were sensitized to all other three legumes, whereas only two patients (5%) were mono-sensitized to peanut.

As cross-reactivity is certainly a prominent feature of the IgE response, we studied whether the level of IgE to peanut was correlated with the level of IgE to the other legumes. A significant correlation was observed between the IgE level to peanut and the IgE level to respectively lupine [correlation coefficient (r) = 0.6, P < 0.01], pea (r = 0.42, P < 0.01), and soy (r = 0.69, P < 0.01). There was also a significant correlation between the SPT reactivity to peanut and lupine (r = 0.36, P = 0.03), whereas the correlations between peanut and respectively pea (r = 0.31, P = 0.05), and soy (r = 0.3, P = 0.06) were borderline significant.

Table 2. Number of peanut-sensitized patients with sensitization to other legumes

Lupine	Pea	Soy	n (%)
–	–	–	2 (5)
+	–	–	3 (8)
+	+	–	1 (3)
+	–	+	7 (18)
+	+	+	20 (53)
–	–	+	5 (13)
–	+	–	0 (0)
–	+	+	0 (0)

Sensitization: SPT ratio ≥ 0.25 and/or specific IgE ≥ 0.35 kU/l.
+, sensitization present; –, no sensitization.

Clinical reactivity to lupine and eliciting doses determined by DBPCFC

None of the patients reported symptoms to lupine by history because they were unaware that lupine was used as a food ingredient and can cause allergic symptoms. In 30 patients, clinical reactivity to lupine was assessed by DBPCFC, and nine of them (30%) had a positive DBPCFC. The first symptom reported during all but one of the challenges was itching in the oral cavity (oral symptoms; OS), which recurred after subsequent higher doses (Table 3). Four patients additionally developed more serious, but still subjective, gastrointestinal symptoms (nausea and abdominal pain). In two patients, this resulted in discontinuation of the challenge because it lasted for more than 45 min. Dyspnea without an objective forced expiratory volume in 1 s decrease was found in three patients. In one of them, this was the first symptom reported.

All the patients tolerated a dose of 0.1 mg lupine flour with neither subjective nor objective symptoms, so the no observed adverse effect level (NOAEL) for our patient group in this study was 0.1 mg lupine flour based upon elicitation of subjective reactions. The minimal ED for subjective symptoms for the individual patients in this study varied from 0.5 to 3000 mg (Table 3), inducing

Table 3. Clinical reactivity to lupine flour during DBPCFC (n = 9*)

	DBPCFC dose (mg)									
Patient	0.01	0.1	0.5	1	10	100	300	1000	3000	ED (mg flour)
L02KP	–	–	–	–	OS	OS	OS	OS, rhinitis	–	10
L11KP	–	–	–	–	–	–	–	–	OS	3000
L18KP	–	–	–	–	–	–	–	OS	OS, nausea	1000
L19KP	–	–	–	–	–	OS	OS	OS	OS	100
L20KP	–	–	–	–	–	–	–	OS	OS	1000
L34KP	–	–	–	–	Dyspnea	Dyspnea	Dyspnea, nausea	Dyspnea	n.t.	10
L36KP	–	–	OS	OS	OS	OS, dyspnea >1 h	n.t.	n.t.	n.t.	0.5
L37KP	–	–	–	OS, abdominal pain	OS, abdominal pain >1 h, dyspnea	n.t.	n.t.	n.t.	n.t.	1
L39KP	–	–	–	OS	OS nausea >45 min	n.t.	n.t.	n.t.	n.t.	1

ED, eliciting dose; OS, oral symptoms; n.t, not tested; –, no symptoms.
*Nine of 30 patients had a positive DBPCFC with lupine.

mild-to-moderate symptoms. The minimal ED based on objective symptoms was 1000 mg and consisted of rhinitis (Table 3). Three patients failed to develop objective symptoms or subjective symptoms more serious than OS even at the highest administered dose of 3000 mg (Table 3).

Sensitization and allergy to lupine in relation to peanut characteristics

As sensitization to different legumes in our peanut-sensitized patients frequently occurred, we evaluated the clinical relevance of these sensitizations separately (Table 4A).

Twenty-three of 30 (77%) lupine-challenged patients had a combined sensitization to peanut and lupine, in line with the co-sensitization frequency in the whole study population, demonstrating that lupine sensitization frequently occurs. In eight of these 23 lupine-sensitized patients (35%), lupine allergy was demonstrated by positive DBPCFC.

Twenty-one patients did not respond during the challenge, of which 15 (71%) were sensitized to lupine, demonstrating a low specificity of CAP and/or SPT. Eight of nine lupine-allergic patients (89%) were lupine-sensitized, showing a high sensitivity (Table 4A).

To study whether symptoms to peanut had an effect on the frequency of symptoms to lupine, peanut-allergic patients were compared with the patients that were only sensitized. The frequency of symptoms to lupine tended to be higher in peanut-allergic patients (8/21) than in patients without symptoms to peanut (1/9), but this difference was not statistically significant ($P = 0.13$) (Table 4B).

Table 4. (A) Sensitization in relation to clinical symptoms to lupine, pea and soy in peanut-sensitized patients (number of patients). (B) Clinical symptoms to lupine, pea, and soy in relation to symptoms to peanut (number of patients)

	Sensitization to lupine		Sensitization to pea		Sensitization to soy	
	Yes	No	Yes	No	Yes	No
(A)						
Symptoms	8	1	6	1	11	3
No symptoms	15	6	15	16	22	2

	Peanut-allergic	Nonpeanut-allergic
(B)		
Symptoms to lupine		
Yes	8	1
No	13	8
Symptoms to pea		
Yes	6	1
No	24	8
Symptoms to soy		
Yes	12	2
No	18	7

Symptoms to lupine were determined by DBPCFC, and to pea and soy by history. Sensitization: SPT ratio ≥ 0.25 and/or specific IgE ≥ 0.35 kU/l.

Sensitization and allergy to pea and soy in relation to peanut characteristics

Twenty-one of 38 peanut-sensitized patients (55%) were also sensitized to pea. Six of them (29%) had a positive history to pea, demonstrating that about one out of three patients with sensitization to pea had clinical symptoms (Table 4A).

Regarding soy, 33 out of 38 peanut-sensitized patients (87%) were also sensitized to soy. Eleven of these 33 patients (33%) reported symptoms to a wide variety of soy-containing products, whereas three of five nonsoy-sensitized patients also had a positive history to soy (Table 4A). Together, these data demonstrate that sensitization to pea or soy might lead to clinical symptoms in about 30% of the patients, comparable to lupine. Having symptoms to peanuts or not had no effect on the frequency of symptoms to pea and soy ($P = 0.35$ and $P = 0.21$, respectively) (Table 4B).

Predictive factors for lupine-allergy

As an increase in the occurrence of allergic reactions to lupine has been suggested, and because many

Table 5. Differences between peanut-sensitized patients with and without lupine allergy

	Lupine-allergic (n = 9)	Lupine tolerant (n = 21)	P-value*
Lupine sensitization	8/9 (89%)	15/20 (75%)	0.29
Median CAP lupine	0.88 (0.50–2.85)	0 (0–0.76)	0.18
Median SPT lupine	0.58 (0.24–0.67)	0.38 (0.21–0.72)	0.31
Sensitization pea	6/9 (67%)	10/20 (50%)	0.23
Sensitization soy	7/9 (78%)	19/20 (95%)	0.20
Symptoms to peanut	8/9 (89%)	13/21 (62%)	0.13
Symptoms to pea	2/9 (22%)	4/21 (19%)	0.36
Symptoms to soy	4/9 (44%)	5/21 (24%)	0.18

*Fisher's exact test.

food-allergic patients are not aware of the use of lupine in food, it is relevant to estimate risk factors which are associated with lupine allergy. Therefore, our lupine-allergic patients were compared with nonlupine-allergic patients (Table 5). The distribution of sensitization to lupine, pea, and soy was similar in both groups. In addition, there was no significant difference in the frequency of symptoms to peanut, pea, and soy.

Independent predictive values of the IgE level and SPT response to lupine for lupine allergy could not be found by logistic regression analyses (data not shown), demonstrating that the sensitization level to lupine is not useful for suspecting an allergy to lupine within a peanut-sensitized population.

Discussion

Allergy to legumes may be mediated by primary sensitization via ingestion (7, 8, 21) or inhalation (7, 22, 23) or may be acquired after primary sensitization to pollen (24–26) or to another legume (27, 28). Although the route of sensitization and the frequency of allergic reactions to lupine are unknown, most reactions have been reported in peanut-allergic patients (1, 2, 4, 6). Therefore, in this study, the patterns and frequencies of sensitization to lupine, pea, and soy were analyzed in an unselected peanut-sensitized population. In addition, clinical symptoms to these legumes were evaluated. We chose to focus not only on peanut-allergic patients but to include all peanut-sensitized patients, because peanut-sensitized patients without symptoms to peanut could have symptoms to other legumes as well. This is illustrated by the fact that one peanut-sensitized patient without symptoms to peanut did have symptoms to lupine during the DBPCFC.

In our population, co-sensitization to lupine (82%), pea (55%), and soy (87%) frequently occurred, in line with previous studies (6, 10, 11). The majority of our patients (53%) was sensitized to all three legumes tested. It is not known whether this reflects co-sensitization towards distinct allergens or cross-reactivity. As the level of peanut-specific IgE was significantly correlated to the levels of lupine-, pea- and soy-specific IgE, similar IgE binding properties of these allergens (cross-reactivity) could be suggested. However, IgE-inhibition experiments are needed, to investigate and to identify allergens within lupine responsible for cross-reactivity. Recently, it was shown that patients allergic to lupine but not to peanut displayed IgE binding to other lupine allergens when compared with the patients with a combined allergy (29), which indicates that there are remarkable differences in allergen recognition between these two groups of patients. IgE binding to lupine allergens could not be inhibited by pre-incubation of the serum with birch pollen, soy flour, and green pea flour (29). In a few patients, cross-reactivity was found between peanut (150 kD allergen) and lupine (18–22 kD allergen) (29). This illustrates also that unique allergens might be involved in lupine-allergic patients.

Allergy to either lupine or to pea or soy was present in one-third of the study population, making it a more common feature than previously reported (12, 30). However, those previous studies were performed in children. It might be that the extents of clinically relevant cross-reactivity are higher in adults when compared with children because of dietary habits. The percentages of reactivity to pea and soy are probably somewhat overestimated. Clinical symptoms to lupine were confirmed by DBPCFC, but for pea and soy the same were only evaluated by history. As soy is usually consumed as an ingredient and not as a single food, it is more difficult to attribute symptoms to this allergen in contrast to pea which is usually eaten as such. Having symptoms to peanut or not had no effect on the grade of sensitization to lupine and on the frequency of symptoms to lupine. This illustrates that the peanut-sensitized patients without symptoms to peanut have comparable high risks for being lupine-allergic as the peanut-allergic patients.

There is little information in the literature on the lowest dose that causes allergic reactions to lupine (6). Our low-dose challenge data demonstrated that the no-observed-adverse effect level for this group of eight lupine-allergic patients was 0.1 mg lupine flour based on the elicitation of subjective symptoms. Thus, we can conclude, with 90% certainty that 75% of lupine-allergic individuals will not react to doses of 0.1 mg lupine flour or less. With objective symptoms, the no-observed adverse effect level was 1 mg of lupine flour although three of eight patients experienced only subjective responses even at the highest dose of 3000 mg. The lowest (cumulative) ED described previously was 265 mg of lupine flour, inducing abdominal pain and asthma in peanut-allergic patients (6). For peanut, we recently established the lowest dose that induced subjective symptoms using the same challenge protocol (9). The ED for subjective symptoms started from 0.1 mg peanut flour, and for objective symptoms from 10 mg, in line with previous reports (31, 32). Comparing the results of both studies, it appeared that the ED for lupine is only fivefold higher than that for peanut. The symptom progression of peanut and lupine

during the DBPCFC procedure with higher doses was similar indicating that the allergenicity of lupine might be more similar to peanut than, for example, to soy, as in our population soy usually induces mild symptoms. However, systemic reactions to soy have been described (33). Because our study included only 8 patients with clinical symptoms to lupine, further studies are needed in a larger group of lupine-allergic patients to confirm the ED findings in this study to a higher degree of statistical certainty (34).

Considering the potential severity of lupine allergy and the likelihood that reactions will occur in unsuspecting peanut-allergic consumers, factors were investigated to predict which patients were most likely to have lupine allergy. In our peanut-sensitized study population, no predictive factors could be identified by information that is commonly gathered in routine practice.

Food-allergic individuals are typically advised to employ specific avoidance diets to prevent reactions (35). The success of avoidance diets implies that food-allergic patients would be aware of their allergy and the use of that ingredient in foods. Currently, the EU requires the declaration of commonly allergenic foods and ingredients derived from those foods on labels of packaged foods (5). Peanut is included on the existing list of commonly allergenic foods in the EU. While the prevalence of lupine allergy is unknown, our results suggest that one-third of peanut-allergic individuals could also be allergic to lupine. As the prevalence of peanut allergy is approximately 0.5% of the overall population (36), the prevalence of lupine allergy could be as high as 0.15%. Furthermore, lupine-allergic patients reacted at doses as low as 0.5-mg lupine flour so modest exposures could provoke reactions. So, it is arguably justified that lupine is added to the EU list since December 2006 (Annex III A; 2000/13/EG). However, the declaration of lupine on food labels will be of limited benefit to individuals who may be unaware of their lupine allergy. This is shown by the fact that peanut-sensitized individuals are neither aware of their potential lupine allergy nor about the use of lupine in foods while clinically relevant sensitization to lupine occurs with a reasonably high frequency in the peanut-sensitized population. Moreover, we were unable to identify any diagnostic criteria other than use of lupine challenges to identify the subgroups of patients being lupine-allergic.

Thus, education is important to build awareness because labeling strategies alone are unlikely to be sufficient.

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