

Original article

Diagnosis and natural course of allergy to cooked potatoes in children

Background: Allergy to heat stable potato proteins can cause severe allergic disease in children.

Objective: To study diagnostic criteria for allergy to cooked potatoes and to describe its clinical characteristics and natural history.

Methods: Thirty-six children, aged 4–36 months, with atopic symptoms and having a positive potato-CAP and/or skin prick test (SPT) were included. Potato allergy was documented by means of provocation, or elimination and reintroduction or an unequivocal clinical history. Potato-CAP and SPT with a commercial extract were evaluated for diagnostic performance.

Results: Presenting symptoms in children with proven potato allergy ($n = 17$) were eczema (16 of 17), gastrointestinal complaints (eight of 17), urticaria and/or angioedema (five of 17), wheezing/rhinitis (three of 17) and anaphylaxis (two of 17). Fifteen children had previously diagnosed cow's milk protein allergy and were egg-sensitized. Potato-CAP at cut-off > 2 kU/l provided a 100% sensitivity and a 62.5% specificity for diagnosis of potato allergy, while a SPT score ≥ 3 had a 100% sensitivity and a score ≥ 4 had a 100% specificity. Tolerance to cooked potato was achieved in 80% of subjects at age 16–102 months. Of 12 subjects having reached the age of 3 years during the study, 10 were re-evaluated at age 3–6 years: seven of 10 subjects had developed clinical pollen allergy, compared with four of 18 atopic controls ($P < 0.05$).

Conclusions: Potato-CAP and SPT at specific cut-off are valuable tools in the diagnosis of allergy to cooked potato. Most children with potato allergy develop tolerance at mean age of 4 years. Allergy to cooked potatoes is a risk factor for the development of pollen allergy.

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Key words: allergy to cooked potato; diagnosis; eczema; natural course; pollen allergy.

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White potato (*Solanum tuberosum*) is highly consumed in Europe, and in its cooked form it often is introduced in the child's diet around the age of 5–6 months (1, 2). Allergy to raw potato has mainly been described in adults, most frequently as a cause of oral allergy syndrome (3, 4), generally caused by heat-labile allergens displaying immunoglobulin (Ig) E cross-reactivity with tree pollen (5, 6). Allergy to cooked potato has been reported in children only (7–9), with both immediate and late severe reactions, and even with anaphylaxis (7, 8). In previous studies, children with allergy to cooked potatoes were found to have positive skin prick tests (SPT) with commercial as well as with raw and cooked potato extract and they also had positive SPTs with one or more purified potato allergens (8, 10, 11). However, only skin prick testing with cooked potato extract provided highly

specific results for the diagnosis of clinical allergy to cooked potato (8). Unfortunately, the use of such self-made extracts may not be feasible in current allergy practice. Furthermore, as with food sensitization in general, the presence of potato-specific IgE does not necessarily implicate clinical allergy to potato (12, 13). Therefore, in this study we aimed to investigate the diagnostic performance of SPT with commercial potato extract and of both a commercial and a home-made potato-CAP.

Up till now the natural course of allergy to cooked potato has not been studied. In a preliminary study we suggested that allergy to cooked potato is a risk factor for the early development of pollen allergy (14). Here, we report on 36 children who presented with a positive SPT to potato and/or potato-specific IgE. In 17 of them a clinical allergy to cooked potatoes was documented. We describe their demographic data, presenting symptoms and concomitant allergies, as well as their evolution

Abbreviations: SPT, skin prick test; HDM, house dust mite; CMPA, cow's milk protein allergy.

towards tolerance for cooked potato and the development of other sensitizations.

Materials and methods

Subjects and control group

In this study, we included 36 children seen at the paediatric department's outpatient allergy clinic between the age of 4 and 36 months who were positive in potato SPT and/or CAP. Eight of 36 subjects had participated in a previous study (8). Clinical history was noted, as were already documented clinical allergies or sensitizations. All subjects received appropriate treatment including specific dietary restrictions for food allergies diagnosed so far; in case of eczema they all had adequate topical treatment with emollients and corticosteroids.

The subjects were defined to have a clinical allergy to cooked potato if they (1) were positive in a provocation test with cooked potato as reported elsewhere (8) or (2) showed a significant improvement after elimination of potato from the diet and recurrence of symptoms on its reintroduction or (3) had an unequivocal history of allergic symptoms elicited by the ingestion of cooked potato. Subjects with a diagnosis of allergy to cooked potato were put on a potato-free diet. On follow up the subjects were seen at different time intervals, depending on their individual clinical problems. They were invited for a control visit with extensive allergic re-evaluation at the age of 3–6 years. A questionnaire asking for signs and symptoms of pollen allergy was filled in at that moment and a blood sample was taken. For this part of the study we included a control group of 18 atopic age-matched subjects known with proven cow's milk protein allergy (CMPA) in their first years of life and with a negative potato SPT and a potato-CAP < 0.35 kU/l at that time. Fifteen of 18 controls were also egg-sensitized. Clinical pollen allergy was defined as having (1) experienced exacerbation of symptoms during the pollen season requiring medication and disappearance of those symptoms after the pollen season and (2) a CAP > 0.35 kU/l for the pollen corresponding with the seasonal symptoms.

Ethics

The study was approved by the Ethics Committee of the University Hospital Gasthuisberg, Leuven. All parents gave their informed consent to participate in the study.

Reintroduction of potato at home

For patients who did not show immediate allergic reactions in relation to potato previously, reintroduction of potato was carried out at home. The subjects were on a potato-free diet for at least 4 weeks and they had to be free from any acute disease and from exacerbations of allergic symptoms. Medication if any and topical treatment in case of eczema were kept unchanged. All subjects received home-made meals only. The parents were instructed to exclusively introduce cooked potato (small pieces of potato boiled in water for at least 25 min) in an amount of 60–120 g/day. They noticed the frequency and aspect of stools before and after the introduction of potato and were asked to come for a control visit whenever they suspected a reaction. In case of gastrointestinal complaints two stool samples were examined for pathogens and parasites (15, 16).

Scoring of the severity of atopic dermatitis

The severity of atopic dermatitis was scored according to the SCORAD method accepted by the European Task Force on Atopic Dermatitis (17). For subjects in whom potato was reintroduced at home this scoring was performed during a doctor's visit immediately before and after the introduction of potato.

Potato extract and preparation of the CAPs

Potato extract was prepared from the Bintje cultivar, essentially according to Rudeschko et al. (18). Five hundred grams of potato bulb were put for 10 min in 1 l of prechilled diacetone alcohol at -20°C . Then, 1.5 l of prechilled acetone was added, and the mixture was kept overnight at -20°C . The precipitate was rinsed at 4°C , twice with acetone and once with acetone : ether (1 : 1), and left to dry. The resulting powder was dissolved in 900 ml of 0.02 M sodium phosphate buffer pH 7.2 for at least 1 h while stirring. After centrifugation, the supernatant was first filtered through a 0.45- μm membrane, then through a 0.2- μm membrane. Half the supernatant was boiled for 10 min, cooled to ambient temperature before storage at -20°C until use. This is referred to as home-made cooked potato extract (HMCP). The other half was immediately stored at -20°C , and is referred to as home-made non-cooked potato extract (HMNCP).

About 400 ml of HMCP and HMNCP were used by Phadia (Uppsala, Sweden) for coupling to CAP matrix, which are referred to as HMCP-CAP and HMNCP-CAP, respectively.

Total IgE levels and CAP

At enrolment total serum IgE (Phadia) was determined in all subjects. Specific serum IgE to potato, bromelain and latex was measured by means of CAP (Phadia). The commercial CAP potato is referred to as potato-CAP. HMCP-CAP, HMNCP-CAP and potato-CAP were determined simultaneously on 16 sera. Potato-CAP determination was repeated at different time intervals in individual subjects.

On blood samples taken at age 3–6 years we determined CAP potato, grass pollen, birch pollen, mugwort and house dust mite (HDM) (Phadia). CAP values > 0.35 kU/l were considered positive.

Skin prick tests

Skin prick tests were performed with a commercial potato extract (HAL, Haarlem, the Netherlands) by means of a microlance (HAL prick-lancette) and read after 15 min (19). Maximal and orthogonal diameters of the weal reaction were recorded and mean diameters were calculated. Histamine diphosphate 1 mg/ml (HAL) and Coca solution in 50% glycerol were used as positive and negative control, respectively. After subtraction of the mean weal diameter of the negative control, an SPT with a mean weal diameter of < 2 mm was scored 1+, of 2–3 mm as 2+, of > 3 mm to 6 mm as 3+, of > 6 mm as 4+ and an urticarial reaction was scored 5+. SPTs with a score 2+ or more were regarded as positive (20, 21).

Statistical analysis

Comparison between groups was done by chi-square, Fisher's exact, Mann-Whitney *U* and Kruskal-Wallis tests; significances were tested two-tailed.

Results

Demographic and clinical data

At enrolment the subjects, 27 boys and nine girls, were aged 4–35 months (mean 14.2 months). Of them, 35 subjects presented with eczema, 11 with vomiting or gastrointestinal complaints, nine with urticaria and/or angioedema, eight with wheezing and rhinitis and three subjects had experienced anaphylaxis, which was elicited by cooked potato in two subjects and by cow's milk in another one. Of the 36 subjects, seven children who participated in a previous study underwent a provocation test which was positive in all of them (8); two subjects had a clear history of allergy to cooked potato: one boy who participated in the previous study and who showed an impressive clinical evolution after the sole withdrawal of potato with a decrease in SCORAD index from 117 to 28, and one girl who had experienced angioedema, urticaria, vomiting and gastrointestinal complaints immediately after ingestion of cooked potato; 16 subjects underwent elimination and reintroduction of cooked potato at home, which in eight of them resulted in significant improvement after elimination and in recurrence of symptoms on reintroduction, while the eight other subjects showed neither improvement on elimination, nor worsening on reintroduction; 11 subjects experienced a better control of symptoms on avoiding cooked potatoes, but a trial with reintroduction was refused by the parents. Hence, the 36 subjects could be divided into three groups (Table 1): group I – 17 subjects with confirmed allergy to cooked potato, as proven by provocation, elimination and reintroduction or clinical history; group II – 11 subjects suspected of having allergy to cooked potato, but in whom reintroduction of potato was not done because of

refusal by the parents; group III – eight subjects without clinical allergy to cooked potato. Sex and age distribution in the three groups are depicted in Table 1. For group I subjects, the primary symptoms, the symptoms subsiding on elimination of cooked potato and the outcome of potato challenge are summarized in Table 2. Gastrointestinal complaints if present consisted of protracted diarrhoea and abdominal pain in all and loss of appetite in some children. In all those subjects two stool samples remained negative in search for pathogens and parasites.

Concomitant allergies and sensitization

Thirty of 36 subjects had a proven clinical CMPA (Table 1). Thirty-one subjects were sensitized to egg white, 10 of them having a proven clinical allergy to it. Allergy to fish, banana and nuts was documented in two, one and two subjects, respectively. Further, four subjects suffered from allergy to pet dander, while allergy to HDM, grass pollen and birch pollen was suspected in two, one and one subject, respectively, according to the subject's clinical history together with a positive SPT and/or specific IgE to the respective allergens. Of note, of the two patients with nut allergy one belonged to group I, the other one to group III and this one was sensitized to birch pollen.

Total and specific serum IgE

Median total IgE was 952 kU/l (range: 16–6100) in group I, whereas it was 167 kU/l (range: 40–2010) and 125 kU/l (range: 13.6–1748) in group II and group III, respectively (differences ns; Table 1).

Commercial potato-CAP was determined in all subjects at enrolment. In group I, potato-CAP ranged from 2.05 to >100 kU/l (median 24 kU/l), while it ranged from 0.78 to 48.4 kU/l (median 7.51 kU/l) and from 0.63 to 23.1 kU/l (median 1.48 kU/l) in group II and group III, respectively (group I and group III: $P < 0.001$; Fig. 1A). Commercial potato-CAP at cut-off > 2 kU/l detected all group I subjects with proven clinical allergy to cooked potato, but also three of eight subjects of group III without clinical potato allergy. Hence, potato-CAP at cut-off > 2 kU/l has a sensitivity of 100% and a specificity of 62.5% for the diagnosis of clinical allergy to cooked potato.

In 16 subjects (nine subjects of group I, one of group II and six of group III), we performed simultaneous determination of HMNCP-CAP and commercial potato-CAP and of HMNCP-CAP and HMCP-CAP. This yielded closely correlating results with r_s 0.998 and 0.966, respectively (Spearman Rank). HMNCP-CAP was positive in all tested subjects, while HMCP-CAP was positive in nine of nine subjects of group I and in one of six subjects of group III ($P < 0.01$). CAP bromelain was positive in two of 10 subjects in group I and in one of six and zero of seven in group II and group III, respectively, with levels ranging

Table 1. Demographic data, clinical characteristics and total immunoglobulin (Ig) E in three groups of potato-sensitized subjects at presentation

	Group I (n = 17)	Group II (n = 11)	Group III (n = 8)
Age (months)			
Range	4–35	7–35	6–21
Mean	13	15.1	12.9
M/F	15/2	6/5	6/2
Cow's milk allergy	15	9	6
Egg white sensitized	15	8	8
Presenting symptoms			
Atopic dermatitis	16	11	8
Gastrointestinal	8	2	1
Urticaria/angioedema	5	3	1
Wheezing/rhinitis	3	3	2
Anaphylaxis	2	0	1
Total IgE (kU/l)			
Range	16–6100	40–2010	14–1748
Median	952	167	125

Group I: subjects with proven clinical allergy to cooked potato; group II: subjects with clinical improvement after withdrawal of potato, but in whom no trial with reintroduction was done; group III: subjects without clinical allergy to cooked potato; differences between groups are not significant.

Table 2. Primary symptoms, age at first introduction of potato and at diagnosis of potato allergy, symptoms subsiding on elimination of cooked potato and provocative dose, time lapse of onset of symptoms and symptoms elicited by cooked potato in group I

Subject	Primary symptoms	Age (months) at:		Symptoms subsiding on elimination of cooked potato	Potato provocation† or reintroduction at home§		
		introduction	diagnosis		Dose ingested‡	Time lapse¶	Symptoms**
1*	E, U, A	5	7	U, A	5 (day 1)†	15 min	U, A
2	E, GI	5.5	8	E, GI	30–60 (days 1–4)§	3 days	E (10 → 16.5), GI
3	E, GI	26	35	GI	60–120 (days 1–10)§	7 days	GI
4	E, GI	13	14	GI	60 (days 1–4)§	4 days	GI
5*	E, V	5	15	E, V	15 (day 1)†	30 min	V
6*	E	6	14	E	120 (days 1–2)†	24 h	E (0 → 16)
7*	E	6	9	E	120 (days 1–3)†	48 h	E (11 → 24.5)
8	E, V, GI	6	12	V, GI	60–120 (days 1–10)§	7 days	GI
9*	An (U, A, V, Rh, Wh)	3.5	5	An (U, A, V, Rh, Wh)	50 (day 1)†	1 h	An (U, A, V, Rh, Wh)
10	E	4	6	E	60–120 (days 1–4)§	48 h	E (10 → 25)
11	E	4.5	8	E	30–60 (day1–4)§	48 h	E (0 → 28.5)
12	E, U	5	12	E	30–60 (day1–4)§	48 h	E (0 → 28.5)
13*	E, Rh, Wh	6	25	E, Wh	120 (days 1–3)†	5 h	E, Wh
14*	E	4	8	E	nd	nd	nd
15	E, An (U, A, V, GI), F	6	18	An (U, A, V, GI)	nd	nd	nd
16	E, U	6	15	E	60–120 (days 1–4)§	48 h	E (0 → 16)
17*	E, V	5	10	E, V	35 (day 1)†	45 min	U, V

E, eczema; U, urticaria; A, angioedema; GI, gastrointestinal complaints; V, vomiting; An, anaphylaxis; Rh, rhinitis; Wh, wheezing; F, failure to thrive; CMPA, cow's milk protein allergy; HDM, house dust mite.

*Subjects who participated in a previous study (8).

†Provocation in the hospital.

‡Potato dose ingested on the first challenge day and repeated during the following days.

§Reintroduction of potato at home.

¶Time lapse in minutes, hours or days between onset of challenge and onset of symptoms.

**Data between brackets: SCORAD index before and after introduction of potato.

from 0.39 to 0.99 kU/l. CAP latex was positive in three of eight subjects in group I and in two of six and zero of seven subjects in group II and group III, respectively, with values ranging from 0.46 to 5.04 kU/l. None of these subjects had a history of clinical allergy to latex, in particular they did not show any reaction on repetitive contact with balloons.

Skin prick tests

Potato SPT was performed in 15 of 17 subjects in group I and in 11 of 11 and six of eight subjects in group II and group III, respectively. In all tested subjects of group I the SPT score was $\geq 3+$, whereas in group III only one subject had a score of $3+$ ($P < 0.001$; Fig. 1B). In group II, the score ranged from 0 to $4+$. Considering groups I and III, SPT at cut-off score $\geq 3+$ detected all group I subjects with proven clinical potato allergy, while using a cut-off score $\geq 4+$ it detected group I subjects only. Hence, SPT with the commercial extract at cut-off score $3+$ (=weal diameter ≥ 3 mm) provides a 100% sensitivity for the diagnosis of clinical allergy to cooked potato, while at cut-off score $4+$ (=weal diameter ≥ 6 mm) it provides a 100% specificity for it.

Development of tolerance to potato

Fifteen of the 17 subjects of group I were followed over a mean period of 4 years. The other two subjects were lost

from follow up. After a potato-free period of 6 months at least, a potato provocation test was performed as described previously (8) in seven subjects who had shown immediate allergic reactions previously, while in the other eight subjects reintroduction of potato was attempted at home. In seven of 15 subjects (subject 2, 3, 5, 7, 12, 14, 16 in Table 2) provocation/reintroduction was immediately successful. In the other eight subjects it resulted in exacerbation of symptoms at the first attempt, but an attempt 6–20 months later was successful in five of them. The other three subjects have not been rechallenged up till now. One of them, a girl who had been on a potato-free diet for more than 6 years, underwent a potato provocation test at the age of 7.5 years. This resulted in anaphylaxis with generalized itching, urticaria, angioedema, vomiting, abdominal pain and diarrhoea starting 90 min after the ingestion of 60 g cooked potatoes. Hence, after being on a potato-free diet for 8–77 months (mean 37.5 months) tolerance was achieved in 12 of 15 group I subjects at an age ranging from 16 to 102 months (mean 47.5 months). Figure 2 shows the evolution of potato-CAP in 11 group I subjects becoming tolerant (Fig. 2A,B) and in the three group I subjects remaining intolerant up till now (Fig. 2C).

On achievement of tolerance, potato-CAP was determined in 11 subjects of group I and it had decreased in all of them (Fig. 2A,B). It ranged from <0.35 to 19.7 kU/l (mean 6.1 kU/l). The percentage of decrease in

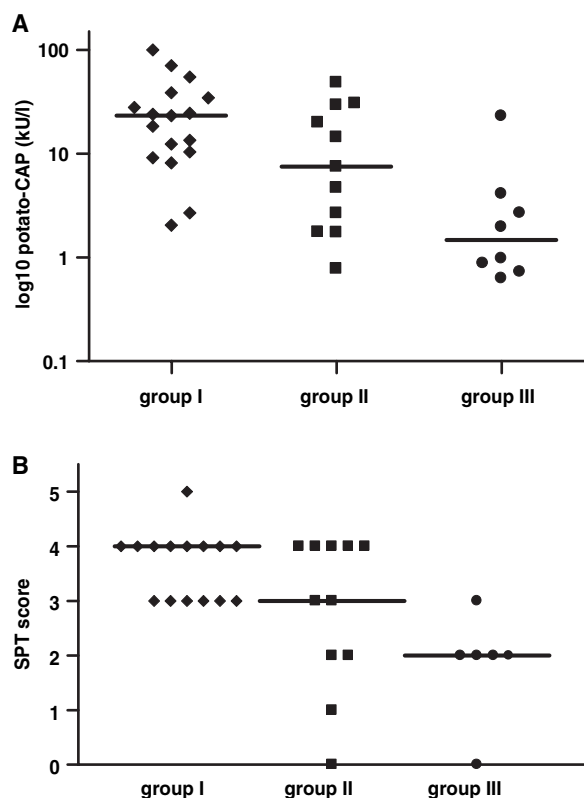


Figure 1. (A) Potato-CAP in three groups. Distribution of potato-CAP values in three groups of potato-sensitized subjects: group I [◆]: potato-allergic subjects; group II [■]: subjects with highly suspected, but no clearly documented potato allergy; group III [●]: subjects without potato allergy. Kruskal–Wallis: $P < 0.01$. Groups I and III: Mann–Whitney U : $P < 0.001$. (B) Potato skin prick test (SPT) in three groups. Potato SPT in three groups of potato-sensitized subjects: group I [◆]: potato-allergic subjects; group II [■]: subjects with highly suspected, but no clearly documented potato allergy; group III [●]: subjects without potato allergy. Kruskal–Wallis: $P < 0.01$. Group I and group III: Mann–Whitney U : $P < 0.001$. The horizontal bar indicates the median.

potato-CAP on achievement of tolerance in those 11 subjects ranged from 11.1% to 92.5% (median decrease 75.5%). In contrast, in the five subjects of group I who were not yet tolerant at the time of first reintroduction and in the three subjects of group I remaining intolerant till now, the change in potato-CAP ranged from a decrease of 68% to an increase of 82% (median decrease 34%; Fig. 3).

Development of pollen allergy/sensitization

Of the 17 subjects of group I with proven allergy to cooked potato, 12 reached the age of 3 years during the study. Of them, 10 subjects were seen again between the age of 3–6 years for evaluation of signs and symptoms of pollen allergy, the other two subjects being lost from follow up. Seven of the 10 subjects had developed clinical

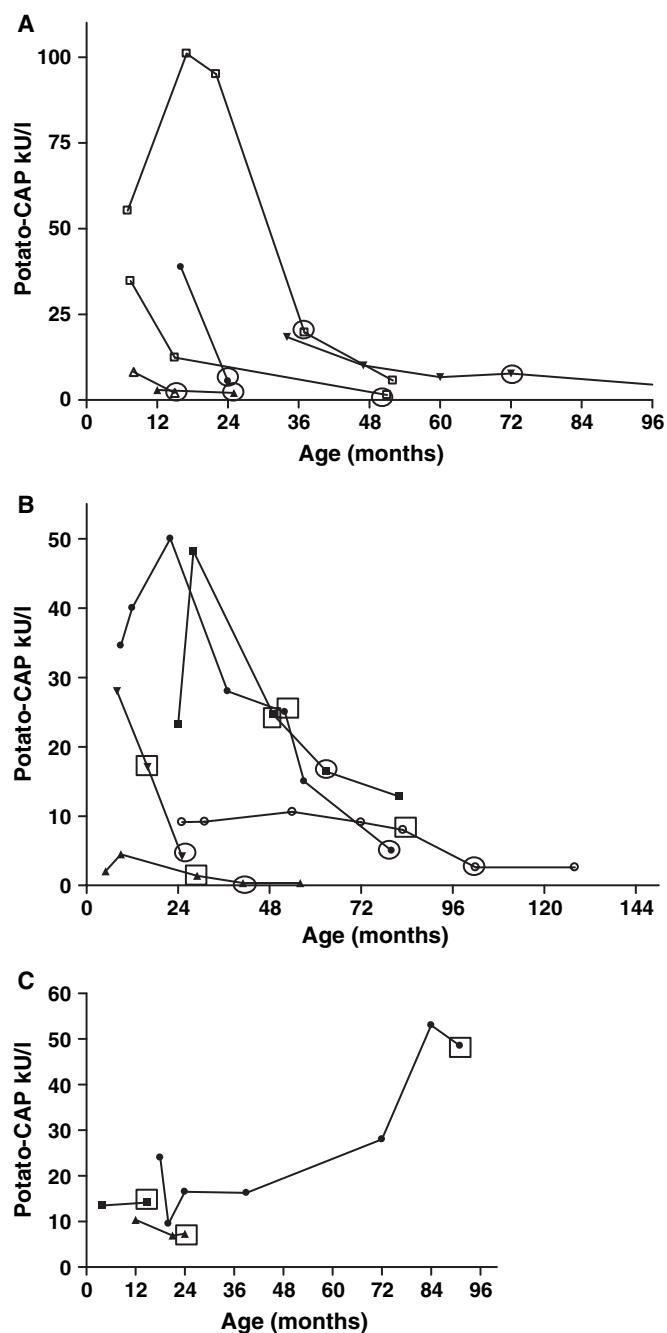


Figure 2. Evolution of potato-CAP in group I at follow up. Evolution of potato-CAP in six subjects in whom introduction of potato was successful at first attempt (A), in five subjects who experienced a positive rechallenge but who had a successful introduction of potato afterwards (B), and in three subjects non-tolerant up till now (C). The squares indicate potato-CAP values at the moment of positive challenge; the circles indicate values on achievement of tolerance.

symptoms of pollen allergy, with rhinoconjunctivitis (seven of 10), asthma (five of 10) and/or eczema (two of 10). In comparison, only four of 18 atopic age-matched controls had developed clinical allergy to pollen, with

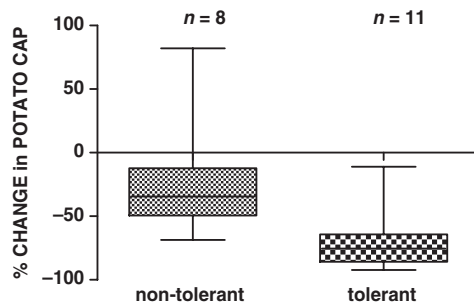


Figure 3. Change in potato-CAP in tolerant and non-tolerant subjects of group I. Percentage change in potato-CAP at follow up in eight subjects not yet tolerant (five subjects becoming tolerant later on and three subjects not tolerant up till now) and in 11 subjects on achievement of tolerance. Results are expressed as the percentage change in CAP value between enrolment and at the moment of positive provocation for the non-tolerant group (median: 34) and as the percentage change in CAP between the highest value before tolerance and the value on achievement of tolerance for the tolerant group (median: 75.5).

Table 3. Development at age 3–6 years of pollen sensitization, clinical pollen allergy and HDM sensitization in potato-allergic subjects and in atopic controls without potato-sensitization

	Potato-allergic subjects (n = 10)	Atopic controls (n = 18)	P-value
Mean age (months)	53.4	53.5	ns
Total IgE (kU/l)			
Range	46–1643	43 to >3000*	ns
Median	918	347*	ns
Pollen sensitization	9/10	10/18	< 0.01
Grass	9/10	10/18	< 0.01
Birch	8/10	6/18	< 0.05
Mugwort	3/8	3/17	ns
Clinical pollen allergy	7/10	4/18	< 0.05
HDM sensitization/allergy	7/9	11/18	ns

HDM, house dust mite; IgE, immunoglobulin E.

*Determined in 12 controls.

rhinoconjunctivitis (two of 18), asthma (one of 18) and/or eczema (two of 18) ($P < 0.05$). Of the 10 subjects of group I, nine had a positive CAP for one or more kind of pollen, nine of 10 being sensitized to grass pollen, eight of 10 to birch pollen and three of nine to mugwort, compared with 10 of 18, six of 18 and three of 17 in the atopic control group (Table 3). On the other hand, seven of 10 subjects of group I became sensitized to HDM, compared with 11 of 18 controls.

Discussion

This is the first study describing the natural history of allergy to cooked potatoes in children and the development of tolerance to it.

At the moment of diagnosis of potato allergy, most patients were receiving potatoes in their diet since at least 1 month and some did so for more than 1 year. The relative delay in diagnosis of potato allergy may be partly explained by the fact that all but two patients had one or more previously diagnosed concomitant food allergies, for which they already were on a cow's milk and egg-free diet. For that reason, exacerbation of symptoms might have been mistaken for being elicited by accidental intake of previously documented causal food allergens. Hence, this might explain that the two patients being allergic only to potato have been diagnosed rather early, at age 9 and 5 months, respectively. On the other hand, the time lapse between onset of ingestion and onset of clinical symptoms may reflect a variable duration of the sensitization process and can differ between individual patients.

At the exception of one, all subjects with potato allergy presented with eczema. This is concordant with the findings of a previous study reporting positive oral potato challenges in children with eczema (9). The higher frequency of gastrointestinal complaints in group I with proven potato allergy, when compared to group III without clinical potato allergy, did not reach statistical significance, but this might be due to the small number of cases. Nevertheless, in young atopic children with ongoing gastrointestinal complaints, the possibility of allergy to cooked potatoes should be taken into account.

The high frequency of CMPA in our potato-allergic subjects is compatible with current knowledge that children with CMPA often show multiple food allergies (22).

The potato allergens responsible for clinical allergy and sensitization in our patients clearly are stable allergens, resisting cooking and digestion and persisting in commercial extracts for skin testing. The potato tuber protein patatin (Sol t 1) has been identified as a major food allergen among atopic children (10). Although patatin is considered as an heat-labile allergen, it has been shown that the heat lability of its IgE-interaction is strongly influenced by other potato proteins (23). Four other potato tuber proteins, belonging to the family of soybean trypsin inhibitors, have been identified as allergens in potato-sensitive children (11). Those allergens known to resist processing and digestion might be involved in clinical reactions to cooked potato. Further studies are actually going on to identify the allergens involved in allergy to cooked potato.

We used an home-made potato-CAP (HMCP-CAP) prepared from cooked potato in order to exclude IgE-binding to heat-labile allergens. This HMCP-CAP proved to be a highly sensitive and a fairly specific tool in the diagnosis of allergy to cooked potatoes, as it was positive in all tested subjects of group I with proven potato allergy and in only one subject of group III with potato-sensitization only. This particular subject was strongly sensitized, with a potato-CAP of 23 kU/l and a SPT score of 3+.

The closely correlating results of the commercial potato-CAP and of the HMCP-CAP suggest that heat-stable allergenic proteins are well represented in the commercial CAP and that the latter is a useful diagnostic tool for allergy to cooked potato. Indeed, applying a cut-off of ≥ 2 kU/l for the commercial potato-CAP, a 100% sensitivity and a 62.5% specificity for the diagnosis of allergy to cooked potato could be calculated. Of note, positivity in potato-CAP in group III was caused by IgE-binding to potato allergens and not by non-specific CAP-binding. Indeed, on IgE-immunoblots performed on sera of group III subjects, at least one protein band was recognized in five of five subjects (unpublished data). Furthermore, CAP bromelaine in groups I and II was positive in three of 23 subjects only, with levels not exceeding 0.99 kU/l, while it was negative in five of five subjects of group III. This clearly indicates that, at least in our study population, IgE binding to carbohydrate determinants plays to the utmost a minor role in potato-CAP results (12).

For SPT-scoring, we defined a SPT of 2–3 mm as the lowest limit of positivity. We did so, because 15 of 32 skin prick-tested subjects were aged 1 year or younger and because in this age group, a SPT with weal diameter ≥ 2 mm should be interpreted as positive (20, 21). Considering groups I and III, all subjects with a SPT-score $\geq 4+$ belonged to group I and none of the group I subjects, with proven potato allergy, had a score $< 3+$, while in group III, with potato-sensitization only, all but one subjects had a score $< 3+$. Therefore, by using a cut-off score $4+$ (≥ 6 mm weal diameter), skin prick testing with a commercial extract provides a highly specific tool in the diagnosis of allergy to cooked potatoes, while by using a cut-off score $3+$ (≥ 3 mm weal diameter) as the lowest limit of positivity it provides a highly sensitive tool. Applying the above-discussed diagnostic criteria to the subjects of group II, who remained unidentified as to whether or not potato-allergic, we can assume that at least five of 11 subjects are clinical reactors. In a previous study we showed that a HMCP extract is a highly specific and sensitive tool in detecting patients with allergy to cooked potato (8). Hence, possibly the use of both, a cooked and a non-cooked commercial extract might provide an even better way in discriminating between clinical reactors and non-reactors among sensitized patients.

Potato is one of the foods implicated in the latex-fruit syndrome (24–26) and it has been questioned whether latex sensitization precedes or follows the onset of food allergy. In this study, five subjects, three of group I and two of group II, were latex-CAP-positive, but none had an history of clinical allergy to latex. Furthermore, the only subject in whom latex-CAP was determined twice had a negative latex-CAP first, which became positive

after sensitization to potato. This suggests that, at least in young children with potato allergy/sensitization, latex sensitization is a bystander phenomenon. Of note, the banana-sensitized subject, which belonged to group I, had a negative latex CAP and SPT.

During follow up 12 of 15 group I subjects became tolerant to ingested potatoes. On achievement of tolerance, potato-CAP determined in 11 of 12 group I subjects had decreased clearly in all of them, but it covered a broad range from < 0.35 to 19.7 kU/l. Therefore, a cut-off CAP-value for the prediction of tolerance cannot be proposed. Possibly the percentage of decrease in potato-CAP might be a suitable tool in this respect, as a median decrease of 75.5% preceded the achievement of tolerance. Such a strong decrease in the potato-CAP might be a useful parameter suggesting that introduction of potato could be attempted.

This study confirms our preliminary findings, suggesting that potato allergy is a risk factor for the early development of pollen sensitization and of clinical symptoms due to pollen allergy (14). Whether this is due to a causal connection between the development of allergy to cooked potatoes and to pollen, or is purely an expression of a stronger atopic predisposition remains to be investigated. However, our finding that HDM sensitization was comparably high in potato-allergic subjects and in atopic controls might favour the former possibility.

Conclusion

Children with allergy to cooked potatoes present with eczema in most cases, gastrointestinal complaints in 50% and immediate hypersensitivity reactions in 30%. Most of them suffer from CMPA. Skin prick testing with a commercial extract using different cut-offs provides a highly specific and sensitive tool in the diagnosis of allergy to cooked potatoes. Determination of potato-sIgE by means of an experimentally prepared cooked potato-CAP, but also by commercial CAP proved to be valuable for diagnosis. In subjects developing tolerance on avoidance of cooked potato, this was achieved at a mean age of 4 years. Allergy to cooked potatoes is a risk factor for the early development of pollen allergy.

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