

Kiwi fruit is a significant allergen and is associated with differing patterns of reactivity in children and adults

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Summary

Background Allergy to kiwi fruit appears increasingly common, but few studies have evaluated its clinical characteristics, or evaluated methods of investigating the allergy.

Objective To characterize the clinical characteristics of kiwi fruit allergy and to study the role of double-blind placebo-controlled food challenge (DBPCFC), skin tests and specific IgE in the diagnosis of this food allergy.

Methods Two-hundred and seventy-three subjects with a history suggestive of allergy to kiwi completed a questionnaire. Forty-five were investigated by DBPCFC, prick-to-prick skin testing with fresh kiwi pulp, and specific IgE measurement. Nineteen subjects were also skin tested using a commercially available solution.

Results The most frequently reported symptoms were localized to the oral mucosa (65%), but severe symptoms (wheeze, cyanosis or collapse) were reported by 18% of subjects. Young children were significantly more likely than adults to react on their first known exposure ($P < 0.001$), and to report severe symptoms ($P = 0.008$). Twenty-four of 45 subjects (53%) had allergy confirmed by DBPCFC. Prick-to-prick skin test with fresh kiwi was positive in 93% of subjects who had allergy confirmed by DBPCFC, and also in 55% of subjects with a negative food challenge. The commercial extract was significantly less sensitive, but with fewer false-positive reactions. CAP sIgE was only positive in 54% of subjects who had a positive challenge.

Conclusions Kiwi fruit should be considered a significant food allergen, capable of causing severe reactions, particularly in young children. DBPCFC confirmed allergy to kiwi fruit in 53% of the subjects tested, who had a previous history suggestive of kiwi allergy. Skin testing with fresh fruit has good sensitivity (93%), but poor specificity (45%) in this population. CAP sIgE and a commercially available skin test solution were both much less sensitive (54%; 75%) but had better specificity (90%; 67%).

Keywords *Actinidia*, allergens, double-blind methods, immunoglobulin E, kiwi fruit, skin tests

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Introduction

Kiwi fruit (*Actinidia deliciosa*) has been recognized as a food allergen for over 20 years [1], but although several studies have evaluated the immunological reactivity to kiwi fruit and examined cross-reactivity with pollens and latex allergens, there is little information about the clinical aspects of the allergy. The first report of kiwi fruit allergy in 1981 [1] described an adult who developed wheeze and urticaria on contact with the fruit, and there have subsequently been a handful of case reports of people reacting with a range of symptoms from oral allergy syndrome to life-threatening anaphylaxis [2–6]. Studies of immunological reactivity to kiwi fruit have predominantly focused on subjects with oral allergy

syndrome [7–10]. We report the first study designed to investigate the clinical characteristics of kiwi fruit allergy in children and adults, and the diagnostic value of clinical investigation by skin-prick tests and specific IgE antibody assay compared with a double-blind placebo-controlled food challenges (DBPCFC).

Methods

The Southampton and South West Hants Joint Research Ethics Committee approved the study.

Subjects

Subjects with self-reported kiwi fruit allergy were recruited from three sources: the paediatric and adult allergy clinics at Southampton General Hospital, respondents to an advertise-

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ment in The Anaphylaxis Campaign Magazine and people who contacted the study following a press release on national radio and in newspapers. Four hundred and twenty subjects were sent a self-administered postal questionnaire, with 291 (69%) completed questionnaires being returned between April 2001 and September 2002. Non-respondents were not followed-up. Subjects who completed a questionnaire and reported symptoms suggestive of IgE-mediated allergy to kiwi fruit were invited to come to the centre for clinical investigation of their reported symptoms to kiwi fruit. Our study was funded sufficiently to challenge 40–50 subjects, constituting by far the largest clinical study of kiwi fruit allergy to date. Subjects were primarily selected by their availability and motivation to attend the research centre. We selected volunteers to be representative of all ages (over 6 years) and to include people with isolated oral symptoms as well as those with a history of systemic reactions. Subjects with a history of severe anaphylaxis were excluded from challenge.

In addition skin tests and specific IgE to kiwi fruit were measured in five atopic and five non-atopic controls who eat kiwi fruit with no adverse symptoms.

Questionnaire

The postal questionnaire included questions on age of onset of allergy, symptoms, frequency of kiwi ingestion prior to a reaction, treatment received and co-existing allergies and atopic diseases. Reported symptoms were considered mild if they involved a tingling or sore mouth, or a rash; moderately severe if they included abdominal pain, a tight throat, facial swelling or breathing difficulties other than wheeze. Severe symptoms were those involving wheeze, cyanosis or collapse [11].

Diagnostic investigations

Skin-prick testing was performed on the volar aspect of the distal forearm using standard commercially available solutions of latex (1 in 10 wt: vol), birch pollen, house dust mite (HDM), egg albumin and cow's milk allergens (all from ALK-Abelló). Prick-to-prick testing was performed using fresh pulp of kiwi, apple, banana and avocado. The fruit was cut, and the lancet was pricked into the pulp and then immediately afterwards into the skin at 90°. A negative control of saline 0.9% and a positive control of histamine 10 mg/mL were used. The reaction was regarded as positive if the mean wheal diameter was at least 3 mm in the presence of appropriate reactions to the positive and negative controls. Nineteen subjects also had skin testing using a commercially available kiwi extract (Alyostal, France). Because children were amongst the subjects, the number of skin tests was limited, and not all allergens known to cross-react with kiwi fruit (eg. Timothy pollen) were included in the skin test panel.

Serum was tested for total IgE and specific IgE to kiwi fruit, latex and avocado using the CAP system (Pharmacia, Uppsala, Sweden) in the immunology laboratory, Southampton University NHS Trust Hospital. Skin tests and specific IgE to kiwi fruit were measured in five atopic and five

non-atopic controls who eat kiwi fruit with no adverse symptoms.

All DBPCFC took place in the Wellcome Trust Clinical Research Facility, which is fully equipped for physiological monitoring and resuscitation. All subjects were well on the day of the challenge, and intravenous access was established prior to the challenge commencing. Double-blind food challenges proved difficult to interpret in some subjects, and the recipe and methodology changed in an attempt to overcome this. Adequate blinding was confirmed by non-allergic volunteers. (A typical kiwi fruit weighs 60 g.)

Recipe 1: Peeled, pureed pulp of kiwi fruit, including seeds, was masked in a sorbet or ice cream vehicle (at room temperature) that contained ground dried tea leaves and liquid food colouring. Four placebo doses were randomly dispersed with nine active doses in incremental doses of kiwi fruit (1, 10, 50, 100, 500, 1000, 2000, 4000, 8000 mg). The doses were given to the subject at intervals appropriate to the reported reaction time. This was generally 15 min. The subject wore a nasal clip whilst ingesting the challenge.

Recipe 2: Peeled, pureed pulp of kiwi fruit, including seeds, was masked in yogurt containing a mix of orange pulp, tea leaves and liquid food colouring. Three placebo doses were randomly dispersed with four active doses in incremental doses of kiwi fruit (2.5, 10, 20 and 60 g). The doses were given to the subject at intervals of 30 min.

One subject had an open challenge due to known allergy to the challenge vehicle. Subjects who had a negative or inconclusive DBPCFC were offered an open challenge with whole kiwi fruit (60 g). In addition to being medically assessed, subjects had facial photographs prior to the challenge and following the development of visible signs. A dietitian and clinician reviewed the challenge signs and symptoms data. Challenges were considered positive if the subject had subjective symptoms which conformed to the pattern of active/placebo doses, or if they developed an objective sign, for example, urticaria, angioedema or a fall in peak expiratory flow. The open challenge was only considered positive if the subject developed physical signs indicative of an IgE-mediated response.

SDS-PAGE

SDS-PAGE analysis was used to determine the protein profile of an extract of fresh kiwi fruit (made using the methodology of Pastorello [12]) and a commercially available kiwi skin test extract (Alyostal, France). Protein content of the two extracts was measured by the Lowry method. Samples were run in 12% NuPAGE gel (Invitrogen, Paisley, UK) with 40, 20, 10 and 5 µg of extract per lane. Reference markers with known molecular weight (Mark 12 unstained standard, Invitrogen) were run in the same gel. Following electrophoresis, the gel was fixed and then stained with Brilliant Blue G Colloidal concentrate.

Statistics

Data were doubly entered in SPSS for Windows (SPSS version 10.0, Chicago, USA), and were analysed using

Pearson's χ^2 test and Fisher's exact test where appropriate. All reported *P*-values are two-tailed.

Results

Questionnaire

Two hundred and ninety-one questionnaires were returned, but 18 were excluded because the symptoms were not suggestive of IgE-mediated kiwi fruit allergy. Two hundred and seventy three valid questionnaires were therefore analysed, 189 (69%) of which were from female respondents. The age range of cases was 5 months to 86 years (mean 38.8 years, SD 21.1 years). The age of subjects at the time of their first reaction ranged from 4 months to 71 years (mean 31.5; SD 18.9), 13% reacting below the age of 5 years. Respondents reported very little allergy to kiwi fruit in the 1970s, particularly in the now adult population who were children at the time. Allergic reactions were increasingly reported in the 1980s, again predominantly in adults. It was not until the 1990s that kiwi fruit allergy was commonly reported in children and young infants (Fig. 1).

Timing of reactions Seventy-three percent of children of 5 years or less (22 of 32 children) reacted on their first known exposure to kiwi fruit in comparison with only 21% of subjects over the age of 15 years (39 of 189 adults) (Pearson's $\chi^2 = 33.3$, $P < 0.001$). Sixty-four percent of the total subjects reported immediate (< 5 min) symptoms on contact with the fruit, 90% of the total subjects had reactions within 30 min and only 3% reported a delay of more than an hour. All subjects with delayed reactions had mild symptoms.

Associated allergies Kiwi allergy in this UK population was associated with self-reported latex allergy (9%) and allergies to avocado (5%), banana (6%), apple (6%), grass pollen (29%) and tree pollen (23%). Allergies to allergens not known to cross-react with kiwi fruit were also common. Commonly reported co-existing allergies included peanuts (14%), tree nuts (17%), milk (6%) and egg (8%). Children

under the age of 5 years were particularly likely to have a strong atopic predisposition. Ninety per cent had been treated for asthma, eczema or hayfever. Nineteen of 33 of these young children (58%) reported peanut allergy, 15 (45%) tree nut allergy, five (15%) milk allergy and 10 (30%) egg allergy.

Allergic symptoms The symptoms reported on first and most recent reactions are summarized in Table 1. Localized oral reactions were the most commonly described symptoms. Severe symptoms were reported on the first reaction by 18% of respondents and by 12% of subjects on their most recent reaction. The most common severe symptom described was wheeze but subjects who had been treated for asthma were not more likely to have a severe reaction (Pearson's $\chi^2 = 2.00$; $P = 0.40$). Severe symptoms were significantly more likely to occur in young children (< 5 years) than adults over 15 years (Pearson's $\chi^2 = 7.1$; $P = 0.008$) (Fig. 2). If subjects had severe symptoms on their first reaction, the most recent reaction was also likely to be severe. However, more than 30% of those who initially had a mild reaction subsequently had moderate or severe symptoms (Table 2).

Treatment of reactions Fifteen per cent of respondents had attended hospital on at least one occasion during an acute reaction to kiwi fruit, 3% had been admitted overnight and three subjects (1%) had been admitted to an intensive care unit. Thirty-one per cent of respondents had used antihista-

Table 1. Reported symptoms on first and most recent reaction

Symptom	First reaction <i>N</i> = 276 (%)	Most recent reaction <i>N</i> = 206 (%)
Tingling, sore mouth	180 (65)	144 (69)
Throat tightening/difficulty swallowing	125 (45)	103 (50)
Swelling of lips/tongue	106 (38)	77 (37)
Face swelling	74 (27)	42 (20)
Rash	60 (22)	31 (15)
Breathing difficulty	49 (18)	33 (16)
Vomiting	49 (18)	35 (17)
Abdominal pain	46 (17)	37 (18)
Wheeze	39 (14)	26 (13)
Collapse	13 (5)	7 (3)
Cyanosis	9 (3)	3 (1)

Subjects could report more than one symptom.

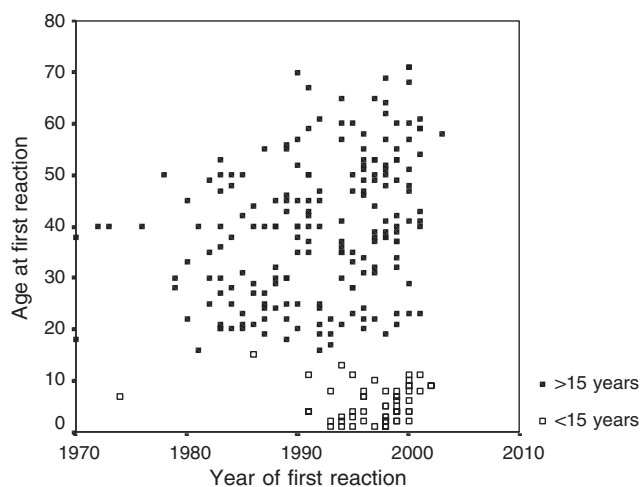


Fig 1. The development of allergy to kiwi fruit in adults and children since 1970. Each point represents one subject plotted in the year of their first reaction, and their age at that time.

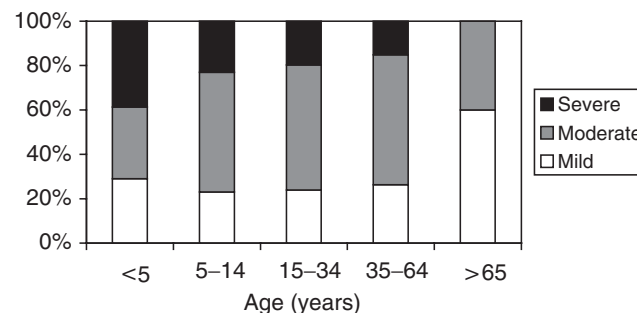


Fig 2. Severity of first reactions according to age at the time of first reaction.

Table 2. Comparison of first and most recent reactions

Most recent reaction	First reaction		
	Mild	Moderate	Severe
Mild	46	7	1
Moderate	16	86	5
Severe	4	5	23

Data missing for 13 subjects.

Table 3. Clinical manifestations during challenges

Clinical signs and symptoms	Ages at test (years)
DBPCFC	
Isolated oral symptoms	29, 36, 42, 44, 49, 53, 53, 55, 57
Facial swelling and oral symptoms	9, 22, 51, 55
Urticaria $\pm$ angioedema	6, 9, 9, 10
Drop in peak flow, urticaria and facial oedema	9
Wheeze	42
Urticaria and abdominal pain	9, 10, 26
Erythema and oral symptoms	15
Erythema and abdominal pain	46
Open challenge	
Swelling of the lips and facial erythema	54
Swelling of tongue (observable)	54
Urticaria + angioedema	22
Stridor and dysphonia	36

mines to treat a reaction to kiwi fruit, 7% injected epinephrine, 6% a bronchodilator and 4% steroids.

Food challenge

Oral challenges were performed in 46 subjects with self-reported allergy to kiwi fruit (45 DBPCFC $\pm$ open challenge, one open food challenge). Subjects ranged in age from 6 to 64 years (mean 33 years; SD 18 years), and included 12 children under the age of 15 years. Twenty-six (57%) of subjects had a history of symptoms localized to the oral mucosa, the remaining 20 subjects reported systemic symptoms.

Thirty subjects received recipe one, 15 recipe two and one child had an open challenge. In total, 24 DBPCFCs were positive (Table 3), 12 were negative and nine challenges were inconclusive. The inconclusive challenges were in subjects with subjective symptoms. They had symptoms that did not strictly correlate with the placebo/active dose regime, but who we believed were probably positive. The child who only had an open challenge developed swelling of the lips and facial erythema after 2.5 g of kiwi (25 mg protein). In addition, three subjects developed objective clinical signs suggestive of allergy during an open challenge following a negative or inconclusive DBPCFC (Table 3). Therefore, 24 subjects (53%) had kiwi fruit allergy confirmed by DBPCFC, with a further four (total 60%) developing signs suggestive of IgE-mediated food allergy during an open challenge. We had hoped that recipe two would eliminate the inconclusive results in subjects with OAS, but this was not the case with two of 15 subjects having inconclusive symptoms with this improved recipe.

Table 4. Skin test results with fresh kiwi fruit pulp in 45 subjects (prick to prick) and with a commercial extract in 19 subjects

	DBPCFC result		
	Positive	Negative	Inconclusive
Fresh kiwi SPT wheal			
<3 mm	1	4	1
$\geq$ 3 mm	22	9	8
Commercial kiwi SPT wheal			
<3 mm	3	2	2
$\geq$ 3 mm	8	1	3

Table 5. Specific kiwi IgE results

Specific IgE to kiwi fruit	DBPCFC result		
	Positive	Negative	Inconclusive
<0.35	9	10	7
0.4–0.7	6	1	0
0.7–3.5	6	1	1
3.5–17.5	2	0	1

Skin tests

Of the 24 subjects who reacted on DBPCFC, only one had a negative skin test on prick-to-prick testing with fresh fruit. However, there was a high rate of false-positive skin test results (Table 4). In this population prick-to-prick skin tests had a sensitivity of 95% and a specificity of 31%. Skin tests were negative in the five atopic and five non-atopic controls.

Nineteen subjects were also tested with a commercial kiwi skin test extract (Table 4). The commercial solution would appear to be significantly less sensitive, but the number of false-positive skin test reactions was reduced.

The most common allergens causing positive skin tests in the 46 subjects were birch pollen (14), HDM (24), apple (six), banana (four) and avocado (five).

Serum IgE measurements

The results of specific IgE in 45 subjects who had undergone a DBPCFC challenge are shown in Table 5. In this population, the sensitivity of the test was 60% and the specificity was 83%. The level of specific IgE did not correlate with reported severity of symptoms or age. One atopic control had kiwi-specific IgE. A challenge was not performed because this subject reported regular consumption of kiwi fruit with no problem. None of the other nine control sera had detectable kiwi sIgE.

Gel

Protein content of the fresh kiwi extract was 0.49 mg protein/mg extract (49%), and the skin test solution contained 50 mg protein/mL. The protein profiles of the two extracts are shown in Fig. 3. The fresh fruit extract had protein bands at $\approx$ 14, 15, 17, 22, 36 and 40 kDa. The skin test solution only had a band at $\approx$ 23 kDa. The study was repeated running neat skin test solution with similar results (not shown).

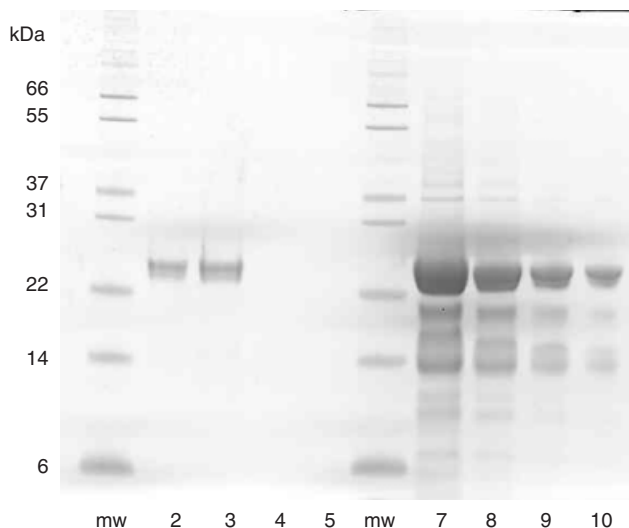


Fig 3. Kiwi skin test extract (Alyostal, France) lanes 2–5; fresh kiwi extract lanes 7–10; molecular marker lanes 1 and 5. Samples were run in 12% SDS-PAGE gel with 40, 20, 10 and 5 µg of extract per lane.

Discussion

Kiwi fruit was introduced into the UK diet in the late 1960s/early 1970s. Since the first world-wide report of allergy in 1981 [1], very few studies have evaluated IgE-mediated hypersensitivity to kiwi fruit. We report the largest detailed study of kiwi fruit allergic patients. Subjects presented with typical symptoms of IgE-mediated allergy, including anaphylaxis, highlighting the growing importance of this allergen. We were able to confirm definite clinical reactivity to kiwi fruit in 53% of 45 patients who reported adverse reactions to kiwi fruit.

The retrospective questionnaire survey of 273 subjects shows that the first people to develop allergy to kiwi fruit were adults, and despite an increasing consumption of the fruit throughout the 1970s and 1980s, it was not until the mid-1990s that a large increase in the number of children developing kiwi allergy started to occur. The large number of self-selecting respondents to this study suggests that kiwi fruit allergy in the UK may be more common than previously recognized by the medical profession. There has been a demonstrable increase in the incidence of food allergy in general [13], and this has been coincident with an increase in the consumption of kiwi fruit. The combination of these factors probably accounts for the increase in reports of reactions to kiwi fruit. World production figures certainly support a massive increase in kiwi fruit consumption over the past 20 years. Estimates of world kiwi production of 162 398 t during the 3 years 1983–1986, had increased seven-fold to 1 142 316 by 1998–2001 (World Kiwi Fruit Report, Belrose Inc., Pullman, WA, USA). Import data suggest that UK consumption is similarly increasing, with imports of 22 193 t in 1996 rising to 31 563 t in 2002 (UKtradeinfo.co.uk, HM Customs and Excise). In a recently published series of paediatric patients with sesame seed allergy, 30% presented with anaphylaxis, and all of them under the age of 1 year [14]. The authors suggested that their findings could be due to both early exposure in life and the heavy consumption of sesame in their population.

Until now clinical knowledge about kiwi allergy has depended on reports of small groups of patients and scientific information has concentrated on cross-reactivity between birch pollen and latex allergens. Some of the studies investigating cross-reactivity have specifically recruited subjects with OAS. This may have led to misconceptions that kiwi fruit allergy is almost exclusively a 'mild' allergy presenting as a result of cross-reactivity, with symptoms of oral allergy syndrome. Data from this study clearly demonstrates that kiwi fruit allergy can result in severe, life-threatening reactions, particularly in young children. This highlights the fact that a new food should not be immediately categorized as having low allergenicity just because the first reactors (usually adults) have mild symptoms; children may react differently.

The reasons why children did not start developing kiwi fruit allergy until some 30 years after its introduction into the diet will require further investigation. It is possible that kiwi fruit has only been consumed by children in the UK in recent years, but there are no data about kiwi fruit consumption in the general population. Children in this study were reported to react differently to kiwi than the adults in the study. They were more likely to react on their first known exposure to kiwi fruit, whilst adults commonly reported multiple exposures before developing symptoms.

In a similar study characterizing peanut allergy we found that only 19% of subjects reported being exposed to peanut before the exposure that caused the first reaction [11]. Because our understanding is that prior exposure is required for sensitization before an IgE-mediated reaction occurs, 'hidden' routes of sensitization are likely. These potentially include *in utero* sensitization [15], transfer of allergens in breast milk [16] or topical application of allergens [17]. Cross-reactivity to latex and pollens is an additional potential route of sensitization to kiwi fruit. Perhaps the highly atopic young child becomes sensitized by the 'hidden' early routes of exposure, and is capable of mounting an allergic reaction on their first known exposure. Older subjects tended to be less atopic, and may need a larger dose of sensitizing antigen before developing clinical food allergy.

Children who reacted to kiwi fruit were likely to be strongly atopic, with 90% reporting atopic disease, and 58% reporting allergy to peanuts. Children were also more likely to have severe reactions. The youngest subject in our study had a severe anaphylactic reaction at 4 months of age, requiring resuscitation with epinephrine and oxygen, having eaten kiwi fruit prepared using a recipe provided by a health professional. The severity of reactions experienced by young children may simply reflect that they represent a population with a strong allergic predisposition, and as such are more likely to have severe reactions. Alternatively they may be recognizing different IgE binding protein or may be consuming kiwi fruit in a different preparation to adults. Kiwi fruit has only been easily available in the UK for the past 20–30 years, and the adult population must therefore be less likely to have had exposure to the allergen in early life. The striking clinical differences between adults and children with kiwi fruit allergy require further evaluation.

The finding of severe reactions occurring more in younger children is unlike that which exists in peanut allergy, where the deaths predominantly occur in later adolescence and early

adulthood, and more severe symptoms are reported in the older age groups [11]. One could speculate that if we had looked at the range of severity of reaction to peanuts only 30 years after it had been introduced into the UK diet, then we might have seen the same pattern seen in this study. If there is a cohort effect, reflecting a critical age of first exposure to a food allergen, then in 20 years time the most severe reactors to kiwi fruit will be in adolescence and early adulthood, possibly leading to fatalities that have not been seen to date. This has significant implications for the way in which one monitors the development of allergy to a new food. It would be wrong to assume that a food is not particularly allergenic just because the first set of reactors have mild reactions.

The clinical association of pollinosis with allergy to fresh fruit including kiwi is well recognized [18]. Initial respiratory sensitization results in IgE antibodies to pollen proteins, which are homologous to those found in some fruits or vegetables. For example, antigens in birch pollen and apples share allergenic epitopes leading to cross-reactivity that may cause clinical symptoms of OAS when a birch pollen allergic subject eats an apple [19]. Many allergens in kiwi fruit are readily digested by simulated gastric fluid [20], and per oral sensitization to these unstable allergens is therefore unlikely. However, presensitization by inhaling birch pollen allergens could predispose to allergic symptoms to kiwi fruit. The lability of the kiwi allergens may explain why allergic reactions are restricted to the oral cavity (OAS) in some patients with pollen allergy. However, in our study population, subjects with seasonal rhinitis, or reported allergy to pollens, reported rates of systemic symptoms similar to those without pollen-related allergy. Further work is required to determine why some subjects react with symptoms localized to the oral mucosa, while others have severe systemic reactions. Perhaps these two groups are reacting to different allergens, the systemic reactors responding to more stable epitopes. There is no published work comparing different immune responses in the oral mucosa and systemically in subjects with OAS and systemic reactions, and it is perhaps likely that the different responses to allergen are due to differences between subjects rather than differences in the characteristics of the allergens. Allergy to kiwi fruit is increasingly reported, but the role of clinical investigations has received little critical evaluation. Skin testing with fresh kiwi fruit is the most common clinical investigation reported in case reports and series [2, 5, 9, 21–23]. Previous reports suggest that prick-to-prick testing with fresh kiwi or skin testing with home-made kiwi extract are extremely sensitive in subjects in whom kiwi allergy was suspected. We too have found prick-to-prick testing with fresh kiwi fruit very sensitive with only one of 23 subjects having a negative skin test but positive challenge (sensitivity 95%). Although highly sensitive, some studies have described poor specificity, with skin test reactivity in subjects without symptoms of allergy to kiwi fruit, but clinical reactivity to pollens [21] or latex [24, 25]. In this study, 96% of subjects who had a negative DBPCFC had a positive skin test (specificity 31%). However, given the problems of confirming whether oral challenge was positive or negative in some of our subjects (discussed below), the specificity in this study is a worse-case scenario. Skin tests were negative in all our atopic and non-atopic controls.

Commercial skin test extracts are significantly less sensitive. In a study from Spain of 43 subjects with kiwi allergy, only 40% of subjects had positive skin reactions to one commercial extract, and 28% to another make of skin test solution – all subjects had had positive reactions when tested by prick-to-prick with fresh kiwi [26]. We have also found that a commercially available extract was less sensitive than fresh fruit, and that the wheals tended to be smaller. Comparing SDS-PAGE gels of commercial extract and an extract of fresh kiwi fruit, it is evident that most protein bands are absent from the commercial extract, presumably reflecting the lability of kiwi fruit proteins.

Reports to date are contradictory about the role of measuring specific IgE to confirm kiwi fruit allergy. Although positive in some case reports of patients with kiwi allergy [4–6, 23], other authors have found sIgE measurement unhelpful [3, 27]. We found the test to have poor sensitivity (sensitivity 60%). It might well be that the CAP system has a similar problem with the lability of allergens as were identified in the skin test solution.

Double-blind food challenges (DBPCFC) are the 'gold standard' for confirming food allergy [28], but blinded food challenges have rarely been used in the context of oral allergy syndrome. Our recipes were designed to identically challenge all subjects with reported allergy to kiwi fruit, both subjects with oral allergy syndrome, and those with more generalized reactions. Some subjects with OAS complained of severe oral symptoms but these did not correlate with the dosing schedule. These subjects may well not be allergic to kiwi fruit, but our subjective feeling as clinicians is that some of the subjects with oral allergy syndrome were experiencing persistence of symptoms from one dose beyond the next or fluctuating severity of symptoms that did not necessarily coincide with the doses. These subjects were labelled negative or inconclusive in the absence of objective signs, but the subjects were insistent that they experienced symptoms similar to their 'usual' symptoms both during the closed and open challenge. Despite changing the protocol, we continued to have inconclusive results, particularly in subjects with OAS. This highlights a need to tailor challenges to the individual. Many of the people with systemic reactions, particularly young children, reacted at low doses. However, in order to maximize the safety of the test safe for the systemic reactors, subjects with OAS also started at low doses with relatively small increments. We now believe that this group would have been characterized better using even larger increments with longer (e.g. an hour) between doses.

This study has limitations. It is not an epidemiological study, and therefore cannot provide an estimate of the prevalence of the problem. The volunteers are self-selected, which may explain the greater number of adult females, as well as a fairly high percentage of subjects with severe symptoms. As with all questionnaire studies, there is likely to be recall bias. However, this report highlights important features of kiwi fruit allergy, which further our clinical progress in the field.

It has clearly shown that allergy to kiwi fruit is an important problem, with most severe reactions occurring in young children. A significant number of subjects have required resuscitation with epinephrine, and three adult subjects had been admitted to intensive care following

ingestion of kiwi fruit. Although kiwi allergy is known to occur as a consequence of cross-reactions with pollens and latex, half of our population was only allergic to kiwi fruit. These findings emphasize the need for further studies to explain the apparent increasing prevalence of this allergy, and to explain the differences between reactions in children and adults.

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