Allergy 2003: 58: 98–113
Printed in UK. All rights reserved

ALLERGY
ISSN 0105-4538

Review article

Food allergy in adulthood

J. F. Crespo, J. Rodriguez
Servicio de Alergia, Hospital Universitario Doce de Octubre, Madrid, Spain

Dr Jesus F. Crespo
Servicio de Alergia
Hospital Universitario Doce de Octubre
Avda. de Cordoba s/n
28041 Madrid
Spain

Accepted for publication 2 July 2002

In the last decades, the results of studies involving controlled food challenges have provided a reliable scientific basis on the role of foods as a cause of hypersensitivity reactions. Most of these investigations have been focused on paediatric populations, highlighting the role of food allergy in the pathogenesis of atopic dermatitis, identifying foods that most commonly cause allergic reactions, and calling attention to the limited value of skin tests and *in vitro* assays in the diagnosis of clinical allergy (1). However, less evidence for specific features of adverse reactions to foods in adults has been available. Loveless (2) and Graham et al. (3) verified the association between the ingestion of food and development of symptoms in adults in the 1950s. Further, the remarkable studies conducted by Bernstein et al. (4) and Atkins et al. (5, 6) in the early and mid 1980s, definitely confirmed the role of foods as a cause of IgE-mediated allergic reactions in adults and evaluated the relationship between diagnostic procedures and reactivity to food on oral challenge. In 1987, Amlot et al. (7) coined the term, *oral allergy syndrome* (OAS) to describe the symptoms experienced by a subgroup of patients with positive skin tests to food, typically oral symptoms such as oral irritation and throat tightness, followed in a proportion of patients with systemic symptoms. The OAS was a 'new term' to describe an old featured clinical condition, the association between local oropharyngeal signs and symptoms with the ingestion of foods such as hazelnuts, apples, pears, carrots, celery, and potatoes with allergy to pollen, particularly birch. At that time, Ortolani et al. (8) published a large case series of adult patients who had oral symptoms after ingestion of fresh fruits and vegetables under the title 'The oral allergy syndrome'. From then on, this term has rapidly gained acceptance, although its exact meaning has not been kept out of some controversy (9, 10). For some years, however, most studies of food allergy in adults were anecdotal reports of anaphylactic reactions after ingestion of a specific food or based mainly on the clinical history supported by positive allergy skin testing and *in vitro* studies. In the last few years, a number of studies have evaluated adverse reactions to plant-derived foods in adults using DBPCFC models (11–17). Further, by identifying well-characterized clinically allergic patients, these studies have been the basis for detailed immunochemical analysis of allergenic components.

The objective of the present review is to provide an overview of the complex nature of the relationship of foods and IgE-mediated allergic reactions in adults, focusing on distinctive features. Following the recommendations of the EAACI Nomenclature Task Force (18), the term food hypersensitivity (FH) will be used to designate an adverse reaction to food, food allergy (FA), when immunological mechanisms have been demonstrated, and IgE-mediated food allergy, if the role of IgE is highlighted.

Prevalence

Recent population surveys have estimated rates of prevalence of perceived FH of 12% to 20% in adults (19–22). In a large multicentre study involving subjects aged 20–44 years of age from 15 countries, about 12% of adults reported adverse reactions following particular food ingestion (23). The rate of perceived adult FH varied largely across different countries (e.g. Spain, 4.6%; Australia, 19.1%) despite a common standardized methodology. By performing skin prick tests for five food

allergens, after a postal questionnaire, Woods et al. (24) found that 1.3% of adults in Australia were consistently sensitized and perceived adverse food reactions to the same allergen. It is generally considered that true FH is less common in adults than in children. In two population studies performed in the mid 1990, which used DBPCFCs in a selected subgroup of the study population, the prevalence was estimated at 2.4% for FH in Dutch adults (19) and 1.4–1.8% for IgE-mediated FA to eight everyday foods in the UK (20). A slightly higher prevalence was found in a study conducted in a selected population; Bischoff et al. (25) found that 3.2% of 375 adult patients with inflammatory and functional gastrointestinal disease had FA, confirmed by endoscopic allergen provocation and/or elimination diet and re-challenge. However, the prevalence of FA confirmed by DBPCFC in patients infected with HIV seems to be similar to that found in the general adult population (26). Moreover, a recent epidemiological survey performed in France estimated the prevalence of perceived FA to be 4.2% in patients aged from 1 to 3 years and approximately 4% in adults (27). This study was performed only by questionnaire, but it included specific symptoms consistent with FA. Perceived hypersensitivity reactions to milk were estimated to occur in 3–6% of Finnish young adults (28), to peanut and tree nut in 1.1% of the general population of the USA (29) and to peanut in 0.5% of adults in the UK (30). Gender differences, with a female predominance of FH, have been noted in several studies performed on adults. In subjects aged 25–74 years, women (27.5%) were found to report significantly more allergic reactions to foods than men (14.0%) (22).

The rate of near-fatal and fatal reactions to food in adults is unknown. However, fatalities have been described (31,32) and 91% of 32 casualties reported to a national registry established by the American Academy of Allergy Asthma, and Immunology occurred in adolescents and young adults (10–19 years of age, 17 subjects; 20–30 years, 10; and 30–33 years, 2) (33). After 6 years of age, peanut and tree nut caused all the fatalities; all but one of the subjects were known to have food allergy, most of them were known to have asthma, and only four subjects received epinephrine shortly after the reaction. In addition, foods were identified as the major causative agent of severe anaphylaxis with loss of consciousness (42% of 12 cases) and anaphylaxis (38.5% of 127 patients) treated in the emergency department of a general hospital (34) and in 42% of 142 cases of anaphylaxis (35).

Food allergens

The foods most likely to cause proved FH in adults have not been identified through specifically designed community-based studies. Peanuts, fish, shellfish, and tree nuts are frequently listed in textbooks as the most relevant offenders in adult food allergy. Nonetheless, the increasing frequency of pollen allergy, which is found in approximately 15–20% of the general population in developed countries (36), and its relationship with allergy to fruits, suggest that these foods might be a leading cause of FH in adults. Clinical studies have verified clinical allergy to fresh fruits in approximately 20% of pollen-allergic adult patients, therefore more than 2% of the adolescents and young adults might be affected by fruit hypersensitivity (37). This is consistent with findings in the French population, where fruits and vegetables were identified as the most frequent cause of perceived FA from 7 to 30 years of age (27). Likewise, fruits (particularly Rosaceae) and tree nuts were the most common foods perceived as offenders in German adults (22). Also, fruit and vegetables were identified, by case history and positive skin testing, as the main cause of food allergy in patients with onset after 10 years of age in Israel, whereas milk and eggs were the least common (38). In Spain, two case series featured fresh fruits, shellfish, and nuts as the most common causes in adult patients, as diagnosed by case history and allergy testing (39, 40).

The immunochemistry and molecular aspects of food allergens have been recently reviewed elsewhere (41, 42). There is scarce information on qualitative differences of IgE-binding to allergenic components in foods by children and adults. Paediatric and adult fish-allergic patients were shown to have a similar *in vitro* IgE binding to a 12.5- kDa protein from fish extracts, immunochemically similar to Gad c 1 (43). However, in other foods the primary route of sensitization and phenomena of cross-allergy may influence the antigenic recognition. As demonstrated by Pastorello et al. (44) two models of sensitization to apples seem to exist, one depending on sensitization to birch pollen, particularly Bet v 1, causing reactions on subsequent oral contact with the homologous allergen Mal d 1, and the other arising directly from ingestion of apples, in which the allergen Mal d 3 (LTP) is particularly relevant. Tropomyosin has been well characterized as the major allergen in shrimp-allergic patients through ingestion, however, an airborne heat-labile 94/97- kDa shrimp allergen was identified as relevant in patients having IgE-mediated respiratory symptoms through inhalation (45, 46). The major allergens from egg white are ovomucoid (Gal d 1), ovalbumin (Gal d 2), conalbumin (Gal d 3), and lysozyme (Gal d 4), but egg-yolk alpha livetin (chicken serum albumin) was identified as an important allergen in adults allergic to eggs in the context of bird-associated egg allergy (47).

Pathophysiology

Food allergy found in adult subjects could represent a persistence of reactions starting early in childhood and children or be primarily initiated in adulthood. Food

allergy is characteristically one of the first manifestations of the atopic syndrome and affects young children. The most important allergens are cow's milk, hen's egg, fish, and legumes. However, a number of studies have documented the adult onset of food-induced anaphylactic reactions through ingestion, particularly caused by shellfish, nuts, fruits and vegetables. Although more common in the developing gut-associated lymphoid tissue of young children, it is clear that sensitizing processes through the gastrointestinal tract and both cellular and IgE-mediated hypersensitivity responses to ingested foods could operate at any age. In addition, recently evidence has been presented to suggest the presence of localized IgE-mediated responses (duodenal presence of IgE-bearing cells, activated eosinophils, and T cells in patients) in adult patients with food allergy-related gastrointestinal symptoms confirmed by DBPCFC, but negative results of skin and *in vitro* testing (48).

Furthermore, food allergy in adulthood seems to be commonly associated with sensitization to other allergens, particularly inhalants. This condition has had been the subject of special attention during the last decade. Several terms have been used to define this situation, such as OAS and wide variety of 'syndromes', which associated food allergy to other allergies (i.e., pollen, house-dust mite, bird, cat, latex). The immunological basis for these food allergies is IgE cross-reactivity, which might be clinically manifest or irrelevant. Experimental evidence suggests that inhalant allergens could represent the primary sensitizing agents for some patients, particularly with pollen-associated food sensitivity, which has been designated recently as class 2-food allergy. In most studies, these associations are mentioned as syndromes (e.g. pollen–food allergy syndrome, egg–bird syndrome), although they hardly fit the classical definition of syndrome as just a set of symptoms that occur together.

Pollen-associated food allergy

Immunological and molecular aspects of birch pollen-associated food allergies have been studied intensively. A number of studies have shown that between 50 and 93% of birch pollen-allergic patients have immunological reactivity to plant-derived foods. In addition, homologues of the birch pollen allergens Bet v 1, Bet v 2, and Bet v 6, as well as glycoproteins carrying cross-reactive carbohydrate determinants, have been identified as important cross-reactive families in foods of vegetable origin (49). About 50% (30–80% depending on patients, clinical data, and test method; e.g. case history, IgE quantification, skin tests) of birch pollen allergic-patients has been claimed to be 'allergic' to apple (50–53). However, the frequency of clinical reactivity to apple confirmed by oral provocations in large case series of birch pollen-allergic patients remains unidentified, even though a slight increase in reactivity during the birch pollen season has been confirmed by oral challenge tests (54). In a birch pollen-free area, Cuesta-Herranz et al. (37) found that 37% of 95 adult pollen-allergic patients (mainly to grass and olive) had positive skin tests to plant-derived foods; but clinical reactivity confirmed by open provocation ranged from 10% (plum) to 50% (melon, peach) of sensitized individuals. Hence, clinically insignificant cross-reactivity is a common finding in pollen-associated food allergy, a fact that greatly limits the value of skin testing and specific IgE determinations on the diagnosis of true clinical fruit and vegetable allergy. Kazemi-Shirazi et al. (55) using sera from patients reporting isolated oral symptoms verified that pollen allergens (rBet v 1, rBet v 2, birch, and timothy grass) produced an almost complete inhibition of IgE binding to plant food allergens (apple, peach, hazelnut, celery, and carrot). In contrast, recombinant plant food allergens (Bet v 1-homologous) poorly inhibited IgE binding to Bet v 1. Thus, pollen allergens could represent the primary sensitizing agents in some patients, further reacting to fruits with OAS. However, although oral manifestations are very common in patients allergic to fresh fruits co-sensitized to pollen allergens, constraining the concept of fruit allergy to a pollen-related model causing mild or moderate symptoms could underestimate its potential to elicit severe anaphylactic reactions. Life-threatening allergic reactions induced by fresh fruits have been reported in patients with and without associated pollen allergy. The rate of systemic symptoms, following or not oral symptoms, was slightly higher in peach-allergic subjects without than with pollen allergy, but differences were not significant (25% vs. 46%), in a series of 61 adult peach-allergic patients having positive allergy testing and open food challenges (56). Therefore, sensitization to fresh fruit and vegetables is probably a complex event, since individuals are not only exposed to cross-reactive pollen allergens through the respiratory tract, but also to primary fruit allergens by ingestion.

Bird-associated egg allergy

De Maat-Bleeker et al. (57) first reported the association of sensitivity to ingested egg yolk with rhinitis and asthma caused by exposure to a parrot in an older woman. By RAST-inhibition, Mandallaz et al. (58) demonstrated that livetin, the water-soluble fraction of egg-yolk proteins, is the major cross-reacting antigen found in bird dander and hen's egg proteins. They coined the term bird-egg syndrome to designate this association of inhalant and food allergy and suggested that egg allergy in adults could be mainly due to sensitization to egg-yolk livetins and provoked by inhalation of pet bird dander. Further, IgE from patients with bird-related egg allergy was shown to recognize alpha-livetin (chicken serum albumin) in egg yolk and some major allergens in bird feather extract (47, 59). A conclusive clinical explanation for this syndrome has been provided recently by Quirce et al. (60),

who demonstrated by specific bronchial and oral challenges that chicken albumin may cause both respiratory and food-allergy symptoms in patients with the bird-egg syndrome.

HDM-related food allergy

Case reports have described patients with combined shrimp and HDM allergy in adults. In a study of 48 patients allergic to shellfish (various species, but mainly shrimp), 82% appeared to be sensitized to HDM as well (61). Tropomyosin seems to be the protein involved in shrimp–HDM cross-reactivity, and it may be the only allergen involved. In a study of 17 HDM patients receiving immunotherapy, three had IgE against shrimp, and two of these having IgE against tropomyosin had oral allergy symptoms after ingesting shrimp (62). In addition, cross-reactivity between shrimp and German cockroach has been demonstrated by IgE-inhibition experiments (63). However, the primary sensitizing route and the clinical significance of cross-allergy among HDM, cockroach, and shrimp remains undefined. Some patients with HDM have been reported to experience severe anaphylactic symptoms when ingesting snails (64, 65). In a study (66), 31% of the allergic subjects to HDM were sensitized to snails, and cross-reactivity has been demonstrated by IgE-inhibition studies, which identified HDM as the primary sensitizing agent (67). In addition, several reports suggested that allergen immunotherapy with mite extract can worsen snail-induced allergy (68).

Latex-associated food allergy

Immunological reactivity to foods (skin test, food-specific IgE determinations) in natural rubber latex-allergic adult patients has been found to be common in several studies. Based on the clinical history, Blanco et al. (69) diagnosed 42 food allergies in 52% of 25 latex-allergic patients, and over half (55%) of these consisted of systemic anaphylaxis. The foods most commonly involved were avocado, chestnut, banana, kiwi, and papaya. Beezhold et al. (70) demonstrated that immunological reactivity to foods was more common in latex-allergic individuals than in controls. In this study, a total of 100 out of 376 food skin-prick tests were positive in 33 latex-allergic subjects. Twenty-seven percent of 100 positive food skin tests were associated with clinical symptoms. Thirty-seven percent of patients manifested a clinical allergy to at least one food including 11 with anaphylaxis, and 14 with local sensitivity reactions. Positive food skin tests occurred most frequently with avocado (53%), potato (40%), banana (38%), tomato (28%), chestnut (28%), and kiwi (17%). Brehler et al. (71) found that 42.5% of 136 patients with well-documented, clinically relevant, immediate-type hypersensitivity against latex proteins reported allergic symptoms after ingestion of fruits (papaya, avocado, banana, chestnut, passion fruit, fig, melon, mango, kiwi, pineapple, peach, and tomato).

Clinical studies

The potential severity of allergic reactions to ingested allergens in adults was illustrated long ago by Golbert et al. (72), who in 1969 depicted the clinical characteristics of the reactions in six adults, including most commonly dyspnoea, angioedema, abdominal distress, urticaria, cyanosis, and, less frequently, chest pain and syncope. Atkins et al. (5, 6) offered a detailed analysis of the reaction patterns during double-blind food challenges in a series of adult patients with a history of immediate allergic-like reactions after specific food ingestion. A number of clinical studies have provided evidence of adult onset of allergic reactions to a large group of foods, however, some particular features in adulthood deserve to be mentioned.

Milk

Adult onset of cow's (73–75), mare's (76) and goat's (77) milk allergy has been objectively confirmed in several studies. In a retrospective study of 34 adult milk-allergic patients, the main organ manifestations of cow's milk allergy in adults were the respiratory tract and the skin, with gastrointestinal and cardiovascular symptoms occurring less often than in children (78). Only 28% of cow's milk-allergic adults were symptom-free when ingesting milk products after 4 years of disease. Compared with the existing studies on children, the results suggest that allergies to cow milk proteins in adults are less frequent but tend to persist longer. In addition, anecdotal reports have illustrated the adult onset of asthma induced by occupational exposure to aerosolized cow's milk proteins (79–81).

Egg

Although egg allergy has been confirmed in adults by DBPCFC studies (82), most reports on egg-allergic adult patients have been focused on the bird-associated egg allergy. It has been suggested that the occurrence of a bird-egg syndrome is typical in adulthood, with a predominance of the female sex, and in most patients the onset of symptoms of allergy to birds preceded the clinical reaction to egg ingestion. In a study to compare IgE-binding components in bird feather and egg extracts, Szepfalusi et al. (47) found that the median age in subjects with the bird-associated egg allergy was 46 years, whereas the median age in the egg-white-allergic subjects was 11 years. In a recent case series of eight patients who reported respiratory symptoms upon exposure to bird feathers, as well as allergy symptoms after ingestion of egg yolk, the age range being between 21 and 41 years,

the onset of respiratory symptoms with birds preceded egg allergy in half of patients, with a simultaneous onset in the remaining subjects (60). All patients were reported to experience OAS, followed in most cases by facial angioedema and less frequently by acute asthma. Most patients could tolerate well-cooked eggs and ingestion or manipulation of well-cooked chicken produced no symptoms in any patient. A DBPCFC with chicken albumin provoked digestive and systemic allergic symptoms in two patients challenged.

In addition, exposure to inhaled egg proteins among workers in egg processing facilities has been verified as a cause of occupational respiratory allergy to airborne egg proteins with consecutive ingestive IgE-mediated egg allergy, which has been recently designed as 'egg–egg syndrome' (83–86).

Meat

Beef is a major source of protein, but there is limited information on allergic reactions to beef or the main allergens implicated in these reactions. A case of exercise-induced anaphylaxis was confirmed in a 72-year-old woman who suffered this clinical manifestation only when performing mild physical activity after eating pork and beef (87). Also, allergy to chicken and turkey meat has been reported in adults without sensitization to egg proteins (88, 89). Anaphylactic shock caused by pork was reported long ago (90). Interestingly, cross-reactivity among pork kidney and pork and lamb gut have been demonstrated in a patient able to tolerate pork meat (91). Crossed IgE-reactivity between pork and cat epithelia, due to serum albumin, was described by Drouet et al. (92), who coined the term pork–cat syndrome. However, the clinical significance of immunological cross-reactivity has not been extensively evaluated, despite a case of fatal anaphylaxis that was recently reported in a patient with pork–cat syndrome who had eaten wild boar meat (93).

Fish, crustaceans, and molluscs

Hansen and Bindslev-Jensen (94) established a definite relationship between codfish and clinical allergy in adults. Further, Helbling et al. (95) confirmed clinically relevant cross-reactivity among various species in fish-allergic adults evaluated using DBPCFC. However, allergy to a single fish species, such as swordfish, probably due to the presence of species-specific allergens has been described (96). The diagnosis of fish allergy covers additional difficulties since scombroid poisoning, which is caused by ingestion of scombrotoxin accumulated during fish spoilage, closely resembles an acute allergic reaction (97). Moreover, an increasing number of reports have documented, in the last few years, the role of anisakis parasitizing fish as a cause of recurrent anaphylactic reactions after ingesting fish (98, 99). Airborne fish allergenic-components have been detected in the environment (100), explaining the capacity of fish to induce reproducible asthmatic responses in exposed workers (101–104). Fish skin contact has been reported as a cause of occupational protein contact dermatitis in food handlers (105, 106), as well as immunological contact urticaria (107–109).

Bernstein et al. (4) confirmed the clinical reactivity to shrimp in adults by double-blind food challenge. Further studies indicated that serum levels of shrimp-specific IgE are significantly elevated in shrimp-hypersensitive subjects who exhibit positive food challenges (110). Castillo et al. (61) studied a case series of adult patients with shellfish hypersensitivity. The most frequent causes of symptoms were shrimp and squid. The most commonly found symptoms were urticaria/angioedema, asthma, and rhinitis. Tropomyosin has been identified as a cross-reactive allergen between crustaceans, molluscs and members of the phylum Arthropoda. However, sera from shrimp-sensitive patients were able to recognize qualitatively different allergens in different shrimp species extracts, supporting the hypothesis that there are species-specific shrimp allergens (111). In addition, Castillo et al. (112) have also investigated hypersensitivity to squid, describing a series of adults having symptoms highly suggestive of IgE-mediated reactions after ingesting squid or inhaling vapours from cooking squid, most of them also after shrimp ingestion.

Grains

Although grains and grain products have been primarily implicated in IgE-mediated occupational asthma (113), only anecdotal reports have illustrated their ability to induce allergic reactions upon ingestion in adults. Severe anaphylactic reactions in adults have been reported after ingestion of millet seeds (114–116), buckwheat (117), and corn (118). Recently, Pastorello et al. (119) evaluated 22 patients with systemic symptoms after maize ingestion and identified a lipid transfer protein (LTP) as the major allergen. Wheat flour allergy in adults seems to be infrequent and especially described as anaphylactic shock for the most part induced by exercise (120, 121). Harada et al. (122) first verified a synergistic effect of aspirin in inducing urticaria/anaphylaxis after ingestion of wheat, which was confirmed using challenge tests in two patients with food-dependent exercise-induced anaphylaxis (FDEIA). In a further study (123) performed on 12 patients with FDEIA, the ingestion of wheat and aspirin without exercise provoked symptoms in two patients. Aspirin provoked symptoms even with a small amount of wheat and exercise in one patient. Only the combination of aspirin, wheat and exercise provoked anaphylaxis in one patient. Specific IgE, SPT and/or the histamine release test with gluten were positive in most patients with wheat-dependent FDEIA. A small number of case reports of reactions induced by barley have been published, generally as contact urticaria (124) and systemic reactions

(125–127) due to barley malt. Recently, barley LTP and protein Z were identified as the main allergens in beer from barley malt (128, 129). In addition, several reactions have been reported occurring after ingestion of grain products, but caused by contaminating mites (130, 131).

Seeds (pulses, nuts, and kernels)

Allergy due to ingestion to edible seeds of legumes has been rarely reported in adults (132, 133), with the exception of peanut. Recently, in a clinical study performed in India, Patil et al. (16) confirmed by DBPCFC clinical allergy in 54% of 59 patients complaining of adverse reactions to chickpea. Of these, seven patients showed DBPCFC-positive results with other legumes. Respiratory symptoms alone such as breathlessness, wheezing, and coughing were observed in the course of the DBPCFC in 32.3% of patients, 38.7% of patients showed only cutaneous reactions such as urticaria and angioedema, and anaphylactic reactions occurred in 3.3% of patients. Moneret-Vautrin et al. (134) have demonstrated crossed lupine allergy in approximately 30% of 24 patients allergic to peanuts. In addition, the inhalation of lupine flour has been demonstrated as a cause of allergic sensitization in exposed workers that might give rise to occupational asthma and food allergy (135). In adults, sensitization to soybean occurs mainly by inhalation of soybean dust, which has been identified as the causative agent of occupational asthma and asthma epidemics (136).

Nuts have been traditionally enunciated as one of the leading causes of severe allergic reactions in adults. However, most epidemiological and clinical established facts on nut allergy were based on studies including both children and adults. In an epidemiological survey in France, peanut and tree nut were found to account only for 4% of the reported reactions to foods (27). Onset of nut allergy seems to be most common in children, as illustrated in a clinical study from Ewan (137), in which onset in teens or older was found only in 8% of 62 patients diagnosed with nut allergy by skin testing and clinical history. However, in this study the most severe reactions occurred in adults, who were aware of their allergy and had inadvertently ingested nuts. The frequency of reactivity to individual or combinations of nuts has not been addressed specifically in adults. However, in a study exploring the pattern of specific IgE to peanut, hazelnut and Brazil nut in patients of all ages with a history of possible nut allergy, 61% of 731 sera were found to have specific IgE antibodies to more than one nut (138). The probability of a patient with nut allergy having specific IgE to a particular combination of peanut, hazelnut and brazil nut was found to be similar, whatever their age or sex. In a follow-up (more than 13 610 patient months) study of patients (adults and children) allergic to peanut and nut, approximately 15% of 567 patients had a follow-up reaction. Interestingly, severe follow-up reactions occurred only in 0.5% of patients, aged 27–40 years (139).

Recently, a rigorous, multicentre double blind, placebo-controlled, food challenge study has extensively investigated hazelnut allergy in adults (11). Of the symptoms observed during positive DBPCFs, there were 59 cases of OAS localized to the oral cavity, three cases of oral and gastrointestinal symptoms, and five cases of oral and systemic symptoms. Almost all patients were found to be sensitized to pollen, particularly birch and hazel. Further, sera from clinically reactive patients were used to identify hazelnut allergens, confirming that the most important allergen of hazelnut is the 18-kd protein homologous to Bet v 1 (140). In addition, three new major allergens were recognized in hazelnut as proteins of 32, 35, and 47 kd and a 9-kd LTP was identified as an allergen associated with anaphylactic reactions.

Allergic reactions caused by seed and kernel ingestion (linseed (141, 142), sunflower (143, 144), poppy (145, 146), cotton (147), sesame (148–152)) have been reported in adults, most of them being case reports clinically featured as severe anaphylactic reactions.

Vegetables

Allergy to celery has been of particular interest because of its relationship to pollens (birch and mugwort) and other foods from the Apiaceae and because of its propensity to induce anaphylactic reactions. In fact, more than 20 years ago, the term celery–mugwort–spice syndrome was coined to illustrate a broad cross-reactivity (153). However, until recently clinical and immunological features of celery allergy were established from studies based only on case history and allergy testing. In 2000, Ballmer-Weber et al. (12) published a complete clinical study on celery allergy in adult patients. Actual clinical allergy to celery was confirmed for the first time by DBPCFCs in 69% of 32 subjects complaining of adverse reactions to celery root. Half of the patients had symptoms strictly localized to the oral cavity, whereas the remaining patients showed systemic reactions. All patients with positive DBPCFC results were sensitized either to birch (91%) or to mugwort (64%) pollen. Allergy to carrots, another member of the Apiaceae family, is commonly associated with a sensitization to celery, spices, mugwort, and birch pollen. However, previous studies on carrot allergy lacked controlled oral challenges. Further, the same group has investigated clinical and *in vitro* features of carrot allergy confirmed by DBPCFC (17). The history of allergic reactions to carrot was confirmed by means of DBPCFC in 77% of 26 patients tested. History revealed systemic reactions in 14 patients and symptoms strictly localized to the oral cavity on carrot consumption in six patients. All patients with positive DBPCFC results for carrot were found to be sensitized to birch pollen and 60% to mugwort pollen. In addition, the Bet v 1-related major carrot allergen Dau c 1 was recognized by IgE from 85%

of patients; 45% were sensitized to cross-reactive carbohydrate determinants and 20% to carrot profilin. In a small number of patients, IgE binding to Dau c 1 was not inhibited or was weakly inhibited by rBet v 1 or birch pollen extract. This fact could be attributed to a clinically relevant primary sensitization to food allergens of the Bet v 1 family independently of a primary sensitization to birch pollen allergens.

Clinical allergy to other vegetables has hardly ever been reported. Leaf vegetables are a very infrequent cause of IgE mediated allergic reactions. Lettuce has been described to induce allergic contact dermatitis (154), but it has been scarcely documented as a cause of allergic reactions as a result of ingestion (155, 156). Bronchial responses after specific bronchial challenges indicated that inhalation of vapour from boiling Swiss chard might be the causative factor for the acute asthma (157, 158). Despite their wide use, onion-family vegetables rarely cause allergic symptoms. Only some cases of occupational asthma (159) or contact dermatitis (160) have been reported, as have anecdotal cases of IgE-mediated allergy caused by garlic (161) and onion (162). Asparagus has been rarely described as a cause of occupational asthma when harvesting these shoot vegetables (163); in addition immediate contact urticaria (164), and acute urticaria after ingestion (165) have been described. Recently, Pascual et al. (166) have identified a common band of 44–46 kDa, probably corresponding to patatin, in tomato, potato, and latex using the sera from children and young adults with tomato allergy confirmed by open provocations. Patients were divided in two groups according to concomitant sensitization to latex. In tomato-allergic patients lacking sensitization to latex, the most frequent clinical symptom with tomato was OAS, whereas urticaria and anaphylaxis were found to be the most common manifestations in tomato–latex allergic subjects. Sensitization to pollens, mainly grass, was found to be a common finding particularly in tomato-allergic patients lacking latex allergy. A few cases of contact urticaria (167) and respiratory symptoms (168) induced by potato have been published; probably due to the heat liability of the major potato allergen patatin, Sol t 1 (169).

Fruits

The fruiting body of different plants is commonly consumed as a dessert or an appetizer. Although a wide number of botanical families include foods usually designated as fruits, only a small number of species have been identified in clinical studies as a cause of clinical IgE-mediated allergy. The Rosaceae and the Cucurbitaceae families have been the subject of particular interest in clinical studies. Others have been widely studied from an immunological and molecular view, but information on their clinical relevance is limited. Recent changes in dietary habits and the global market have made possible the consumption of fruits considered as exotic only a few years ago, so also providing novel allergenic sources. Table 1 lists fruits that have been reported in clinical studies as a cause of IgE-mediated allergic reactions. Different immunological and clinical aspects of the cross-reactions between birch pollen and apple have been investigated in numerous studies, but only a small group has included food challenges as revised by Skamstrup Hansen et al. (15). Apple allergy has been traditionally reported as a birch pollen-associated phenomenon caused by homologous structures in apples and birch pollen, being the OAS with by far the most predominant clinical finding. In a noteworthy case series of 100 Italian patients with OAS, apple was found to be the most prevalent food (170). The major allergens identified in apple extract (Mal d 1 and Mal d 2) are structurally homologous to the birch pollen major allergens Bet v 1 (PR-10) and Bet v 2 (profilin) (171). Recently, by evaluating 43 adults with allergy to apple confirmed by open provocation, Pastorello et al. (44) demonstrated that a lipid transfer protein (Mal d 3) was an important allergen in patients allergic to apple but not to birch pollen, whose sensitization may occur primarily through the oral route. Seventy-two percent of 43 patients had isolated oral symptoms during the oral challenge, 5% oral and gastrointestinal, 7% oral and systemic symptoms (urticaria, rhinoconjunctivitis, or asthma) during the course of the oral challenge. The remaining patients (16%) had a convincing history of life-threatening reactions (laryngeal oedema, anaphylactic shock). Interestingly, the rate of patients having only oral mucosa symptoms was not different in subjects with and without associated birch pollen allergy.

Prunus species fruits, particularly peach, have been found to be among the foods most frequently reported as a cause of allergic reactions in adults in the Mediterranean area (172). In the late 1980s, Ortolani et al. (170) first documented by open food challenges that peach was a common cause of OAS. Further, Cistero et al. (173) noted that most of the allergenicity of peach is confined to the skin and corresponds to a protein of 8–10 kd.

Table 1. Fruits reported as a cause of allergic reactions in clinical studies

Botanical family	Fruits
Anacardiaceae	Mango
Anonaceae	Custard apple
Cucurbitaceae	Cucumber, melon, pumpkin, watermelon, zucchini
Actinidiaceae	Kiwi
Ebenaceae	Persimmon
Lauraceae	Avocado
Moraceae	Fig
Musaceae	Banana
Palmaceae	Coconut, date
Punicaceae	Pomegranate
Rosaceae (Pomoideae)	Apple, pear
Rosaceae (Prunoideae)	Apricot, peach, plum, cherry
Sapindaceae	Ackee, litchi
Vitaceae	Grape

A number of recent studies has improved the knowledge of allergenic components, cross-reactive structures, and clinical features of peach allergy. At the same time, two different groups (174, 175) published their findings identifying an LTP as the most relevant allergen in peach. Further investigations have demonstrated that approximately 90% of peach-sensitive patients have positive *in vivo* responses to peach LTP (176). It has been shown that this protein is an important allergen in the Rosaceae, including *Prunus* species (peach, apricot, plum, and cherry) and Malaceous (apple, pear) fruits (177–179). In a large case series of 70 peach-allergic patients diagnosed by allergy testing, rub tests, and open oral challenges, Cuesta Herranz et al. (56) found the OAS as the most common symptom (86% of patients), followed by contact urticaria (61%) and systemic symptoms (26%). Most of the peach-allergic patients (81%) also had pollen allergy, which was significantly associated with asthma. In a DBPCFC study (180) of 34 adults complaining of adverse reactions to Rosaceae, peach was proved to be the most common offender, followed by apple and apricot. Although isolated oral symptoms were the most common manifestations of peach allergy (59%), severe systemic anaphylaxis was found in 23% of peach-allergic patients. In addition, 46% of 22 patients with clinical peach allergy were found to be clinically reactive to other Rosaceae as confirmed by DBPCFCs.

Recently, clinical allergy to melon has been confirmed in a DBPCFC study in 36% of 53 adults complaining of adverse reactions (14). Onset of melon-induced reactions was reported to occur from 6 to 45 years (median, 20 years), preceded by seasonal rhinitis, asthma, or both in 88% of patients. Isolated oral mucosa symptoms occurred in 74% of patients, but anaphylactic shock was documented in 11%. All but one patient were shown to react clinically to an extensive group of foods; predominantly avocado (37%), banana (37%), kiwi (32%), and watermelon (32%). Previous studies have demonstrated an association between sensitivity to melon, watermelon, banana and ragweed pollen allergy (181). On the other hand, it has been demonstrated that in a ragweed-free area, sensitization to melon occurred mainly in patients with *Plantago* and orchard grass pollen allergy, which share antigenic components with melon (182). Regarding other member of gourd family, Reindl et al. (183) have confirmed four cases of clinical allergy to zucchini by DBPCFC, clinically manifest as OAS in half of the patients. IgE-inhibition experiments showed cross-reactivity with the birch pollen profilin (Bet v 2).

Kiwi fruit has been reported as a cause of OAS as well as severe systemic reactions. Kiwi fruit contains a large number of allergens widely cross-reacting with allergens in grass and birch pollen extracts (184), however, the major allergen, Act c 1, appears to be specific for kiwi (185). Other clinical studies of fruit-allergic patients have focused mainly on latex-associated fruits, particularly avocado, banana, and chestnut. Blanco et al. (186) reported a case series of 17 adult patients with a history consistent with avocado hypersensitivity. Clinical manifestations were particularly severe, as systemic anaphylaxis was found in 40% of patients. In addition, a number of other allergies were reported in these patients, such as latex (59% of patients), banana (47%), chestnut (47%), kiwi (24%), and walnut (24%). In this regard, chestnut and avocado class I chitinases with an N-terminal hevein-like domain have been identified as the major allergens that cross-react with latex (187).

Diagnostic evaluation

Several consensus guidelines support the idea that evaluation of FH relies on a clinical history, physical examination, appropriate skin and/or *in vitro* testing, and double blind, placebo-controlled food challenges (188, 189). However, the evaluation of subjects with histories of adverse reactions after ingestion of fresh fruits and vegetables, which is a frequent complaint in adults, deserves additional comments. IgE-mediated sensitization is frequently not detected by using allergenic extracts because of the lability of the responsible allergen. In 1942, Tuft and Blumstein (190) first documented the frequent failure of some fruit extracts to induce positive skin reactions in clinically sensitive patients. Later on, the introduction of the prick–prick technique with fresh fruits and vegetables increased the potential of skin testing to detect immunological hypersensitivity. In a study of 100 adults with a history of OAS after ingestion of fruits and vegetables, Ortolani et al. (170) demonstrated that skin tests with the prick + prick technique were more sensitive for fruits and vegetables, such as carrot, celery, cherry, apple, tomato, orange, and peach. In contrast, skin testing with commercial extracts was the most sensitive option for peanut, hazelnut, and pea. However, the accuracy of skin and *in vitro* tests with most plant-derived foods for predicting true clinical allergy remains unsettled. Tables 2 and 3 show studies evaluating the clinical utility of skin and *in vitro* testing in adults with case histories of adverse reactions to specific foods. Regarding plant-derived foods, Ortolani et al. (11) noted that skin testing with natural hazelnut and IgE tests had a reasonable sensitivity and positive predictive value (PPV) (over 0.9), but a very low specificity and negative predictive value (NPV) (under 0.15). A PPV of the prick–prick and specific IgE ($\geq$ 0.7 kU/l) of 0.88 and 0.96 was obtained for celery, whereas the specificity and negative predictive values were poor for this food (12). In contrast, significant lower PPV (0.42 and 0.44) of prick–prick and specific IgE ($\geq$ 0.35 kU/l) to melon have been reported by Rodriguez et al. (14). In general, these figures strongly contrast with previous studies evaluating the clinical utility of allergy testing in food allergy. Poon et al. (191) performed a cost-effectiveness analysis of *in vitro* and skin testing based on data taken from literature published

Table 2. Performance characteristics for skin tests in studies conducted with the DBPCFC method in adults

Food	Positive DBPCFC	Sensitivity	Specificity	PPV	NPV
Hen's egg extract (1 : 100 w/v) (82)	7/13 (0.54)	0.71	0.33	0.59	0.46
Cow's milk extract (1 : 20 w/v) (82)	4/11 (0.36)	0.75	0.57	0.36	0.88
Codfish extract (1 : 20 w/v) (94)	7/10 (0.70)	1	0.67	0.94	1
Hazelnut extract (0.64–6.2 mg/ml*) (11)	67/78 (0.86)	0.90	0.06	0.93	0.04
Natural hazelnut (prick–prick) (11)	67/78 (0.86)	0.88	0.28	0.94	0.15
Celery extracts (44 μg/ml–1.5 mg/ml*) (12)	22/30 (0.73)	0.48–0.96	0.13–0.88	0.87–0.96	0.11–0.43
Raw celery root (prick–prick) (12)	22/30 (0.73)	0.96	0	0.88	0
Carrot extract (17)	20/24 (0.83)	0.26	1	–	–
Raw carrot (prick–prick) (17)	20/24 (0.83)	1	0	0.92	0
Fresh melon (prick–prick) (14)	19/53 (0.36)	0.79	0.38	0.42	0.77
Chickpea extract (2 mg/ml*) (16)	31/59 (0.53)	1	0.64	0.75	1

* Proteins.

Table 3. Performance characteristics for food-specific IgE determinations in studies conducted with the DBPCFC method in adults

Food	Positive DBPCFC	Sensitivity	Specificity	PPV	NPV
Egg* (82)	7/13 (0.54)	0.58	0.17	0.62	0.15
Milk* (82)	4/11 (0.36)	1	0.71	0.53	1
Codfish* (94)	7/10 (0.70)	1	0.67	0.94	1
Hazelnut† (11)	67/78 (0.86)	0.75	0.16	0.92	0.05
Celery† (12)	22/30 (0.73)	0.73	0.38	0.09	0.17
Carrot† (17)	20/24 (0.83)	0.90	0.50	0.97	0.23
Melon‡ (14)	19/53 (0.36)	0.53	0.62	0.44	0.70
Chickpea§ (16)	31/59 (0.53)	0.74	1	1	0.78

* Phadebas RAST ≥ class 1.
† CAP-FEIA ≥ 0.7 kU/l.
‡ CAP-FEIA ≥ 0.35 kU/l.
§ ELISA.

between 1975 and 1996. In comparison with the oral challenge test, skin tests and *in vitro* were found to have PPV ranging between 2% and 30%, and NPV ranging between 95% and 100%. Reasons for these differences could be related to the study design, selection criteria (e.g. age, associated atopic disorders, type of symptoms), food/s evaluated, and the sample size.

Establishing a valid model for verifying the diagnosis of true clinical allergy to fresh fruits and vegetables continues to be a controversial issue. In the late 1980s, standards were set for the use of the DBPCFC technique both for establishing uniform patient populations for controlled studies on the mechanism involved in food allergy and for use, in clinical practice, for diagnostic purposes in individual patients (192, 193). More recently, the EAACI subcommittee on adverse reactions to food endorsed the value of this method by 'considering that a positive DBPCFC is the only conclusive evidence of a food allergy provided it is performed properly' (189). Nevertheless, clinical features of fresh fruit reactions, commonly manifested as OAS, and the decrease of allergenicity of processed fruits (i.e., cutting, heating) have been invoked as major concerns limiting the usefulness of the DBPCFC method. Therefore open challenges have been generally considered confirmatory for these allergenic reactions. OAS is considered a form of contact urticaria confined to the oropharynx, therefore proper oral provocations should allow direct contact of the fresh fruit with the oropharyngeal mucosa. This has been typically accomplished by using one or more uncontrolled open food challenges (OFC), which incorporate chewing increasing doses of fresh fruits before the patient is asked to swallow the final doses. However, the effectiveness of these procedures to provide an appropriate control of psychogenic factors and patient or observer bias is possibly limited. The capability of DBPCFCs using liquid vehicles to reproduce OAS has been documented in several studies. Symptoms strictly localized to the oral cavity were elicited in 16 and 11 adult patients during the course of DBPCFCs with carrot and celery in liquid vehicles, respectively (12, 17). On the other hand, although the true rate of false negative results from DBCFCs with fresh fruits and vegetables in adequate vehicles has been addressed in very few studies, it seems to be close to other foods, such as fish (Table 4). Skamstrup Hansen et al. (15) evaluated three methods of DBPCFC with apple, including fresh apple juice, freshly grated apple, and freeze-dried apple powder in 65 patients with a positive open oral challenge with apple. The first model had an unacceptably low sensitivity (0.43) combined with a high rate of reactions to placebo. The sensitivity of the last two challenge models was comparable (0.74/0.60). These findings are consistent with several studies, in which DBPCFCs with fresh fruits confirmed approximately 70% of precedent positive OFC with fresh fruits (14,180). The remaining DBPCFCs results were considered apparently as false negative, but when patients underwent additional final OFCs, after negative results of DBPCFCs, they remained unreactive. It is quite probable that the design of the DBPCFC procedure with adequate vehicles and placeboes could provide an objective method for determining the validity of a history of an adverse reaction to fresh fruits and vegetables.

Table 4. Results of DBPCFCs with plant-derived foods in adults

	Hazelnut (11)	Celery (12)	Carrot (17)	Melon (14)	Apple (15)	Chickpea (16)
Case histories	86	32	26	53		59
Positive OFC	–	–	–	25/51* (49%)	19	–
Positive DBPCFC	67/86† (78%)	22/32‡ (69%)	20/26‡ (77%)	17/25 (68%)	14/19 (74%)	31/59 (53%)
Cumulative dose	20 g	20 g	70 g	200 g	20 g§	10 g¶
Vehicles (and placeboes)	Water, sugar, peppermint syrup, rice flour, cocoa powder, saffron, milled rice grains	Broccoli, cream, yogurt, water, salt	Cooked pumpkin, cream, yogurt, water, saffron, salt, pepper	Orange and pineapple juice, sugar, wheat meal, liquid colouring	Grated cabbage, apple juice	Capsules (dextrose)
Positive final OFC	5/11	4/8	1/4	0/8	–	
Cumulative dose	10 g	35 g	35 g	200 g	–	50 g
False-negative DBPCFC	5/78 (6%)	4/30 (13%)	1/24 (4%)	0	–	0

* Two patients reported severe anaphylaxis which precluded further challenges.
† Eight placebo responders.
‡ Two placebo responders.
§ Grated apple (other two models were also evaluated in the same study).
¶ Chickpea flour.

An additional issue in the diagnostic evaluation of food allergy arises from possible clinical cross-allergy to related foods, whose relevance is quite unknown if these foods have not been ingested recently. Rodriguez et al. (14) addressed the clinical reactivity to avocado, banana, kiwi, and chestnut in each of 19 patients with confirmed allergy to melon. Seven reactions (avocado, five patients; banana, one patient; and kiwi, one patient), which had not been reported by the patients as problem foods, were uncovered in the course of routine challenges with these foods. Because of the extensive immunological cross-reactivity among plant-derived foods (e.g. Rosaceae), which is clinically not relevant, skin testing and *in vitro* tests provide a limited guidance for diagnosis of true clinical allergies to potential cross-reactive foods. In a systematic double-blind placebo-controlled food challenge study of reactivity to seven foods of the Rosaceae in adult patients, 121 skin prick tests to some fruits were found to be positive in 26 patients, but only 40 tests were clinically relevant (180). Therefore, potential cross-reactive fruits should be specifically tested by oral challenges before patients are advised that these foods can be safely consumed. Skin and *in vitro* tests with other foods of the same plant family (Rosaceae fruits) or antigenically linked (i.e., avocado, chestnut, kiwi, banana) should be acceptable only as front-line diagnostic tools to be used for selecting foods to be evaluated through oral challenges when they have not been ingested recently (194, 195).

Managing food allergy in adults

As in children, once the diagnosis of clinical allergy in adults is established, the only effective intervention therapy is strict elimination of the offending food (196). In addition, an appropriate avoidance plan should include recommendations on which other potentially cross-reactive foods could be consumed. Although there is a lack of an evidence-based guideline to prescribe avoidance of botanical families or antigenic-related foods, several studies have provided insights regarding clinical relevance of cross-reactivity among related foods, as reviewed somewhere else (197). Since a very low rate of clinical cross-allergy has been demonstrated among legumes, cereal grains, egg-chicken, and milk-cooked beef, it is generally considered as inadequate to restrict entire families or groups that include these foods (198–200). Some studies have recommended that fish-allergic patients should be specifically tested by oral food challenge before being advised that any fish species to which they manifest a positive skin test can be safely consumed (201). Avoidance of the entire food group has been suggested as advice to patients with allergy to nut or shellfish families (202, 203). Elimination diets restrained to fruits reported in history as offenders and proven to induce allergic symptoms might overlook the risk of potential clinical cross-reactivity, when the patient has not consumed other related fruits after the reaction. Therefore, a comprehensive therapeutic management of fruit allergy should consider that other foods of the same plant family (Rosaceae fruits) or antigenically linked (i.e., avocado, chestnut, kiwi, banana in latex-allergic patients) to be specifically tested by oral challenges before advising the patient that these fruits should be safely consumed.

The unpredictability of the first episode of food-induced allergy in adults makes this episode quite unavoidable; however, further reactions could and should be prevented. A number of studies have revealed that food-allergic patients will experience subsequent

reactions, particularly as a result of inadvertent ingestion of the causative food allergen. Therefore, as suggested recently by Bock et al. (33) from the analysis of a case series of patients who suffered fatal anaphylactic reactions to foods, most of them being adolescents and adults, interventions should be implemented to reduce the risk of further reactions by more stringent food-labelling requirements and improving education of patients, physicians, and the general public. The education plan of the allergic individuals should include providing the patient with detailed instructions on how to avoid foods to which they are allergic, early identification of signs of anaphylaxis and an adequate training in the use of self-injectable epinephrine, and an emergency plan in case of accidental ingestion. Unfortunately, the adherence to these recommendations has not been addressed in adult patients. However, paediatric studies presented evidence to support the usefulness of a protocol for emergency care including a ready-to-use intramuscular epinephrine injection (204).

Currently, no proactive treatment of food allergy is yet available. In a randomized clinical trial, the effect of treatment with antihistamines on OAS elicited by ingestion of hazelnuts in birch pollen-allergic patients was investigated by Bindslev-Jensen et al. (205) This study showed that treatment with antihistamines significantly reduced the symptoms compared with placebo, without, however, completely abolishing the symptoms. In view of the potential risk of severe reactions in patients with OAS, antihistamines do not seem a safe approach. As opposed to immunotherapy for hymenopteran venom or certain aeroallergen sensitivities, the few studies that have been conducted in food-allergic adults have studied the possible effects of immunotherapy with pollen allergens in OAS patients, providing controversial results (206, 207). More recently, in a prospective study carried out in 49 birch pollen-sensitive patients with apple-induced OAS, immunotherapy with birch pollen extracts was shown to reduce clinical apple sensitivity and skin reactivity in most cases after only 1 year of treatment (208). In addition, oral hyposensitization with celery juice was shown to be effective to prevent further severe reactions in a 49-year-old woman with celery-induced anaphylaxis (209). It is quite probable that some of the several therapeutic modalities currently under investigation such as peptide immunotherapy, DNA immunization, immunization with immunostimulatory sequences, anti-IgE therapy, and genetic modification of foods, will provide a safe and effective treatment and prevention of food allergy in the near future (210, 211).

References

1. Anderson JA. Milestones marking the knowledge of adverse reactions to food in the decade of the 1980s. Ann Allergy 1994;**72**:143–154.
2. Loveless MH. Milk allergy: a survey of its incidence: experience with masked ingestion test. J Allergy 1950;**21**:489.
3. Graham DT, Wolf S, Wolf HG. Changes in tissue sensitivity associated with varying life situations and emotions: their relevance to allergy. J Allergy 1950;**21**:478.
4. Bernstein M, Day JH, Welsh A. Double-blind food challenge in the diagnosis of food sensitivity in the adult. J Allergy Clin Immunol 1982;**70**:205–210.
5. Atkins FM, Steinberg SS, Metcalfe DD. Evaluation of immediate adverse reactions to foods in adult patients. I. Correlation of demographic, laboratory, and prick skin test data with response to controlled oral food challenge. J Allergy Clin Immunol 1985;**75**:348–355.
6. Atkins FM, Steinberg SS, Metcalfe DD. Evaluation of immediate adverse reactions to foods in adult patients. II. A detailed analysis of reaction patterns during oral food challenge. J Allergy Clin Immunol 1985;**75**:356–363.
7. Amlot PL, Kemeny DM, Zachary C, Parkes P, Lessof MH. Oral allergy syndrome (OAS): symptoms of IgE-mediated hypersensitivity to foods. Clin Allergy 1987;**17**:33–42.
8. Ortolani C, Ispano M, Pastorello E, Bigi A, Ansaloni R. The oral allergy syndrome. Ann Allergy 1988;**61**:47–52.
9. Lessof MH. Pollen–food allergy syndrome. J Allergy Clin Immunol 1996;**98**:239–240.
10. Kelso JM. Oral allergy syndrome? J Allergy Clin Immunol 1995;**96**:275.
11. Ortolani C, Ballmer-Weber BK, Hansen KS et al. Hazelnut allergy: a double-blind, placebo-controlled food challenge multicenter study. J Allergy Clin Immunol 2000;**105**:577–581.
12. Ballmer-Weber BK, Vieths S, Luttkopf D, Heuschmann P, Wüthrich B. Celery allergy confirmed by double-blind, placebo-controlled food challenge: a clinical study in 32 subjects with a history of adverse reactions to celery root. J Allergy Clin Immunol 2000;**106**:373–378.
13. Ballmer-Weber BK, Hoffmann A, Wüthrich B et al. Influence of food processing on the allergenicity of celery: DBPCFC with celery spice and cooked celery in patients with celery allergy. Allergy 2002;**57**:228–235.
14. Rodriguez J, Crespo JF, Burks W et al. Randomized double-blind, crossover challenge study in 53 subjects reporting adverse reactions to melon (*Cucumis melo*). J Allergy Clin Immunol 2000;**106**:968–972.
15. Skamstrup Hansen K, Vestergaard H, Stahl Skov P et al. Double-blind, placebo-controlled food challenge with apple. Allergy 2001;**56**:109–117.
16. Patil SP, Niphadkar PV, Bapat MM. Chickpea a major food allergen in the Indian subcontinent and its clinical and immunochemical correlation. Ann Allergy Asthma Immunol 2001;**87**:140–145.
17. Ballmer-Weber BK, Wüthrich B, Wangorsch A, Fotisch K, Altmann F, Vieths S. Carrot allergy: double-blinded, placebo-controlled food challenge and identification of allergens. J Allergy Clin Immunol 2001;**108**:301–307.
18. Johansson SG, Hourihane JO, Bousquet J et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy 2001;**56**:813–824.

19. Jansen JJ, Kardinaal AF, Huijbers G, Vlieg-Boerstra BJ, Martens BP, Ockhuizen T. Prevalence of food allergy and intolerance in the adult Dutch population. J Allergy Clin Immunol 1994;**93**:446–456.
20. Young E, Stoneham MD, Petruckevitch A, Barton J, Rona R. A population study of food intolerance. Lancet 1994;**343**:1127–1130.
21. Altman DR, Chiaramonte LT. Public perception of food allergy. J Allergy Clin Immunol 1996;**97**:1247–1251.
22. Schafer T, Bohler E, Ruhdorfer S et al. Epidemiology of food allergy/food intolerance in adults: associations with other manifestations of atopy. Allergy 2001;**56**:1172–1179.
23. Woods RK, Abramson M, Bailey M, Walters EH. International prevalences of reported food allergies and intolerances. Comparisons arising from the European Community Respiratory Health Survey (ECRHS) 1991–94. Eur J Clin Nutr 2001;**55**:298–304.
24. Woods RK, Thien F, Raven J, Walters EH, Abramson M. Prevalence of food allergies in young adults and their relationship to asthma, nasal allergies, and eczema. Ann Allergy Asthma Immunol 2002;**88**:183–189.
25. Bischoff SC, Herrmann A, Manns MP. Prevalence of adverse reactions to food in patients with gastrointestinal disease. Allergy 1996;**51**:811–818.
26. Tubiolo VC, Vazzo LA, Beall GN. Food allergy in human immunodeficiency virus (HIV) infection. Ann Allergy Asthma Immunol 1997;**78**:209–212.
27. Kanny G, Moneret-Vautrin DA, Flabbee J, Beaudouin E, Morisset M, Thevenin F. Population study of food allergy in France. J Allergy Clin Immunol 2001;**108**:133–140.
28. Pelto L, Impivaara O, Salminen S, Poussa T, Seppanen R, Lilius EM. Milk hypersensitivity in young adults. Eur J Clin Nutr 1999;**53**:620–624.
29. Sicherer SH, Muñoz-Furlong A, Burks AW, Sampson HA. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. J Allergy Clin Immunol 1999;**103**:559–562.
30. Emmett SE, Angus FJ, Fry JS, Lee PN. Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut allergy in other household members. Allergy 1999;**54**:380–385.
31. Yunginger JW, Sweeney KG, Sturner WQ et al. Fatal food-induced anaphylaxis. JAMA 1988;**260**:1450–1452.
32. Foucard T, Edberg U, Malmheden Yman I. Fatal and severe food hypersensitivity. Peanut and soya underestimated allergens. Lakartidningen 1997;**94**:2635–2638.
33. Bock SA, Muñoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. J Allergy Clin Immunol 2001;**107**:191–193.
34. Pastorello EA, Rivolta F, Bianchi M, Mauro M, Pravettoni V. Incidence of anaphylaxis in the emergency department of a general hospital in Milan. J Chromatogr B Biomed Sci Appl 2001; **756**:11–17.
35. Yocum MW, Khan DA. Assessment of patients who have experienced anaphylaxis: a 3-year survey. Mayo Clin Proc 1994;**69**:16–23.
36. Wüthrich B, Schindler C, Leuenberger P, Ackermann-Liebrich U. Prevalence of atopy and pollinosis in the adult population of Switzerland (SAPALDIA study). Swiss Study on Air Pollution and Lung Diseases in Adults. Int Arch Allergy Immunol 1995;**106**:149–156.
37. Cuesta-Herranz J, Lazaro M, Figueredo E, Igea JM, Umpierrez A, De-Las-Heras M. Allergy to plant-derived fresh foods in a birch- and ragweed-free area. Clin Exp Allergy 2000;**30**:1411–1416.
38. Kivity S, Dunner K, Marian Y. The pattern of food hypersensitivity in patients with onset after 10 years of age. Clin Exp Allergy 1994;**24**:19–22.
39. Castillo R, Delgado J, Quiralte J, Blanco C, Carrillo T. Food hypersensitivity among adult patients: epidemiological and clinical aspects. Allergol Immunopathol (Madr) 1996;**24**:93–97.
40. Joral A, Villas F, Garmendia J, Villareal O. Adverse reactions to food in adults. J Invest Allergol Clin Immunol 1995;**5**:47–49.
41. Burks W, Helm R, Stanley S, Bannon GA. Food allergens. Curr Opin Allergy Clin Immunol 2001;**1**:243–248.
42. Lehrer SB, Ayuso R, Reese G. Current Understanding of Food Allergens. Ann N Y Acad Sci 2002;**964**:69–85.
43. James JM, Helm RM, Burks AW, Lehrer SB. Comparison of pediatric and adult IgE antibody binding to fish proteins. Ann Allergy Asthma Immunol 1997;**79**:131–137.
44. Pastorello EA, Pravettoni V, Farioli L et al. Clinical role of a lipid transfer protein that acts as a new apple-specific allergen. J Allergy Clin Immunol 1999;**104**:1106.
45. Asero R, Mistrello G, Roncarolo D, Amato S. A case of allergy to airborne, heat-labile shrimp allergens. J Allergy Clin Immunol 2002;**109**:371–372.
46. Griffin P, Allan L, Gibson M, Elms J, Wiley K, Curran AD. Measurement of personal exposure to aerosols of *Nephrops norvegicus* (scampi) using a monoclonal-based assay. Clin Exp Allergy 2001;**31**: 928–933.
47. Szepfalusi Z, Ebner C, Pandjaitan R et al. Egg yolk alpha-livetin (chicken serum albumin) is a cross-reactive allergen in the bird–egg syndrome. J Allergy Clin Immunol 1994;**93**: 932–942.
48. Lin XP, Magnusson J, Ahlstedt S et al. Local allergic reaction in food-hypersensitive adults despite a lack of systemic food-specific IgE. J Allergy Clin Immunol 2002;**109**:879–887.
49. Vieths S, Scheurer S, Ballmer-Weber B. Current understanding of cross-reactivity of food allergens and pollen. Ann N Y Acad Sci 2002;**964**:47–68.
50. Kremser M, Lindemayr W. Frequency of the so-called 'apple allergy' ('apple contact urticaria syndrome') in patients with birch pollinosis. Z Hautkr 1983;**58**:543–552.
51. Dreborg S, Foucard T. Allergy to apple, carrot and potato in children with birch pollen allergy. Allergy 1983;**38**:167–172.
52. Mowat A, Eriksson NE, Formgren H, Svenonius E. Food hypersensitivity in patients with pollen allergy. Allergy 1982;**37**:437–443.
53. Vieths S, Jankiewicz A, Schöning B, Aulepp H. Apple allergy: the IgE-binding potency of apple strains is related to the occurrence of the 18-kDa allergen. Allergy 1994;**49**:271.
54. Skamstrup Hansen K, Vieths S, Vestergaard H, Skov PS, Bindslev-Jensen C, Poulsen LK. Seasonal variation in food allergy to apple. J Chromatogr B Biomed Sci Appl 2001;**756**:19–32.
55. Kazemi-Shirazi L, Pauli G, Purohit A et al. Quantitative IgE inhibition experiments with purified recombinant allergens indicate pollen-derived allergens as the sensitizing agents responsible for many forms of plant food allergy. J Allergy Clin Immunol 2000;**105**:116–125.
56. Cuesta-Herranz J, Lazaro M, de las Heras M et al. Peach allergy pattern: experience in 70 patients. Allergy 1998;**53**:78–82.

57. de Maat-Bleeker F, Van Dijk AG, Berrens L. Allergy to egg yolk possibly induced by sensitization to bird serum antigens. Ann Allergy 1985;**55**:245–248.
58. Mandallaz MM, de Weck AL, Dahinden CA. Bird–egg syndrome. Cross-reactivity between bird antigens and egg-yolk livetins in IgE-mediated hypersensitivity. Int Arch Allergy Appl Immunol 1988;**87**:143–150.
59. de Blay F, Hoyet C, Candolfi E, Thierry R, Pauli G. Identification of alpha livetin as a cross reacting allergen in a bird–egg syndrome. Allergy Proc 1994;**15**:77–78.
60. Quirce S, Maranon F, Umpierrez A, de las Heras M, Fernandez-Caldas E, Sastre J. Chicken serum albumin (Gal d 5) is a partially heat-labile inhalant and food allergen implicated in the bird–egg syndrome. Allergy 2001;**56**:754–762.
61. Castillo R, Carrilo T, Blanco C et al. Shellfish hypersensitivity: clinical and immunological characteristics. Allergol Immunopathol (Madr) 1994;**22**:83–87.
62. van Ree R, Antonicelli L, Akkerdaas JH et al. Possible induction of food allergy during mite immunotherapy. Allergy 1996;**51**:108–113.
63. Crespo JF, Pascual C, Helm R et al. Cross-reactivity of IgE-binding components between boiled Atlantic shrimp and German cockroach. Allergy 1995;**50**:918–924.
64. De Maat-Bleeker F, Akkerdaas JH, van Ree R, Aalberse RC. Vineyard snail allergy possibly induced by sensitization to house-dust mite (*Dermatophagoides pteronyssinus*). Allergy 1995;**50**:438–440.
65. van Ree R, Antonicelli L, Akkerdaas JH et al. Asthma after consumption of snails in house-dust-mite-allergic patients: a case of IgE cross-reactivity. Allergy 1996;**51**:387–393.
66. Vuitton DA, Rance F, Paquin ML et al. Cross-reactivity between terrestrial snails (*Helix* species) and house-dust mite (*Dermatophagoides pteronyssinus*). I. In vivo study. Allergy 1998;**53**:144–150.
67. Guilloux L, Vuitton DA, Delbourg M et al. Cross-reactivity between terrestrial snails (*Helix* species) and house-dust mite (*Dermatophagoides pteronyssinus*). II. *In vitro* study. Allergy 1998;**53**:151–158.
68. Pajno GB, La Grutta S, Barberio G, Canonica GW, Passalacqua G. Harmful effect of immunotherapy in children with combined snail and mite allergy. J Allergy Clin Immunol 2002;**109**:627–629.
69. Blanco C, Carrillo T, Castillo R, Quiralte J, Cuevas M. Latex allergy: clinical features and cross-reactivity with fruits. Ann Allergy 1994;**73**:309–314.
70. Beezhold DH, Sussman GL, Liss GM, Chang NS. Latex allergy can induce clinical reactions to specific foods. Clin Exp Allergy 1996;**26**:416–422.
71. Brehler R, Theissen U, Mohr C, Luger T. 'Latex–fruit syndrome': frequency of cross-reacting IgE antibodies. Allergy 1997;**52**:404–410.
72. Golbert TM, Patterson R, Pruzansky J. Systemic allergic reactions to ingested antigens. J Allergy 1969;**44**:96.
73. Simpson SI, Somerfield SD, Wilson JD, Hillas JL. A double-blind study for the diagnosis of cows' milk allergy. N Z Med J 1980;**92**:458–459.
74. Koers WJ, van der Elst AM, van Dijk AG, Berrens L. Cow's milk allergy in an adult patient. Ann Allergy 1986;**56**:267–269.
75. Norgaard A, Skov PS, Bindslev-Jensen C. Egg and milk allergy in adults: comparison between fresh foods and commercial allergen extracts in skin prick test and histamine release from basophils. Clin Exp Allergy 1992;**22**:940–947.
76. Gall H, Kalveram CM, Sick H, Sterry W. Allergy to the heat-labile proteins alpha-lactalbumin and beta-lactoglobulin in mare's milk. J Allergy Clin Immunol 1996;**97**:1304–1307.
77. Orlando JP, Breton-Bouveyron A. Anaphylactoid reaction to goat's milk. Allerg Immunol (Paris) 2000;**32**:231–232.
78. Stoger P, Wüthrich B. Type I allergy to cow milk proteins in adults. A retrospective study of 34 adult milk- and cheese-allergic patients. Int Arch Allergy Immunol 1993;**102**:399–407.
79. Rossi GL, Corsico A, Moscato G. Occupational asthma caused by milk proteins: report on a case. J Allergy Clin Immunol 1994;**93**:799–801.
80. Bernaola G, Echechipia S, Urrutia I, Fernandez E, Audicana M, Fernandez de Corres L. Occupational asthma and rhinoconjunctivitis from inhalation of dried cow's milk caused by sensitization to alpha-lactalbumin. Allergy 1994;**49**:189–191.
81. Vaswani SK, Sampson HA, Chang BW, Hamilton RG. Adult-onset sensitization to casein after occupational exposure to aerosolized Tryptone powder. J Allergy Clin Immunol 1999;**104**:1108–1109.
82. Norgaard A, Bindslev-Jensen C. Egg and milk allergy in adults. Diagnosis and characterization. Allergy 1992;**47**:503–509.
83. Smith AB, Bernstein DI, Aw TC et al. Occupational asthma from inhaled egg protein. Am J Ind Med 1987;**12**:205–218.
84. Reed C. Occupational asthma in the egg processing industry. Chest 1990;**98**:261–262.
85. Blanco Carmona JG, Juste Picon S, Garces Sotillos M, Rodriguez Gaston P. Occupational asthma in the confectionery industry caused by sensitivity to egg. Allergy 1992;**47**:190–191.
86. Leseries C, Hartmann AL, Praml G, Wüthrich B. The 'egg–egg' syndrome: occupational respiratory allergy to airborne egg proteins with consecutive ingestive egg allergy in the bakery and confectionery industry. J Invest Allergol Clin Immunol 2001;**11**:89–93.
87. Biedermann T, Schopf P, Rueff F, Przybilla B. Exertion-induced anaphylaxis after eating pork and beef. Dtsch Med Wochenschr 1999;**124**:456–458.
88. Liccardi G, Szepfalusi Z, Noschese P, Nentwich I, D'Amato M, D'Amato G. Allergy to chicken meat without sensitization to egg proteins: a case report. J Allergy Clin Immunol 1997;**100**:577–579.
89. Cahen YD, Fritsch R, Wüthrich B. Food allergy with monovalent sensitivity to poultry meat. Clin Exp Allergy 1998;**28**:1026–1030.
90. Pavel AC, Comanescu A. Anaphylactic shock caused by pork. Rev Med Chir Soc Med Nat Iasi 1969;**73**:489–492.
91. Llatser R, Polo F, De La Hoz F, Guillaumet B. Alimentary allergy to pork. Crossreactivity among pork kidney and pork and lamb gut. Clin Exp Allergy 1998;**28**:1021–1025.
92. Drouet M, Boutet S, Lauret MG et al. The pork–cat syndrome or crossed allergy between pork meat and cat epithelia. (1) Allerg Immunol (Paris) 1994;**26**:166–168.
93. Drouet M, Sabbah A, Le Sellin J, Bonneau JC, Gay G, Dubois-Gosnet C. Fatal anaphylaxis after eating wild boar meat in a patient with pork–cat syndrome. Allerg Immunol (Paris) 2001;**33**:163–165.

94. Hansen TK, Bindslev-Jensen C. Codfish allergy in adults. Identification and diagnosis. Allergy 1992;**47**:610–617.
95. Helbling A, Haydel R Jr, McCants ML, Musmand JJ, El-Dahr J, Lehrer SB. Fish allergy: is cross-reactivity among fish species relevant? Double-blind placebo-controlled food challenge studies of fish allergic adults. Ann Allergy Asthma Immunol 1999;**83**: 517–523.
96. Kelso JM, Jones RT, Yunginger JW. Monospecific allergy to swordfish. Ann Allergy Asthma Immunol 1996;**77**:227–228.
97. Smart DR. Scombroid poisoning. A report of seven cases involving the Western Australian salmon, *Arripis truttaceus*. Med J Aust 1992;**157**:748–751.
98. Kasuya S, Hamano H, Izumi S. Mackerel-induced urticaria and *Anisakis*. Lancet 1990;**335**:665.
99. Audicana MT, Fernandez de Corres L, Muñoz D, Fernandez E, Navarro JA, del Pozo MD. Recurrent anaphylaxis caused by *Anisakis simplex* parasitizing fish. J Allergy Clin Immunol 1995;**96**:558–560.
100. Taylor AV, Swanson MC, Jones RT et al. Detection and quantitation of raw fish aeroallergens from an open-air fish market. J Allergy Clin Immunol 2000;**105**:166–169.
101. Droszcz W, Kowalski J, Piotrowska B, Pawlowicz A, Pietruszewska E. Allergy to fish in fish meal factory workers. Int Arch Occup Environ Health 1981;**49**:13–19.
102. Sherson D, Hansen I, Sigsgaard T. Occupationally related respiratory symptoms in trout-processing workers. Allergy 1989;**44**:334–336.
103. Douglas JD, McSharry C, Blaikie L, Morrow T, Miles S, Franklin D. Occupational asthma caused by automated salmon processing. Lancet 1995;**346**:737–740.
104. Rodriguez J, Reano M, Vives R et al. Occupational asthma caused by fish inhalation. Allergy 1997;**52**:866–869.
105. Hjorth N, Roed-Petersen J. Occupational protein contact dermatitis in food handlers. Contact Dermatitis 1976;**2**:28–42.
106. Alonso MD, Davila I, Conde Salazar L et al. Occupational protein contact dermatitis from herring. Allergy 1993;**48**:349–352.
107. Harvima RJ, Tuomisto L, Husman T. Repeated hand urticaria due to contact with fishfood. Scand J Work Environ Health 1999;**25**:151–152.
108. Melino M, Toni F, Riguzzi G. Immunologic contact urticaria to fish. Contact Dermatitis 1987;**17**:182.
109. Goransson K. Contact urticaria to fish. Contact Dermatitis 1981;**7**: 282–283.
110. Daul CB, Morgan JE, Lehrer SB. The natural history of shrimp hypersensitivity. J Allergy Clin Immunol 1990;**86**:88–93.
111. Morgan JE, O'Neil CE, Daul CB, Lehrer SB. Species-specific shrimp allergens: RAST and RAST-inhibition studies. J Allergy Clin Immunol 1989;**83**:1112–1117.
112. Carrillo T, Castillo R, Caminero J et al. Squid hypersensitivity: a clinical and immunologic study. Ann Allergy 1992;**68**:483–487.
113. Houba R, Doekes G, Heederik D. Am J Ind Med 1998;**34**:529–546.
114. Parker JL, Yunginger JW, Swedlund HA. Anaphylaxis after ingestion of millet seeds. J Allergy Clin Immunol 1981;**67**:78–80.
115. Olivieri J, Hauseries C. Anaphylaxis to millet. Allergy 1998;**53**:109–110.
116. Stuck BA, Blum A, Klimek L, Hormann K. Millet a potentially life-threatening allergen. Allergy 2001;**56**:350.
117. Davidson AE, Passero MA, Settipane GA. Buckwheat-induced anaphylaxis: a case report. Ann Allergy 1992;**69**:439–440.
118. Tanaka LG, El-Dahr JM, Lehrer SB. Double-blind, placebo-controlled corn challenge resulting in anaphylaxis. J Allergy Clin Immunol 2001;**107**:744.
119. Pastorello EA, Farioli L, Pravettoni V et al. The maize major allergen, which is responsible for food-induced allergic reactions, is a lipid transfer protein. J Allergy Clin Immunol 2000;**106**:744–751.
120. Varjonen E, Vainio E, Kalimo K. Life-threatening, recurrent anaphylaxis caused by allergy to gliadin and exercise. Clin Exp Allergy 1997;**27**:162–166.
121. Guenard-Bilbault L, Kanny G, Moneret-Vautrin D. Food allergy to wheat flour in adults. Allerg Immunol (Paris) 1999;**31**:22–25.
122. Harada S, Horikawa T, Ashida M, Kamo T, Nishioka E, Ichihashi M. Aspirin enhances the induction of type I allergic symptoms when combined with food and exercise in patients with food-dependent exercise-induced anaphylaxis. Br J Dermatol 2001;**145**:336–339.
123. Aihara M, Miyazawa M, Osuna H et al. Food-dependent exercise-induced anaphylaxis: influence of concurrent aspirin administration on skin testing and provocation. Br J Dermatol 2002;**146**:466–472.
124. Gutgesell C, Fuchs T. Contact urticaria from beer. Contact Dermatitis 1995;**33**:436–437.
125. Curioni A, Santucci B, Cristaudo A et al. Urticaria from beer: an immediate hypersensitivity reaction due to a 10-kDa protein derived from barley. Clin Exp Allergy 1999;**29**:407–413.
126. Fernandez-Anaya S, Crespo JF, Rodriguez JR et al. Beer anaphylaxis. J Allergy Clin Immunol 1999;**103**:959–960.
127. Figueredo E, Quirce S, del Amo A et al. Beer-induced anaphylaxis: identification of allergens. Allergy 1999;**54**:630–634.
128. Asero R, Mistrello G, Roncarolo D, Amato S, van Ree R. A case of allergy to beer showing cross-reactivity between lipid transfer proteins. Ann Allergy Asthma Immunol 2001;**87**: 65–67.
129. Garcia-Casado G, Crespo JF, Rodriguez J, Salcedo G. Isolation and characterization of barley lipid transfer protein and protein Z as beer allergens. J Allergy Clin Immunol 2001;**108**:647–649.
130. Blanco C, Quiralte J, Castillo R et al. Anaphylaxis after ingestion of wheat flour contaminated with mites. J Allergy Clin Immunol 1997;**99**:308–313.
131. Erben AM, Rodriguez JL, McCullough J, Ownby DR. Anaphylaxis after ingestion of beignets contaminated with *Dermatophagoides farinae*. J Allergy Clin Immunol 1993;**92**:846–849.
132. Vidal C, Perez-Carral C, Chomon B. Unsuspected sources of soybean exposure. Ann Allergy Asthma Immunol 1997;**79**:350–352.
133. Taramarcaz P, Hauseries C, Eigenmann PA. Soy anaphylaxis. Allergy 2001;**56**:792.
134. Moneret-Vautrin DA, Guerin L, Kanny G, Flabbee J, Fremont S, Morisset M. Cross-allergenicity of peanut and lupine: the risk of lupine allergy in patients allergic to peanuts. J Allergy Clin Immunol 1999;**104**: 883–888.
135. Crespo JF, Rodriguez J, Vives R et al. Occupational IgE-mediated allergy after exposure to lupine seed flour. J Allergy Clin Immunol 2001;**108**: 295–297.

136. Navarro C, Marquez M, Hernando L, Galvan F, Zapatero L, Caravaca F. Epidemic asthma in Cartagena, Spain, and its association with soybean sensitivity. Epidemiology 1993;**4**:76–79.
137. Ewan PW. Clinical study of peanut and nut allergy in 62 consecutive patients: new features and associations. BMJ 1996;**312**:1074–1078.
138. Pumphrey RS, Wilson PB, Faragher EB, Edwards SR. Specific immunoglobulin E to peanut, hazelnut and brazil nut in 731 patients: similar patterns found at all ages. Clin Exp Allergy 1999;**29**:1256–1259.
139. Ewan PW, Clark AT. Long-term prospective observational study of patients with peanut and nut allergy after participation in a management plan. Lancet 2001;**357**:111–115.
140. Pastorello EA, Vieths S, Pravettoni V et al. Identification of hazelnut major allergens in sensitive patients with positive double-blind, placebo-controlled food challenge results. J Allergy Clin Immunol 2002;**109**:563–570.
141. Alonso L, Marcos ML, Blanco JG et al. Anaphylaxis caused by linseed (flaxseed) intake. J Allergy Clin Immunol 1996;**98**:469–470.
142. Lezaun A, Fraj J, Colas C et al. Anaphylaxis from linseed. Allergy 1998;**53**:105–106.
143. Noyes JH, Boyd GK, Settipane GA. Anaphylaxis to sunflower seed. J Allergy Clin Immunol 1979;**63**: 242–244.
144. Axelsson IG, Ihre E, Zetterstrom O. Anaphylactic reactions to sunflower seed. Allergy 1994;**49**:517–520.
145. Gloor M, Kagi M, Wüthrich B. Poppyseed anaphylaxis. Schweiz Med Wochenschr 1995;**125**:1434–1437.
146. Crivellaro M, Bonadonna P, Dama A et al. Severe systemic reactions caused by poppy seed. J Invest Allergol Clin Immunol 1999;**9**:58–59.
147. Atkins FM, Wilson M, Bock SA. Cottonseed hypersensitivity: new concerns over an old problem. Allergy Clin Immunol 1988;**82**:242–250.
148. Malish D, Glovsky MM, Hoffman DR, Ghekiere L, Hawkins JM. Anaphylaxis after sesame seed ingestion. J Allergy Clin Immunol 1981;**67**:35–38.
149. James C, Williams-Akita A, Rao YA, Chiarmonte LT, Scheider AT. Sesame seed anaphylaxis. N Y State J Med 1991;**91**:457–458.
150. Kagi MK, Wüthrich B. Falafel burger anaphylaxis due to sesame seed allergy. Ann Allergy 1993;**71**:127–129.
151. Asero R, Mistrello G, Roncarolo D, Antoniotti PL, Falagiani P. A case of sesame seed-induced anaphylaxis. Allergy 1999;**54**:526–527.
152. Pajno GB, Passalacqua G, Magazzu G, Barberio G, Vita D, Canonica GW. Anaphylaxis to sesame. Allergy 2000;**55**:199–201.
153. Wüthrich B, Hofer T. Food allergy: the celery–mugwort–spice syndrome. Association with mango allergy? Dtsch Med Wochenschr 1984;**109**:981–986.
154. Krook G. Occupational dermatitis from *Lactuca sativa* (lettuce) and *Cichorium* (endive). Contact Dermatitis 1977;**3**:36.
155. Vila L, Sanchez G, Sanz ML et al. Study of a case of hypersensitivity to lettuce (*Lactuca sativa*). Clin Exp Allergy 1998;**28**:1031–1035.
156. Franck P, Kanny G, Dousset B, Nabet P, Moneret-Vautrin DA. Lettuce allergy. Allergy 2000;**55**:201–202.
157. de la Hoz B, Fernandez-Rivas M, Quirce S et al. Swiss chard hypersensitivity: clinical and immunologic study. Ann Allergy 1991;**67**:487–492.
158. Parra FM, Lazaro M, Cuevas M et al. Bronchial asthma caused by two unrelated vegetables. Ann Allergy 1993;**70**:324–327.
159. Lybarger JA, Gallagher JS, Pulver DW, Litwin A, Brooks A, Bernstein IL. Occupational asthma induced by inhalation and ingestion of garlic. J Allergy Clin Immunol 1982;**69**:448–454.
160. Delaney TA, Donnelly AM. Garlic dermatitis. Australas J Dermatol 1996;**37**:109–110.
161. Asero R, Mistrello G, Roncarolo D, Antoniotti PL, Falagiani P. A case of garlic allergy. J Allergy Clin Immunol 1998;**101**:427–428.
162. Asero R, Mistrello G, Roncarolo D, Amato S. A case of onion allergy. J Allergy Clin Immunol 2001;**108**: 309–310.
163. Lopez-Rubio A, Rodriguez J, Crespo JF, Vives R, Daroca P, Reano M. Occupational asthma caused by exposure to asparagus: detection of allergens by immunoblotting. Allergy 1998;**53**:1216–1220.
164. Sanchez MC, Hernandez M, Morena V et al. Immunologic contact urticaria caused by asparagus. Contact Dermatitis 1997;**37**:181–182.
165. Escribano MM, Muñoz-Bellido FJ, Serrano P, de la Calle A, Conde J. Acute urticaria after ingestion of asparagus. Allergy 1998;**53**: 622–623.
166. Reche M, Pascual CY, Vicente J et al. Tomato allergy in children and young adults: cross-reactivity with 1latex and potato. Allergy 2001;**56**:1197–1201.
167. Jeannet-Peter N, Piletta-Zanin PA, Hauseries C. Facial dermatitis, contact urticaria, rhinoconjunctivitis, and asthma induced by potato. Am J Contact Dermat 1999;**10**:40–42.
168. Quirce S, Diez Gomez ML, Hinojosa M et al. Housewives with raw potato-induced bronchial asthma. Allergy 1989;**44**:532–536.
169. Koppelman SJ, van Koningsveld GA, Knulst AC, Gruppen H, Pigmans IG, de Jongh HH. Effect of heat-induced aggregation on the IgE binding of patatin (Sol t 1) is dominated by other potato proteins. J Agric Food Chem 2002;**50**:1562–1568.
170. Ortolani C, Ispano M, Pastorello EA, Ansaloni R, Magri GC. Comparison of results of skin prick tests (with fresh foods and commercial food extracts) and RAST in 100 patients with oral allergy syndrome. J Allergy Clin Immunol 1989;**83**:683–690.
171. Breiteneder H, Ebner C. Molecular and biochemical classification of plant-derived food allergens. J Allergy Clin Immunol 2000;**106**:27–36.
172. Rodriguez J, Izquierdo G, Poza-Guedes P, Campo P, Daroca P, Crespo JF. Adverse reactions to foods in adulthood assessed by double-blind placebo-controlled food challenges. J Allergy Clin Immunol 2002;**109**:S82.
173. Lleonart R, Cistero A, Carreira J, Batista A, Moscoso del Prado J. Food allergy: identification of the major IgE-binding component of peach (*Prunus persica*). Ann Allergy 1992;**69**:128–130.
174. Sanchez-Monge R, Lombardero M, Garcia-Selles FJ, Barber D, Salcedo G. Lipid-transfer proteins are relevant allergens in fruit allergy. J Allergy Clin Immunol 1999;**103**:514–519.
175. Pastorello EA, Farioli L, Pravettoni V et al. The major allergen of peach (*Prunus persica*) is a lipid transfer protein. J Allergy Clin Immunol 1999;**103**:520–526.
176. Garcia-Selles FJ, Diaz-Perales A, Sanchez-Monge R et al. Patterns of reactivity to lipid transfer proteins of plant foods and *Artemisia* pollen. An *in vivo* study. Int Arch Allergy Immunol 2002;**128**:115–122.
177. Pastorello EA, Farioli L, Pravettoni V et al. Characterization of the major allergen of plum as a lipid transfer protein. J Chromatogr B Biomed Sci Appl 2001;**756**:95–103.

178. Conti A, Fortunato D, Ortolani C et al. Determination of the primary structure of two lipid transfer proteins from apricot (*Prunus armeniaca*). J Chromatogr B Biomed Sci Appl 2001;**756**:123–129.
179. Pastorello EA, Ortolani C, Baroglio C et al. Complete amino acid sequence determination of the major allergen of peach (*Prunus persica*) Pru P 1. Biol Chem 1999;**380**:1315–1320.
180. Rodriguez J, Crespo JF, Lopez-Rubio A et al. Clinical cross-reactivity among foods of the Rosaceae family. J Allergy Clin Immunol 2000;**106**:183–189.
181. Anderson LB, Dreyfuss EM, Logan J, Johnstone DE, Glaser J. Melon and banana sensitivity coincident with ragweed pollinosis. J Allergy Clin Immunol 1970;**45**:310–319.
182. Garcia Ortiz JC, Cosmes Martin P, Lopez Asunolo A. Melon sensitivity shares allergens with *Plantago* and grass pollens. Allergy 1995;**50**:269–273.
183. Reindl J, Anliker MD, Karamloo F, Vieths S, Wüthrich B. Allergy caused by ingestion of zucchini (*Cucurbita pepo*): characterization of allergens and cross-reactivity to pollen and other foods. J Allergy Clin Immunol 2000;**106**:379–385.
184. Gall H, Kalveram KJ, Forck G, Sterry W. Kiwi fruit allergy: a new birch pollen-associated food allergy. J Allergy Clin Immunol 1994;**94**:70–76.
185. Pastorello EA, Pravettoni V, Ispano M et al. Identification of the allergenic components of kiwi fruit and evaluation of their cross-reactivity with timothy and birch pollens. J Allergy Clin Immunol 1996;**98**:601–610.
186. Blanco C, Carrillo T, Castillo R, Quiralte J, Cuevas M. Avocado hypersensitivity. Allergy 1994;**49**:454–459.
187. Blanco C, Diaz-Perales A, Collada C et al. Class I chitinases as potential panallergens involved in the latex–fruit syndrome. J Allergy Clin Immunol 1999;**103**:507–513.
188. American Gastroenterological Association. Medical position statement: guidelines for the evaluation of food allergies. Gastroenterology 2001;**120**:1023–1025.
189. Bruijnzeel-Koomen C, Ortolani C, Aas K et al. Adverse reactions to food. European Academy of Allergology and Clinical Immunology Subcommittee. Allergy 1995;**50**:623–635.
190. Tuft L, Blumstein GI. Studies in food allergy. Sensitization to fresh fruits: clinical and experimental observations. J Allergy 1942;**13**:574–582.
191. Poon AW, Goodman CS, Rubin RJ. In vitro and skin testing for allergy: comparable clinical utility and costs. Am J Managed Care 1998;**4**:969–985.
192. Bock SA, Sampson HA, Atkins FM et al. Double-blind, placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. J Allergy Clin Immunol 1988;**82**:986–997.
193. Bock SA, Atkins FM. Patterns of food hypersensitivity during sixteen years of double-blind, placebo-controlled food challenges. J Pediatr 1990;**117**:561–567.
194. Rodriguez J, Crespo JF. Clinical features of cross-reactivity of food allergy caused by fruits. Curr Opin Allergy Clin Immunol 2002;**2**:233–238.
195. Crespo JF, Rodriguez J, James JM, Daroca P, Reaño R, Vives R. Reactivity to potential cross-reactive foods in fruit-allergic patients. Implications for prescribing food avoidance. Allergy (in press).
196. Sampson HA. Food allergy. Part 2: Diagnosis and management. J Allergy Clin Immunol 1999;**103**:981–989.
197. Sicherer SH. Clinical implications of cross-reactive food allergens. J Allergy Clin Immunol 2001;**108**:881–890.
198. Bernhisel-Broadbent J, Sampson HA. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. J Allergy Clin Immunol 1989;**83**:435–440.
199. Jones SM, Magnolfi CF, Cooke SK, Sampson HA. Immunologic cross-reactivity among cereal grains and grasses in children with food hypersensitivity. J Allergy Clin Immunol 1995;**96**:341–351.
200. Werfel S, Cooke S, Sampson HA. Clinical reactivity to beef in cow milk allergic children. J Allergy Clin Immunol 1997;**99**:293–300.
201. Bernhisel-Broadbent J, Scalon SM, Sampson HA. Fish hypersensitivity I. In vitro and oral challenge results in fish-allergic patients. J Allergy Clin Immunol 1992;**89**:730–737.
202. Bock SA, Atkins FM. The natural history of peanut allergy. J Allergy Clin Immunol 1989;**83**:900–904.
203. Sicherer SH, Burks AW, Sampson HA. Clinical features of acute allergic reactions to peanut and tree nuts in children. Pediatrics 1998;**102**:e6.
204. Moneret-Vautrin DA, Kanny G, Morisset M et al. Food anaphylaxis in schools: evaluation of the management plan and the efficiency of the emergency kit. Allergy 2001;**56**:1071–1076.
205. Bindslev-Jensen C, Vibits A, Stahl Skov P, Weeke B. Oral allergy syndrome: the effect of astemizole. Allergy 1991;**46**:610–613.
206. Moller C. Effect of pollen immunotherapy on food hypersensitivity in children with birch pollinosis. Ann Allergy 1989;**62**:345.
207. Herrmann D, Henzgen M, Frank E, Rudeschko O, Jager L. Effect of hyposensitization for tree pollinosis on associated apple allergy. J Invest Allergol Clin Immunol 1995;**5**:267.
208. Asero R. Effects of birch-pollen specific immunotherapy on apple allergy in birch pollen hypersensitive patients. Clin Exp Allergy 1998;**28**:1368–1373.
209. Rueff F, Eberlein-Konig B, Przybilla B. Oral hyposensitization with celery juice. Allergy 2001;**56**:82–83.
210. Burks W, Bannon G, Lehrer SB. Classic specific immunotherapy and new perspectives in specific immunotherapy for food allergy. Allergy 2001;**56**:121–124.
211. Li XM, Sampson HA. Novel approaches for the treatment of food allergy. Curr Opin Allergy Clin Immunol 2002;**2**:273–278.