

Update on Food Allergy in Adults

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Abstract Though much has been studied and written about food allergy, the majority of the available literature focuses on food allergies in the pediatric population. Unfortunately, it is likely that in regard to food allergies, adults are not just big children, and extrapolating findings from pediatric to adult patient populations might lead to erroneous assumptions. Thus, it is important to validate the correlation between pediatric and adult data, gather data regarding adult food allergy and understand the specific nuances of subsets of adults to better treat their food allergy. This review was conducted by identifying potentially relevant studies regarding food allergies in adults through electronic databases, including PubMed, Medline, and Google Scholar. The search terms included “allergy”, “food” and “adults”. Parameters of 19+ years of age were added to search terms and all journals were written in or translated to English. From these search results, focus was placed on studies from 2010 to 2012. This systematic update on food allergy in adults found that the evidence regarding prevalence, diagnosis and management of food allergies is very limited, with the majority of data derived from children and young adults.

Keywords Food · Allergy · Adults · Component testing · Anaphylaxis · IgE-mediated food allergy · Prevalence ·

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Introduction

The National Institute of Allergy and Infectious Diseases' (NIAID) 2010 guidelines define food allergy as an adverse health effect arising from a specific immune response that occurs reproducibly upon exposure to a given food [1•]. “Food allergens” are characterized, in these guidelines, as those specific components of food or ingredients within food (typically proteins, but also chemical haptens) that are recognized by allergen-specific immune cells and result in elicitation of specific immunologic reactions resulting in characteristic symptoms [1•]. Reactions to foods can be immune mediated or non-immune mediated. Immune mediated food allergies consist of immunoglobulin E (IgE)-mediated (i.e. anaphylaxis), non IgE-mediated (i.e. food protein induced enterocolitis syndrome) as well as mixed IgE- and non IgE-mediated reactions (i.e. eosinophilic esophagitis). This review will focus on IgE-mediated food allergies.

Adverse health responses to food can range from mild allergic reactions to death caused by anaphylaxis. In the United States, food-induced anaphylaxis is the leading cause of anaphylaxis treated in emergency departments (EDs) [2]. It has been estimated that there are close to 30,000 food-induced anaphylactic reactions treated in EDs and 150–200 deaths attributed to food allergy in the United States each year [3]. Though the majority of patients with food-induced anaphylaxis had a prior history of a reaction to foods, patients without a known allergy may also be at risk [4].

Food allergy is largely a disease of the pediatric age group with a prevalence of 6 % among children under

3 years [5]. Though the prevalence of food allergies tends to decrease over the first two decades of life, occurrence in the aged population is often underestimated [6]. Most of our knowledge regarding food allergy is based on studies performed in children and young adults. Many children lose their sensitivity to allergens as they age, while other food allergies can begin in adulthood. Table 1 compares estimated rates of food allergy in North America in children and adults [7]. Deisner et al. suggest that the increased potential for newly acquired food allergy in elderly adults may be a result of age-related changes that can affect the immune system [8•].

This subject review was conducted by identifying potentially relevant studies regarding food allergies in adults through electronic databases, including PubMed, Medline, and Google Scholar. The search terms included “allergy”, “food” and “adults”. Parameters of 19+ years of age were added to search terms and all journals were written in or translated to English. From these search results, focus was placed on studies from 2010 to 2012.

Prevalence of IgE-Mediated Food Allergy

IgE-mediated reactions are characterized by an acute onset of symptoms generally within two hours after ingestion of or exposure to the trigger food. Allergic sensitization occurs when food-specific IgE (sIgE) antibodies are produced by plasma cells that have differentiated from allergen-specific B lymphocytes. The sIgE antibodies bind to the surface of tissue mast cells and blood basophils, and on re-exposure to the food, antigenic proteins in the food bind to and cross-link these cell surface bound sIgE antibodies, which triggers the release of symptom-causing mediators [9••]. Patients can have allergic sensitization (production of sIgE) to food allergens without having clinical symptoms of an allergic reaction on exposure. Thus, to sufficiently fulfill criteria of

food allergy, both sensitization and specific symptoms on exposure to a particular food are required [1••].

Determining the prevalence of food allergies in adults is challenging. A meta-analysis conducted by Rona et al. concluded that many of the prevalence studies are based solely on patient perceptions of food allergy and do not include the more accurate diagnosis made using a double-blind placebo-controlled food challenge (DBPCFC) or even an open food challenge (OFC) [10]. Not surprisingly, from what data is available, prevalence rates determined on the basis of patient self-reporting are higher than those determined on the basis of medical history and clinical testing. Liu et al. found that in the United States from 2005 to 2006, 8,203 of 10,348 participants in the National Health and Nutrition Examination Survey had serum sIgE levels measured to peanut, cow's milk, egg white, and shrimp [11]. Clinical food allergy was then estimated by using sIgE levels and age-based criteria. On the basis of only the four aforementioned foods, the overall prevalence of food allergy was estimated at 2.5 %. The prevalence rates of clinical food allergy varied by food type and age group and overall were 0.4 % for milk, 0.2 % for egg, 1.3 % for peanut and 1.0 % for shrimp [11]. Vierk et al. found the prevalence of doctor-diagnosed food allergy among US adults to be 5.3 % in adults (Table 2) [12]. In 2010, the RAND Corporation's (a non-profit research and analytics group) systematic review of articles regarding the epidemiologic aspects of food allergy concluded food allergy affects more than 1–2 %, but less than 10 % of the total pediatric and adult population [13].

Young et al. sent a questionnaire to two random samples of 7,500 households in the United Kingdom. There were 12,195 responses and 2,257 (18 %) reported reactions to a food. A total of 93 self-reported symptomatic subjects of this group underwent oral challenge, from which a prevalence rate of 1.4–1.8 % was estimated for the general population [14]. Ten years later, Zuberbier et al. undertook a postal questionnaire survey involving 13,300 subjects from the population registry of Berlin, Germany [15]. Of those who responded, 17 % reported reactions to foods, almost identical to the reported rate in the study by Young et al. [16•]. The results from 141 OFCs and 216 DBPCFCs in this group indicated that the actual prevalence of food allergy in the adult subjects was 3.7 %, with the highest frequency for proven IgE-mediated reactions in adults seen in the 20–39-year-old age group [15].

In children the prevalence of food allergy has been increasing over the past several decades. Branum et al. found through a self-reported survey conducted in the United States, that there was an 18 % increase in food allergies in children from 1997 to 2007 [17]. However, a similar trend has not been studied in adults. Further, robust data regarding the actual prevalence of adult food allergy is sparse. Therefore, the burden of food allergy in adults could be

Table 1 Estimated food allergy rates in North America

Food	Young children	Adults
Milk	2.5 %	0.3 %
Egg	1.3 %	0.2 %
Peanut	0.8 %	0.6 %
Tree nuts	0.2 %	0.5 %
Fish	0.1 %	0.4 %
Shellfish	0.1 %	2.0 %
Overall	6 %	3.7 %

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Table 2 The prevalence of reported food allergy by demographic group, 2011 Food Safety Survey

Demographic variable	Total sample, <i>N</i>	Self-reported food allergy, <i>N</i> (%) ^a	Self-reported doctor-diagnosed food allergy, <i>N</i> (%) ^a
All	4482	471 (9.1)	279 (5.3)
Sex ^b			
Female	2744	340 (11.4)	224 (7.6)
Male	1733	131 (6.5)	55 (2.7)
Age, <i>y</i>			
18–29	729	75 (8.1)	37 (4.1)
30–39	907	81 (8.4)	52 (5.5)
40–49	984	118 (9.6)	70 (5.5)
50–59	759	82 (10.0)	50 (5.7)
≥60	991	95 (8.1)	62 (5.3)
Race/ethnicity			
White/non-Hispanic	3510	361 (8.9)	212 (5.1)
Black	321	37 (8.8)	28 (6.5)
Hispanic	355	35 (8.7)	18 (4.3)
Other	291	38 (11.6)	21 (6.3)
Education ^c			
High school education or less	1727	137 (6.6)	86 (3.8)
At least some college education	2710	329 (11.3)	192 (6.6)

^a *N* represents actual numbers, but percentages are weighted (see the Methods)

^b Prevalence significantly different in female compared with male subjects ($P<0.001$)

^c Prevalence significantly different in respondents with at least some college education ($P<0.001$)

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substantial and reinforces that more data regarding the prevalence of food allergy in adults is needed. In conclusion, we do not clearly know the prevalence of food allergy in adults. Likewise, we are uncertain if there is a growth in this rate, as seen in the pediatric population.

Diagnosis of IgE Mediated Food Allergy

The NIAID guidelines recommend that food allergy be considered in any individual presenting with anaphylaxis or any combination of symptoms (listed in Table 3) that occur after ingestion of food [1•]. Medical history can provide detailed information essential to the formulation of the diagnosis. A thorough medical history includes information regarding suspected food triggers, the quantity needed to provoke reactions, the range of symptoms observed, speed of symptom onset, reproducibility of reactions and involvement of cofactors such as alcohol, exercise or medication [16•]. The NAIAD expert panel however reinforces that medical history alone should not be considered diagnostic of food allergies [1•].

Studies demonstrate that 50–90 % of presumed food allergies are not born out; therefore, a suspicious clinical history of food allergy must be confirmed [1•, 18]. To confirm the diagnosis, the clinician should consider the patient's specific clinical history, the epidemiologic aspects of the disease (e.g., common triggers and common associations) and then consider what testing should be performed to confirm the diagnosis [19]. These tests

include: skin prick testing, sIgE levels, component testing, as well as OFC and DBPCFC. The NIAID guidelines do not recommend the use of intradermal testing, total serum IgE or performance of atopy patch testing in the routine evaluation of non-contact food allergies [1•].

Skin Prick Testing

Skin prick testing (SPT) is one method in which food allergy to a specific food can be confirmed. When undertaking SPT, commercial food extracts are placed on the skin and pricked with a lancet or similar device. A resultant wheal of 3 mm or greater than the negative control is considered to be a positive result [1•, 20]. It is important to remember that there is a known discrepancy between commercial SPT (CSPT) and fresh food SPT (FFSPT) [21, 22]. This difference may be due to denaturation of antigens during processing of the commercial extract [23]. Rance et al. demonstrated the overall concordance between a positive prick test and positive challenge was 58.8 % with CSPT and 91.7 % with FFSPT [24]. Comparing CSPT with FFSPT using clinical history as the true-positive result, Ortolani et al. found that FFSPT yielded greater sensitivity in diagnosing oral allergy syndrome [25]. In addition, there is no significant increase in side effects, as Codreanu et al. found the risk of systemic reactions was 0.008 % when using fresh food prick-prick test versus 0.005 % seen with commercial SPT [26, 27]. Thus, in the case of a clear history of food induced reaction in which a negative CSPT is seen, it is

Table 3 Symptoms of food-induced allergic reaction

Target organ	Immediate symptoms	Delayed symptoms
Cutaneous	Erythema Pruritus Urticaria Morbilloform eruption Angioedema	Erythema Flushing Pruritus Morbilloform eruption Angioedema Eczematous rash
Ocular	Pruritus Conjunctival erythema Tearing Periorbital edema	Pruritus Conjunctival erythema Tearing Periorbital edema
Upper respiratory	Nasal congestion Pruritus Rhinorrhea Sneezing Laryngeal edema Hoarseness Dry staccato cough	
Lower respiratory	Cough Chest tightness Dyspnea Wheezing Intercostal retractions Accessory muscle use	Cough, dyspnea, and wheezing
GI (oral)	Angioedema of the lips, tongue, or palate Oral pruritus Tongue swelling	
GI (lower)	Nausea Colicky abdominal pain Reflux Vomiting Diarrhea	Nausea Abdominal pain Reflux Vomiting Diarrhea Hematochezia Irritability and food refusal with weight loss (young children)
Cardiovascular	Tachycardia (occasionally bradycardia in anaphylaxis) Hypotension Dizziness Fainting Loss of consciousness	
Miscellaneous	Uterine contractions Sense of “impending doom”	

GI gastrointestinal

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recommended that the clinician consider FFSPT prior to challenge [24].

Specific IgE

Allergic sensitization occurs when food-specific IgE (sIgE) antibodies are produced by plasma cells that have

differentiated from allergen-specific B-lymphocytes. SIgE, similar to SPT, is a marker of allergic sensitization, not of allergic disease. Sensitization occurs prior to disease onset and individuals may exhibit sensitization in the absence of actual allergic symptoms. Though the probability of allergic reactivity increases with increasing magnitude of sensitization (i.e. concentration of sIgE), there is no absolute cut-off

level at which symptoms necessarily occur upon allergen contact [28]. In many cases the sensitivity of sIgE is similar to SPT and in children sIgE levels have been found to correlate with SPT wheal size [29, 30]. Pongracic et al. however found that there was no such correlation in adults [31].

Component Testing

In light of a high false positive rate in diagnostic testing for food allergies, investigators are exploring the use of new modalities such as component testing to improve the diagnostic utility. Component-resolved diagnostics (CRD) is an *in vitro* diagnostic technique that uses purified natural or recombinant allergens to test for sIgE to individual allergic components of the allergen in question [32•]. Specifying components involved in food allergy may aid in understanding potential severity and likelihood of reactions. Testing for specific allergen components can also aid in diagnosing oral allergy syndrome (OAS). OAS or pollen-food allergy is an allergic reaction resulting from the cross-reactivity between pollen allergens and certain allergens in uncooked fruits and vegetables resulting in reactions limited to the mouth, lips, tongue and throat [33]. As OAS tends to result in mild symptoms; it is important to differentiate symptoms secondary to OAS and true food allergy in order to stratify risk management. Figure 1, from Phadia Laboratory, reviews known components and their cross reactivity. Another example of the benefits of identifying specific epitopes is seen in a study by Movérare et al. in which they found that subjects with IgE reactivity to Ara h 1, 2 and 3 tended to suffer from severe reactions after exposure to peanuts, while those demonstrating reactivity to Ara h 8, which is highly correlated with rBet v 1 and birch pollen, tended to have milder symptoms [34•]. Thus it is hoped that further refinement in the use of component testing will aid the clinician in more appropriate determination of risk when considering food challenge.

Food Challenge

In an attempt to reduce risk, appropriate measures should be taken prior to a food challenge, such as a thorough history, PST/sIgE testing (consideration of FFPST), and appropriate location for food challenge (office, hospital or intensive care unit). Food challenges can be considered a safe procedure when undertaken by qualified personnel, but it must be appreciated that such challenges can elicit severe, and even life-threatening reactions. Thus, the physician must be immediately available and their staff must be proficient in the treatment of anaphylaxis [30, 35]. The DBPCFC is the gold standard of diagnosis of food allergy, however a single-blind or an OFC is often all that is necessary. If the challenge elicits no symptoms, it is a negative challenge. False-

negative rates for DBPCFC are low (usually 3 %) [36]; thus, after a negative challenge, consideration should be given to having the patient eat the food prepared in the same manner and amount that caused the original reaction. When the challenge elicits objective symptoms it is a positive challenge. If those objective symptoms correlate with medical history and are supported by laboratory tests the diagnosis of food allergy is supported [1••]. A detailed review of oral food challenge is beyond the scope of this article; however, the Adverse Reactions to Food Committee of the American Academy of Allergy, Asthma & Immunology is an excellent resource, that provides in depth review of this topic and its review is strongly recommended for those wishing to perform food challenges [37].

Although DBPCFC still represents the gold standard for the diagnosis of food allergy, they are time-consuming, costly, and carry risk of potential systemic reactions [22]. Thus, it should come as no surprise that research is ongoing to find simpler methods to confirm the diagnosis of food allergies with decreased risk. Certainly it is hoped that component testing will be the discriminatory tool in the risk stratification of food challenge. Presently, DunnGalvin et al. studied a non-challenge method to predict food challenge outcomes, by using routinely collected data in children that were considered suitable for food challenges. They found that using six clinical factors (skin prick test, serum specific IgE, total IgE minus serum specific IgE, symptoms, sex, and age) they were able to accurately predict 97 % of cases being positive and 94 % as negative. Given that DunnGalvin group's work was derived from a pediatric population, further data is needed to support this model in adults [38•].

Management

Presently, the only management available for food induced allergy is avoidance and appropriate acute care intervention should a reaction occur. It is hoped that more proactive therapy will be available in the future. This includes use of omalizumab alone or in tandem with immunotherapy, oral immunotherapy (OIT), sublingual immunotherapy (SLIT) and Chinese herbs.

Avoidance

The primary therapy for food allergy is to avoid the causal food or foods. Avoidance may be difficult when the cause of food allergy is unknown; Mehl et al. performed a case review of anaphylaxis in 103 subjects and found that in 8 % of cases the anaphylactic agent was unknown [39]. When the etiology of the food allergy is known, education regarding avoidance includes careful attention to label reading, care in ingesting foods in restaurants and avoidance of

Fig. 1 ImmunoCAP cross-reactivity map (From Phadia Laboratory; with permission)

Allergen Component				Possible Cross-Reactivity																		
	SOURCE	COMPONENT	PROTEIN FAMILY OR FUNCTION	Fruits	Vegetables	Nuts and seeds	Legumes	Cereals	Spices	Grass pollen	Tree pollen	Wheat pollen	Lupine	Milk	Egg	Seafood	Animals	Mollusks	Worms	Insects	Parasites	
FOODS OF PLANT ORIGIN	Kiwi	Act d 1	Cysteine protease	•																		
		Act d 2	Thaumatin-like protein	•																		
		Act d 3	Knollin																			
	Celery	Api g 1	AP-1																			
	Apple	Mal d 1	MD-1																			
	Peach	Prp p 1	Prp-1																			
		Prp p 3	Prp-3																			
	Cashew nut	Ana o 2	Storage protein, 11S globulin																			
	Brazil nut	Ber e 1	Storage protein, 2S albumin																			
	Hazelnut	Cor a 1 (BdH)	Cor-1																			
		Cor a 3	Storage protein, 11S globulin																			
	Walnut	Jug r 1	Storage protein, 2S albumin																			
		Jug r 2	Storage protein, 7S globulin																			
	Sesame	Sea-1	Storage protein, 2S albumin																			
	Peanut	Ara h 1	Storage protein, 7S globulin																			
		Ara h 2	Storage protein, 2S albumin																			
		Ara h 3	Storage protein, 11S globulin																			
		Ara h 4	Storage protein, 2S albumin																			
	Soy bean	Gly m 3	Gly-3																			
		Gly m 4	Gly-4																			
		Gly m 5	Storage protein, Beta-conglycinin																			
		Gly m 6	Storage protein, Glycinin																			
	Buckwheat	Fag e 2	Storage protein, 2S albumin																			
Wheat	Tri a 14	Tri-14																				
	Tri a 19	Omega 1 gliadin																				
	Tri a 48, 51	Alpha-Amylase / Trypsin inhibitor																				
GRASS POLLEN	Bermuda	Cyn d 1	Grass group 1																			
	Timothy	Phl p 1	Grass group 1																			
		Phl p 2	Grass group 2																			
		Phl p 4	Chitinase																			
		Phl p 5	Grass group 3																			
		Phl p 6	Grass group 4																			
		Phl p 7	Protease																			
TREE POLLEN	Alder	Ala g 1	AP-1																			
	Birch	Ber e 1	MD-1																			
		Ber e 2	MD-2																			
		Ber e 4	Protease																			
	Hazel	Cor a 1 (BdH)	Cor-1																			
	Japanese cedar	Cry j 1	Pectate lyase																			
	Cypress	Cyp s 1	Pectate lyase																			
	Olive	Ole a 7	Tri-14																			
		Ole a 9	Glucanase																			
	Plane	Pla e 1	Invertase inhibitor																			
	Pla e 2	Polygalacturonase																				
	Pla e 3	Tri-14																				
WHEED POLLEN	Fig	Ans a 1	Pectate lyase																			
	Wheat	Tri a 1	Grass group 1																			
	Greenleaf	Ole a 1	Tri-14																			
	Wheat	Tri a 1	Grass group 1																			
	Wheat	Tri a 1	Grass group 1																			
	Wheat	Tri a 1	Grass group 1																			
	Wheat	Tri a 1	Grass group 1																			
LATEX	Hevea	Hev b 1	Rubber elongation factor																			
		Hev b 3	Small rubber particle protein																			
		Hev b 5	Acidic protein																			
		Hev b 6 (Bd)	Protease																			
	Hev b 8	Protein																				
CCD	Bromelain	BRU 1	CCD-marker																			
FOOD OF ANIMAL ORIGIN	Cow's milk	Bos d 4	Alpha lactalbumin																			
		Bos d 5	Beta lactoglobulin																			
	Cow's milk and meat	Bos d 6	Serum Albumin																			
	Cow's milk	Bos d 8	Casins																			
	Cod	Gal d 1	Ovalbumin																			
	Egg white	Gal d 1	Ovalbumin																			
		Gal d 2	Ovalbumin																			
		Gal d 3	Cornulobin/Ovalbumin																			
	Egg yolk/Chicken meat	Gal d 3	Lysio-ferritin Albumin																			
	Shrimp	Pen m 1	Penaeoalbumin																			
	Pen m 2	Arginine kinase																				
	Pen m 4	Sarcoplasmic Calcium binding protein																				
ANIMALS	Dog	Can f 1	Lipocalin																			
		Can f 2	Lipocalin																			
		Can f 3	Serum Albumin																			
		Can f 5	Arginine esterase/hyalinase																			
	Horse	Eq c 1	Lipocalin																			
		Eq c 3	Serum Albumin																			
	Cat	Fel d 1	Urochoglycin																			
	Fel d 2	Serum Albumin																				
	Fel d 4	Lipocalin																				
	Mus m 1	Lipocalin																				

cross-contamination of foods. The difficulty in avoiding cross-contaminating foods is well exemplified in a study by Hostetler et al. who demonstrated the difficulty in avoiding cross contaminating food by having a group of peanut/tree nut allergy sufferers attempt to identify 19 specific peanuts and tree nuts [40•]. Only 58.4 % of subjects older than 18 years of age correctly identified each peanut/tree nut [40•]. Additionally, patients should be taught to recognize symptoms, instructed in proper use of self-injectable epinephrine, able to activate emergency services and encouraged to obtain medical identification jewelry [41]. The Food Allergen Labeling and Consumer Protection Act of 2004 mandated the use of clear labeling. Ingredients likely to contain major food allergens (cow's milk, egg, fish, crustaceans, tree nuts, wheat, peanuts, and soybeans) are all required to be labeled [42]. Yet, Vierk et al. found that approximately 40 % of adults with food allergy who did read food labels found problems with: (1) some ingredient lists which give a general name for an ingredient without specifying the source, such as spices and flavors; (2) different words for the food to which a person is allergic being used on different food products; and (3) food labels not always alerting people that new ingredients have been added to a food, although they are stated in the ingredient list [12]. Thus, it is no surprise that a recent study demonstrated that 55 % of patients attempting to avoid a known food allergy will have a reaction over approximately a five-year period [43].

Epinephrine

When considering the topic of food allergy, it is important to remember that it is one of the most common causes of anaphylaxis and thus understanding of the treatment of anaphylaxis is of great importance. Campbell et al. evaluated 220 ED patients and found that food was the most common suspected cause of anaphylaxis for patients younger than 50 (42.2 %) or 65 years (38.5 %) but was much less common in patients 50 (14.8 %, $P < .001$) or over 65 years of age (14.3 %, $P = 0.01$) [44•]. Epinephrine is the first-line treatment in all cases of anaphylaxis. When there is suboptimal response to the initial dose of epinephrine, or if symptoms progress, repeat epinephrine dosing remains first-line therapy over adjunctive treatments, with multiple doses needed in up to one-fifth of reactions [45•]. It should be remembered that adolescents and young adults are at higher risk of anaphylaxis, as they often engage in risky behaviors and tend to deny symptoms [46]. Likewise, asthmatics, adolescents, and those with a prior reaction are also at increased risk for more severe reactions [45•]. Use of medicines such as beta-blockers, angiotensin-converting enzyme (ACE) or monoamine oxidase inhibitors or tricyclic antidepressants, which are more commonly used in adults, may diminish the efficacy of epinephrine or increase the severity of anaphylactic reactions [35, 37, 47].

With regard to the use of epinephrine, it is important to administer epinephrine in a timely manner, because it has been observed that a delay in epinephrine administration predisposed patients to a biphasic response [48]. Recent studies have demonstrated several concerns regarding use of auto-injectable epinephrine, these include lack of worldwide availability [49], delay in use for those who have access, and a delivery device that may be suboptimal [50], as needle length may not be long enough in women and some obese men [51].

Immunotherapy

In the past few years, new forms of therapy for food allergy have been studied, mostly in children, including oral immunotherapy (OIT) and sublingual immunotherapy (SLIT). OIT involves ingesting milligrams to grams of allergen in the form of flour combined in a food vehicle. In contrast, SLIT involves the administration of small amounts (micrograms to milligrams) of allergen extract placed under the tongue. OIT and SLIT are presumed to restore or induce a tolerant state. However, a distinction must be made between desensitization, in which the allergen is ingested without symptoms during treatment but requires continuous uninterrupted ingestion, and tolerance, in which the food can be ingested without allergic symptoms despite periods of abstinence [52]. Studies to date indicate that although OIT results in desensitization, it remains unclear whether tolerance is achieved [41, 53]. Jones et al. enrolled 39 children with peanut allergy in an open study of OIT. Twenty-seven children who completed the maintenance phase tolerated the targeted 3.9-g open peanut food challenge (18 of them without symptoms). Immune parameters revealed a decrease in peanut-specific IgE levels, PST and basophil activation as well as an increase in IgG levels [54]. Kim et al. found that after SLIT to peanut the treatment group safely ingested 20 times more peanut protein than the placebo group (median, 1,710 mg vs. 85 mg). Immune parameters revealed a decrease in peanut-specific IgE levels, PST and basophil activation and an eventual increase in IgG4 levels [55•]. Corinne et al. found that OIT was more efficacious in desensitization to cow's milk than SLIT, but OIT was also accompanied by more systemic side effects. In the same study it was found that clinical desensitization was lost in as early as one week off therapy [56•]. Thus, reinforcing concern that although desensitization was achieved, the tolerated state was not induced. As of 2010, the NIAID expert panel did not recommend using allergen-specific immunotherapy to treat IgE-mediated food allergy; however, it is hoped that further research will better define the future use of immunotherapy in our food allergic patients [1•].

Other Options

Ongoing research may reveal alternate treatments for food allergies. Currently, studies are examining what potential role omalizumab and other anti-IgE therapy may play. Omalizumab is a recombinant DNA-derived humanized IgG1 monoclonal antibody that selectively binds to human IgE. Leung et al. found that using an anti-IgE monoclonal antibody significantly and substantially increased the threshold of sensitivity to peanut on oral food challenge from a level equal to approximately half a peanut (178 mg) to one equal to almost nine peanuts (2805 mg); an effect that the authors believed would translate into protection against most unintended ingestions of peanuts [57]. In a letter regarding this data however, Nicklas and Chowdhury noted that 76 % of subjects were not protected after ingestion of 8 g of peanut flour (equivalent to approximately 24 peanuts), and approximately 25 % were not protected after ingesting as little as 0.5 g of peanut flour (approximately equal to 1.5 peanuts), despite being pretreated with the highest dose of the monoclonal antibody [58].

Nadeau et al. demonstrated that omalizumab treatment combined with oral milk desensitization in a group of children with clinical reaction to cow's milk permitted rapid milk dose escalation in the majority of subjects [59•]. Recent studies have also demonstrated potential efficacy from Chinese herb, Food Allergy Herbal Formula (FAHF) mix [60]. Srivastava et al. have found that FAHF treatment completely eliminated anaphylaxis in mice allergic to peanut, challenged up to five weeks post-therapy [61•]. FAHF-2 is the only investigational herbal formulation currently validated for use in human clinical trials [62•].

Special Subset of Patients

There are subsets of adult patients that require special consideration when confirming a diagnosis and treatment of food allergy, for example, at the beginning of life, the role maternal diet plays on her progeny's susceptibility to food allergy, or at the other end of the spectrum, the role aging may play on food allergy in the elderly.

Pregnant Women

It is unclear whether restricting maternal diet during pregnancy and/or lactation affects the development or clinical course of food allergy in their progeny. Studies are ongoing to help address the potential utility of dietary avoidance maneuvers during pregnancy and/or lactation. A study by Sicherer et al. demonstrated an increased risk of peanut sensitization in a cohort of infants with milk and egg allergy born to mothers who had increased ingestion of peanut during pregnancy.

Interestingly, they did not show an increased risk of peanut sensitization in babies born to mothers who had an increase of peanut ingestion during breast-feeding [63], while DesRoches and colleagues found an association between peanut sensitization and maternal peanut ingestion during pregnancy and breast-feeding [64]. A systematic review reported that larger scale trials are needed to validate any potential benefit that may be seen in antenatal or breastfeeding mothers with restrictive diets [65]. Not surprisingly, the NIAID expert panel did not recommend restricting maternal diet during pregnancy or lactation as a strategy for preventing the development or clinical course of food allergy [1••]. In addition, the NIAID guidelines further recommend that all infants be exclusively breast-fed, without maternal diet restriction of allergens, until 4 to 6 months of age, unless breast-feeding is contraindicated for medical reasons and suggest that the introduction of solid foods should not be delayed beyond 4 to 6 months of age [1••].

Elderly

Deisner et al. proposed that age-related changes could affect the immune system, increasing the potential for newly acquired food allergy in elderly adults [8•]. They found that deficiencies in micronutrients (zinc, iron and/or vitamin D) in the elderly might contribute to the development of allergy. Further potential risk factors for the development of food allergy in the elderly include the decreased digestive ability due to atrophic gastritis as well as increased use of antiulcer medication [8•]. This study highlights that further research is needed to better understand the science of aging and its impact on allergy.

Conclusions

This systematic update on food allergies in adults found that the evidence regarding prevalence, diagnosis and management of food allergies is very limited, with the majority of data derived from children and young adults. Though much has been studied regarding food allergy, it may not be appropriate to extrapolate data from the pediatric to the adult population. It is important to validate correlation between pediatric and adult data, gather new data regarding adult food allergy and understand the specific needs of subsets of adults, to better treat adult food allergy.

The American Academy of Allergy, Asthma & Immunology; the European Academy of Allergy and Clinical Immunology; the World Allergy Organization; and the American College of Allergy, Asthma & Immunology have come together to increase the communication of information at a global level. Within the framework of this collaboration, termed the International Collaboration in Asthma, Allergy and Immunology, a series of consensus documents called

the International Consensus ON (ICON) are being developed to serve as a resource and support to physicians in managing various allergic diseases including food allergy. Included in this charge, will be to describe the natural history, prevalence, diagnosis, and treatment of food allergies in the context of the global community [9••].

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