



An update on the impact of food allergy on anxiety and quality of life

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Purpose of review

Food allergies have become more common, and management involves dietary avoidance that can impair quality of life. Patients and families must manage the daily risk of anaphylaxis at each meal. The purpose of this review is to describe the impact of food allergies on quality of life and to provide an update on new developments in food allergy management, particularly peanut allergy.

Recent findings

Food allergy requires careful avoidance of common and ubiquitous dietary allergens. Living with food allergy is associated with annual economic costs in excess of \$4000 per child, in addition to risks of anxiety and depressive symptoms. An expert panel sponsored by the 2017 National Institute of Allergy and Infectious Diseases published addendum guidelines for the prevention of peanut allergy, which suggest three separate approaches to peanut protein introduction for infants at various levels of risk.

Summary

Clinicians must be aware of underappreciated burdens faced by children and families with food allergies. Management involves a partnership between primary and specialty care. Mitigation strategies to improve quality of life for patients include efforts to avoid overdiagnosis in synergy with balanced counseling about the risks of food allergies. Experimental food allergen desensitization can improve quality of life but remains investigational at this time. For patients with significant anxiety, interdisciplinary management involving professional counseling may be helpful. Risk stratification and early introduction of peanut protein can help prevent the development of peanut allergy.

Keywords

anxiety, food allergy, quality of life

INTRODUCTION

Food allergy has become a common problem managed by pediatricians because it affects 8–10% of children [1,2]. The economic impact of food allergy is significant. Gupta *et al.* [3] estimated the economic burden from food allergy to be \$4184 per year per child with food allergy, including costs of physician visits, emergency care and hospitalization, travel, medication, and special diets.

The risk of fatal food reactions is a source of anxiety for patients and families. In a seminal study, Sampson *et al.* [4] identified six children and adolescents who died of food anaphylaxis and compared these participants with seven others who nearly died and required intubation during a period of 14 months. Risk factors for fatal and near-fatal reactions included asthma, peanut or nut allergy (10 of the 13 participants were peanut or nut allergic), and delayed administration of epinephrine. As peanut and nut allergies are a risk for food allergy

fatality, these specific allergies are often more worrisome to families. Peanut allergy affects 2% (1.5 million) of US children [1,5], and approximately 12% of peanut allergic children experience repeated allergic reactions each year [6,7]. However, many patients and their parents may overestimate the absolute risk of a fatal food allergy reaction, leading to impairment in quality of life.

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KEY POINTS

- Food allergies may be associated with social isolation, fear, anxiety, and depression.
- Management of comorbid impairments in quality of life begins with accurate diagnosis and balanced counseling.
- Early detection of anxiety is important to allow appropriate interdisciplinary management of patients with food allergy and their families.

QUALITY OF LIFE AND ANXIETY

There are several factors that may cause fear and anxiety in patients and families living with food allergy, but paramount among them is risk perception. Although one estimate suggests that the number of food allergy deaths is 150 per year [8], this figure is likely an overestimate. Food Allergy Research and Education (www.foodallergy.com) manages a registry of fatal food reactions, which identified 31 fatal reactions between 2001 and 2006 [9]. Mortality statistics of participants up to 24 years of age from the Centers for Disease Control and Prevention [10] reveal 232 fatalities in an at-risk population of 1 005 422 330 persons between 1999 and 2014 by 'ICD-10 L27.2 (dermatitis due to ingested food)' and 'R57 (shock, not elsewhere classified).' Using these figures, the annual death rate for children and young adults with food allergy would be 6×10^{-7} , assuming an 8% risk of food allergy. This corresponds to one death in 1.7 million at-risk individuals per year, which is consistent with data reported by Umasunthar *et al.* [11] describing a food allergy fatality incident rate of 1.81 per million person years. These authors concluded food allergy fatality anaphylaxis was rarer than the rate of accidental death in the general population. In this analysis, the risk of dying from murder was higher than the risk of dying from food allergy, although food allergy fatality was still more likely than the risk of dying from a lightning strike. Hanna *et al.* [12] recently reported that healthcare professionals often overestimate the risk of food allergy fatality by a mean factor of 13.5-fold (95% confidence interval 5.0–31.6).

Food allergy impacts the quality of life of caregivers, although pediatric allergist specialty care may attenuate this impairment to some degree through correct diagnosis and appropriate counseling [13]. As expected, more severe reactions worsen quality of life [14], and caregiver quality of life impairments can strain relationships. Gupta *et al.* [15] reported in a sample of 2045 parents of food

allergic children that 25% felt food allergy had caused a strain on their marriage or relationship, and 40% had experienced hostility from another parent when trying to accommodate their child's food allergy.

Whether food allergies increase patient anxiety and depression has been questioned, and studies designed to answer this question have been inconsistent [16–19]. An Australian study concluded that symptoms of anxiety and depression were more common among adolescents aged 14–21 years with food allergy, according to maternal (but not self) report, and that levels of depressive symptoms may persist into young adulthood [20]. However, another study did not demonstrate increased anxiety in food allergic children 8–16 years of age compared with children from a general pediatrics clinic [21].

It is important for patients and families to find balance in food allergy management. Fedele *et al.* [22] described four response patterns in 57 food allergy families: balanced psychosocial functioning with high food allergy management skills and adequate vigilance (41%), high responders with adequate management skills and high anxiety (45%), low responders with both low management skills and low vigilance (5%), and anxious high responders with high management skills and extremely high maternal anxiety (9%). One role of the healthcare provider in food allergy management is to help patients and families find the difficult balance between adequate vigilance and excessive anxiety, recognizing that this is part of a developmental process. Polloni *et al.* [23] demonstrated that adolescents with food allergy had greater risk of social difficulties but lower likelihood of conduct and hyperactivity disorders. The authors pointed out that coping with food allergy, rather than being a simple strategy, comprises the cumulative history of repeated interactions of food and relationships in a child's developmental progress. A minority of children may be at risk for alexithymia – a personality construct that can be expressed as 'a lack of words to express emotions'. This impairment may become manifest in some patients as somatoform bodily sensations when the individual misreads physical expression of emotion as a physical expression of disease [24]. This can create unusual clinical conundrums when a patient presents with somatoform manifestations of anxiety misattributed to food allergy. In clinical experience, this is typically accompanied by anxiety and frequent complaints of symptoms attributed to noningestion food exposures. Careful evaluation is required to understand whether symptoms are due to an immunoglobulin E (IgE)-mediated mechanism or anxiety.

Herbert *et al.* [25] recently reviewed clinical management of psychosocial concerns related to food allergy through various stages of childhood; however, published behavioral interventions for patients with food allergy are scant. There has been only one study of an intervention using cognitive-behavioral therapy (CBT), a goal-oriented collaborative traditional psychotherapy treatment used by mental health professionals that involves identifying and addressing maladaptive patterns of thinking and behavior. In this study of five mothers of food allergy children, anxiety, depression, and worry were significantly reduced, and overall mental health and quality of life improved for 12 weeks [26].

It is difficult to compare the impact of food allergy with other health states, but Carroll and Downs [27] published comparative health state utility data comparing 29 health states. Health state utilities (representing patient preferences under conditions of risk) were obtained from 4016 interviews with parents or guardians of at least one child under 18 years of age at pediatric clinics, conventions, and the Indiana State Fair. With perfect health valued at 100% and death at 0, a moderate food allergic reaction scored 93% on the standard gamble instrument, compared with 84% for a moderate seizure disorder, 83% for severe persistent asthma, and 59% for severe mental retardation.

FOOD ALLERGY MANAGEMENT

Although there is comfort for patients in knowing the epinephrine autoinjector is an effective treatment for accidental allergic reactions [4], higher rates of food-related anxiety have been associated with epinephrine carriage. It is unclear whether this increased anxiety is directly related to carrying epinephrine or to the perception that the food allergy is severe enough that epinephrine may be needed [25]. The recent controversy of the unjustified 400% EpiPen cost increase has been met with anger and frustration from patients and providers [28^a]. Although coupon programs have assisted selected patients, the future costs of these devices remain uncertain. Sanofi US (Bridgewater, NJ) voluntarily recalled the Auvi-Q autoinjector due to dosing accuracy concerns in October 2015; however, the device was re-released in early 2017 [28^a,29]. Camargo *et al.* [30] found the Auvi-Q device was preferred by patients given its smaller size and audio instructions. One study demonstrated higher rates of successful device use with the audio-prompted Auvi-Q device compared with other autoinjectors [31^a].

A partnership between primary and specialty care is important in food allergy management because correct diagnosis and balanced counseling

are important in approaching food allergy. This is important to prevent initial overdiagnosis and to provide timely assessment of spontaneous tolerance, which occurs in 79% of patients with milk allergy [32], 68% of patients with egg allergies [33], and 22% of patients with peanut allergies [34]. Recently, Couch *et al.* [35^a] highlighted the importance of specialty care in supervised tree nut challenges, pointing out that peanut–tree nut co-allergy may not be as common as previously assumed. In this study, patients with low-level tree nut sensitization frequently passed tree nut challenges. This report emphasizes the role of allergy referral for evaluation of asymptomatic food allergen sensitization for correct diagnosis of food allergy.

There have been recent changes in the guidance for influenza vaccination of egg-allergic patients. Although most influenza vaccines contain minute measurable amounts of egg protein, data have shown that administration of the influenza vaccine in a single, age-appropriate dose is well tolerated by patients with egg allergy. Egg allergy does not increase the risk of an anaphylactic reaction to influenza vaccine, although milder allergic reactions may occur. Patients with egg allergy should be counseled that they may routinely receive the annual influenza vaccine without any additional precautions apart from those of routine influenza recommendations [36^a].

Although strategies to minimize the likelihood of accidental ingestion of allergens should be provided, overly cautious avoidance strategies may create an unnecessary burden on families. In the United States, the Food Allergen Labelling and Consumer Protection ACT (FALCPA), which took effect in 2006, has clarified some sources of potential food triggers by requiring declaration of several major food allergens (milk, eggs, fish, crustacean shellfish, peanuts, tree nuts, wheat, and soy) in packaged FDA-regulated foods. However, FALCPA only applies to packaged foods and does not extend protection to restaurant food allergen ingredients [37]. Additionally, FALCPA does not regulate the use of precautionary ‘may contain’ statements, which some manufacturers may use as a low-cost liability shield. Although it is common practice to recommend avoidance of products that ‘may contain’ possible food allergens with advisory labeling, Brough *et al.* [38] recently found that risks for non-snack food items may be lower than perceived. The published rate of actual peanut or nut contamination in all foods with precautionary allergen labeling ranges from 0.9 to 32%.

Many patients with both milk and egg allergy can tolerate baked goods that contain milk or egg as minor ingredients, and consuming these foods may

promote tolerance to these allergens. It is important to appropriately educate patients how to incorporate tolerance-boosting practices safely into their diets. Leonard *et al.*'s [39] review of this practice provides useful parameters to guide those baked preparations to include and those to avoid.

Early introduction of food allergens may prevent some cases of food allergy from developing. The Learning Early About Peanut (LEAP) and LEAP-On studies have demonstrated significant peanut allergy risk reduction from early peanut introduction during infancy, and this benefit appears durable even if peanut allergen is subsequently removed from the diet of high-risk children with established tolerance [40,41[¶]]. The recently published 2017 National Institute of Allergy and Infectious Diseases-sponsored expert panel addendum guidelines for the prevention of peanut allergy suggest three separate approaches to peanut protein introduction for infants at various levels of risk:

- (1) For the highest risk infants with eczema, egg allergy, or both, the guidelines recommend strong consideration of evaluation by skin prick testing and/or specific IgE testing, and then supervised oral food challenge in the office, if necessary.
 - (a) If peanut sensitization is negative, peanut protein introduction is recommended at home or in the office (based on provider/parental preference) at 4–6 months of age.
 - (b) For moderate levels of sensitization (peanut prick skin testing 3–7 mm), introduction by supervised feeding or office challenge is recommended at 4–6 months of age. The authors recommend that such supervised feedings occur in a pediatric allergy clinic.
 - (c) If levels of sensitization are high (i.e., peanut skin prick test ≥ 8 mm), peanut allergy is assumed, and continued specialist evaluation and management is recommended.
- (2) Children with mild-to-moderate eczema are considered in a lower stratum of risk, and it is recommended that peanut-containing foods be introduced around 6 months of age.
- (3) For children without any history of eczema or food allergy, it is recommended that peanut-containing foods be introduced in a manner that is 'age-appropriate and in accordance with family preferences and cultural practices'. These guidelines also provide useful tips on preparation of peanut protein, emphasizing strategies for age-appropriate presentation and choking prevention [42^{¶¶}].

Families of food allergic children frequently ask how to approach food introduction for younger

siblings. Although sibling food allergy can increase food allergy risk, the risk of clinically irrelevant food sensitization (i.e., positive skin testing but evidence of food tolerance) is several-fold greater than clinical reactivity. Gupta *et al.* [43[¶]] evaluated 2834 children and found that among siblings of children with food allergy, 53% had a positive food serum specific IgE or skin prick test but no symptoms of food allergy. Only 13.6% of siblings were both sensitized and clinically reactive to the same food. The authors cautioned against overinterpreting the relevance of food allergen sensitization in asymptomatic siblings and suggested that given the high rate of false positive testing, siblings should not have routine screening food testing before introduction. An alternative approach of careful food introduction (gradual introduction of culprit foods under supervision) at home is reasonable in a child without atopic dermatitis or other food allergy.

FUTURE DIRECTIONS

Experimental desensitization to food allergens remains an active area of research. Peanut oral immunotherapy appears to offer some degree of protection for patients in the event of accidental ingestion, but clinical use of the therapy may be limited by the high rate of side effects [44[¶]]. Nonetheless, quality of life still improves with immunotherapy, although it appears that many participants receiving oral immunotherapy could experience fewer allergic reactions and episodes of anaphylaxis by practicing strict food avoidance than by receiving active therapy [6,45]. A longer-term question not addressed in these studies is whether oral immunotherapy can result in a food allergy cure or at least a prolonged sustained unresponsiveness to allergens. If patients received a long-term benefit, the therapy would be more attractive despite the tradeoff of increased immunotherapy reactions. Vickery recently published a study indicating that age at initiation of immunotherapy may be a significant factor in oral immunotherapy. Forty children aged 9–36 months with suspected or known peanut allergy were randomized to receive early peanut oral immunotherapy. Of those treated, 91% achieved 4-week sustained unresponsiveness. With a daily peanut treatment dose as low as 300 mg, treated children were 19 times more likely to successfully consume 5 g of dietary peanut at study completion than matched standard-care controls. The authors suggest that low-dose peanut oral immunotherapy, initiated shortly after diagnosis, may safely and effectively rescue young children with early peanut allergy. Treatment was associated with a risk of adverse effects, and 95% of treated participants

experienced some adverse event (although most were mild). Moderate adverse effects were reported in 17% of participants [46^{***}]. An epicutaneous peanut immunotherapy patch under development is also of interest, as it may produce a modest degree of desensitization with fewer side-effects [47[†]].

Several companies are working on innovations for patients with food allergy, including devices to detect allergens in foods. Although these devices will not be a substitute for careful label reading, an electronic device by Nima to detect gluten-containing foods [48] and a wearable USB-sized food allergen detection device called the Allergy Amulet [49] represent novel approaches. An electronic smart phone app called Allerpal provides a shareable electronic version of an emergency action plan [50], whereas EpiFind in development by Altrix Medical [51] may allow patients without an epinephrine autoinjector to rapidly identify nearby devices through GPS and smart phone technology. Also in development is a device by Windgap Medical (Somerville, Massachusetts) [52], a smaller and longer-lasting epinephrine autoinjector alternative that stores epinephrine in a dry form and mixes it into a solution when the device is activated.

CONCLUSION

Food allergy continues to be a frequent problem encountered in pediatric practice, but fatal food allergy is rare. Appropriate risk stratification for early food introduction is important for prevention of food allergies and involves a partnership between primary and subspecialty care. Accurate diagnosis, timely assessment of potential spontaneous tolerance, counseling, and emergency preparedness must be a part of management, and efforts to detect and manage associated anxiety should be present in every clinical encounter. Further research is needed to determine how experimental therapies may ultimately be incorporated into clinical practice. In the future, clinical applications of oral and transcutaneous immunotherapies will likely involve patient preference sensitive factors. A clearer understanding of longer-term immunotherapy outcomes will better inform decisions about food allergen immunotherapy. These decisions will involve balancing trade-offs of allergic reactions from the immunotherapy treatments themselves with the likelihood of long-term tolerance.

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Conflicts of interest

M.S.S. has a brother who is CEO of Altrix Medical, developer of the EpiFind smart phone application to locate epinephrine autoinjectors by GPS technology. J.S. and M.F. have no conflicts of interest.

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