

MOC-CME Review

Common questions in food allergy avoidance



Maureen Egan, MD; Matthew Greenhawt, MD, MBA, MSc

Section of Allergy and Immunology, Department of Pediatrics, University of Colorado School of Medicine, Children's Hospital of Colorado, Aurora, Colorado

ARTICLE INFO

Article history:

Received for publication August 8, 2017.

Received in revised form September 11, 2017.

Accepted for publication September 12, 2017.

Key Messages

Current food allergy management focuses on avoidance of the allergen. Appropriate counseling is essential to minimize accidental ingestions while also preventing excessive limitations.

- The risk of a systemic reaction to a food allergen is primarily through ingestion with contact and inhalational exposures being low risk.
- Oils derived from foods can differ in their protein content based on the refining process, with full refining of oils leading to complete protein removal and tolerance amongst food allergic individuals.
- Consider referral to a dietician with an expertise in infant/pediatric nutrition for all children with food allergies, particularly young children avoiding ubiquitous foods such as cow's milk.
- Counseling on accurate interpretation of food labels is essential, with the knowledge that precautionary allergen labeling is not standardized.

INSTRUCTIONS

Credit can now be obtained, free for a limited time, by reading the review article in this issue and completing all activity components. Please note the instructions listed below:

- Review the target audience, learning objectives and all disclosures.
- Complete the pre-test.
- Read the article and reflect on all content as to how it may be applicable to your practice.

Reprints: Maureen Egan, MD, Section of Allergy and Immunology, Department of Pediatrics, University of Colorado School of Medicine, Children's Hospital of Colorado, 13123 E 16th Ave, Box 518, Aurora, CO 80045; E-mail: maureen.egan@childrenscolorado.org.

Disclosures: Dr Egan is a consultant for Nestle. Dr Greenhawt is supported by grant 1K08HS024599-01 from the Agency for Healthcare Quality and Research; is an expert panel and coordinating committee member of the National Institute of Allergy and Infectious Diseases–sponsored Guidelines for Peanut Allergy Prevention; has served as a consultant for the Canadian Transportation Agency, Thermo Fisher, and Aimmune Therapeutics; is a member of physician/medical advisory boards for Aimmune, Nutricia, Kaleo Pharmaceutical, Nestle, and Monsanto; is a member of the scientific advisory council for the National Peanut Board; has received honorarium for lectures from Thermo Fisher and multiple state allergy societies, the American College of Allergy, Asthma, and Immunology, and the European Academy of Allergy and Clinical Immunology; is an associate editor for the *Annals of Allergy, Asthma, and Immunology*; and is a member of the Joint Taskforce on Allergy Practice Parameters.

<https://doi.org/10.1016/j.anai.2017.09.078>

1081-1206/© 2018 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

- Complete the post-test/evaluation and claim credit earned. At this time, physicians will have earned up to 1.0 AMA PRA Category 1 Credit™. Minimum passing score on the post-test is 70%.
- Approximately 4–6 weeks later you will receive an online outcomes assessment regarding your application of this article to your practice. Once you have completed this assessment, you will be eligible to receive MOC Part II credit from the American Board of Allergy and Immunology.

Overall Purpose

Participants will be able to demonstrate increased knowledge of the clinical treatment of allergy/asthma/immunology and how new information can be applied to their own practices.

Learning Objectives

At the conclusion of this activity, participants should be able to:

- Discuss the risk of casual contact to allergens in patients with food allergies
- Review appropriate substitutes for patients with cow's milk allergy
- Describe food labeling in regard to appropriate allergen avoidance for food allergic individuals

Release Date: March 1, 2018

Expiration Date: February 28, 2020

Target Audience

Physicians involved in providing patient care in the field of allergy/asthma/immunology

Accreditation

The American College of Allergy, Asthma & Immunology (ACAAI) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Designation

The American College of Allergy, Asthma & Immunology (ACAAI) designates this journal-based CME activity for a maximum of 1.0 AMA PRA Category 1 Credit™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Disclosure Policy

As required by the Accreditation Council for Continuing Medical Education (ACCME) and in accordance with the American College of Allergy, Asthma and Immunology (ACAAI) policy, all CME planners, presenters, moderators, authors, reviewers, and other individuals in a position to control and/or influence the content of an activity must disclose all relevant financial relationships with any commercial interest that have occurred within the past 12 months. All identified conflicts of interest must be resolved and the educational content thoroughly vetted for fair balance, scientific objectivity, and appropriateness of patient care recommendations. It is required that disclosure be provided to the learners prior to the start of the activity. Individuals with no relevant financial relationships must also inform the learners that no relevant financial relationships exist. Learners must also be informed when off-label, experimental/investigational uses of drugs or devices are discussed in an educational activity or included in related materials. Disclosure in no way implies that the information presented is biased or of lesser quality. It is incumbent upon course participants to be aware of these factors in interpreting the program contents and evaluating recommendations. Moreover, expressed views do not necessarily reflect the opinions of ACAAI.

Disclosure of Relevant Financial Relationships

All identified conflicts of interest have been resolved. Any unapproved/investigative uses of therapeutic agents/devices discussed are appropriately noted.

Planning Committee

- Jonathan A. Bernstein, MD (Annals CME Subcommittee): Consultant, Grants/Fees: AstraZeneca, CSL Behring, Novartis, Pharming, Sanofi Regeneron, Shire; Consultant, Grant: BioCryst
- Guha Krishnaswamy, MD (Annals CME Subcommittee): Author, Royalties: UpToDate; Research, Grant: CSL Behring; Reviewer, Honorarium: NIAID/AITC
- Gailen D. Marshall, Jr, MD, PhD (Editor-in-Chief): Research, Grants: AstraZeneca, NIH, PCORI, Stallergenes
- Anna Nowak-Wegrzyn, MD (CME Series Editor, Deputy Editor): Advisory Board, Fees: ALK Abello, Gerber, Merck; Contributor, Fees: UpToDate; Research, Grants: Astellas Pharma, DBV Technologies, Food Allergy Research and Education, NIH/NIAID Immune Tolerance Network, Nutricia, Thermo Fisher Scientific; Speaker, Grant/Fees: Nestle
- John J. Oppenheimer, MD (Annals CME Subcommittee, Associate Editor): Consultant, Fees: AstraZeneca, Boehringer Ingelheim, DBV Technologies, GlaxoSmithKline, Kaleo, Novartis, Sanofi

Author

- Maureen Egan, MD, Consultant, Fees: Nestle
- Matthew Greenhawt, MD, MBA, MSc, Advisory Committee, Honorarium: Kaleo, Nestle Nutrition Institute; Consulting/Speaker, Fees/Honorarium: Aimmune Therapeutics, Thermo Fisher; Speaker, Honorarium: Intrommune

Recognition of Commercial Support: This activity has not received external commercial support.

Copyright Statement: ©2015–2018 ACAAI. All rights reserved.

CME Inquiries: Contact the American College of Allergy, Asthma & Immunology at education@acaai.org or 847-427-1200.

Introduction

Food allergies affect up to 5% to 8% of children in the United States^{1,2} and may be increasing in prevalence³ as evidenced by a report from the Centers for Disease Control and Prevention, which noted a 50% increase in the United States between 1997 and 2011.⁴ Although many foods have been reported to trigger allergic reactions, the most common causes of significant allergic reactions are milk, egg, wheat, soy, peanut, tree nuts, fish, shellfish, and seeds.⁵

Although treatment options for food allergies, such as oral and epicutaneous immunotherapy, have shown potential, they are not currently approved for general use by the Food and Drug Administration. Therefore, current management focuses on avoidance of the allergen.⁵

Because the most common food allergens are ubiquitous, complete avoidance can be difficult and unintentional ingestions are common.^{6,7} Fleischer et al⁶ reported that among children 3 to 15 months old with a diagnosis of milk or egg allergy, the mean rate

of an allergic reaction was 0.81 per year. Similarly, Sicherer et al⁷ reported that among children with peanut and tree nut allergies, 55% of peanut allergic children and 30% of tree nut allergic children had an unintentional ingestion during a median period of 5.5 years, with a mean of 2 accidents per patient with an unintentional ingestion. Although fatalities caused by food allergy are rare,³ unintentional exposures can lead to potentially severe reactions.^{6,7} Fleischer et al⁶ reported severe reactions in 11.4% of unintentional exposures, whereas Sicherer et al⁷ reported that 53% of reactions caused by unintentional exposures had multisystem and/or respiratory symptoms.

Appropriate avoidance includes correctly reading ingredient labels on manufactured products, understanding the risks of casual contact with an allergen, and use of appropriate practices to prevent cross-contact.⁸ However, implementation of these practices can be difficult. In 2013, the Food Allergy Research & Education group administered an online survey to 5,578 individuals with food allergies or parents of a food allergic child identified several knowledge gaps.⁹ Specifically, 26.3% believed that precautionary allergy labeling (PAL) is mandated by law, with 36.7% of participants reporting they believed PAL was based on specific amounts of the allergen present in the food or did not know.⁹ Similarly, Simons et al¹⁰ surveyed individuals who attended the Food Allergy & Anaphylaxis Network conference and noted that 16% had a history of reaction attributable to misunderstanding a food label term. Alternatively, 40% of patients allergic to soy were avoiding soy oil and soy lecithin, which is typically unnecessary.¹⁰ The unnecessary avoidance is important because it may contribute to nutritional deficiencies that for which food allergic patients are at risk.¹¹

In addition, families often have concern and anxiety regarding the risk from exposures from casual contact with the allergen.¹² This is important because it can contribute to social isolation and reduced quality of life (QoL) that has been found among food allergic patients and their family members.^{8,12–14} Specifically, Bollinger et al¹⁵ interviewed 87 families with a food allergic child and reported that food allergies affected family social activities in 49% and school attendance in 34%, with 10% of children being homeschooled because of their food allergies. Primeau et al¹² similarly reported significantly more social disruption in daily activities in food allergic children compared with their peers.

Therefore, it is essential that the practicing allergist be able to correctly diagnose food allergies and able to provide advice on appropriate avoidance behaviors while preventing excessive limitations.¹⁶ Specifically, one must be able to counsel on correctly reading ingredient labels, educate the family on behaviors to prevent cross-contamination, and explain the risks of exposure in commonly encountered situations and with casual contact. Allergists similarly must be able to provide avoidance advice while suggesting age and nutritionally appropriate substitutions. This review therefore focuses on providing an understanding of identifying potential myths that may surround certain aspects of food allergy management, with a focus on redirecting misconceptions, and enhancing communications that can improve how our patients live life with disease.

Case 1

An 11-month-old boy is brought to your office for evaluation of food allergy. He developed hives around his face and chest within 30 minutes after eating peanut butter for the first time, approximately 1 month ago. No other symptoms developed. His symptoms resolved with diphenhydramine alone, and he otherwise has not had any reactions concerning for potential food allergies. He has a comorbid history of mild atopic dermatitis that is well controlled with a skin care regimen of emollient-based moisturization and occasional use of hydrocortisone cream, 0.5%. His pediatrician sent

serum test results for peanut, which reported a peanut specific IgE (slgE) level of 57.84 kUA/L and negative serum test results to tree nuts. In regard to common food allergens, he currently tolerates cow's milk, egg, wheat, fish, legumes, and sesame. Although serum slgE levels had been measured, he had never ingested tree nuts. You perform skin testing to peanut, which has a wheal/flare diameter of 15/30 mm with negative skin test results to tree nuts. You advise avoidance of peanut and home introduction of age-appropriate forms of tree nuts.

Question

The family has an older child who loves peanut butter, so they are questioning whether they can still have peanut butter in their house. What is the risk their child could experience a reaction just by being near peanut products, without actually ingesting that product?

Myth Addressed

There is danger from causal contact or inhalation of peanut dust or vapors from peanut-containing products.

Discussion

Families of food allergic children often question what types of allergen exposure or situations may put their children at risk for a reaction. There is common perception that there is a risk from aerosolization of allergen from peanut-containing products, which has prompted management recommendations, such as bans of peanut-containing products at school (at the classroom, lunch table, or school-wide level), at sporting events and other public venues, and on commercial flights. But is there truly a risk outside ingesting these products? At least 3 recent studies have addressed these questions, reporting that there is no discernable risk from inhalation or casual contact with these products.

Perry et al¹⁷ simulated real-life situations in which one may be exposed to peanut protein, such as eating in a school cafeteria, attending sporting events, and commercial airline travel, by using 19 non-peanut allergic individuals wearing personal air monitors with measurement of Ara h 1, a peanut component, to detect presence of peanut protein. Ara h 1 was undetectable in all simulated situations.¹⁷ Similarly, Brough et al¹⁸ evaluated the presence of peanut protein in homes with household peanut consumption (as part of the home monitoring phase in the Learning Early About Peanut study) and found that airborne levels were lower than the limit possible for quantitation outside a brief period directly after peanuts were deshelled. Peanut was detected at below 5 and 340 $\mu\text{g}/\text{m}^3$ at 1 cm and 1 m above peanuts being actively shelled. However, these levels were undetectable immediately after shelling ceased, demonstrating that the particle does not remain airborne. Odors, such as from peanut butter, are organic compounds that are nonallergenic and must be differentiated from aerosolization of food allergens, which are proteins, created during cooking or processing of foods.⁸ Although Roberts et al¹⁹ identified 5 patients who reacted to aerosolized forms of food while being cooked (fish, chickpea, and buckwheat), the symptoms were similar to inhalation of aeroallergens, and no patient reported symptoms from peanut inhalation. Therefore, evidence demonstrates that inhalational exposures to peanut products are highly unlikely to trigger allergic reactions.^{18,20,21}

The risk of casual contact with a food allergen, such as skin contact from a peanut-containing product or residue from a product, is also a common concern. As was the case with inhalation of peanut dust, the literature on casual nonoral contact with food allergens indicates that the risk of a systemic reaction is exceptionally low,

apart from actual ingestion of the allergen.^{20,21} Simonte et al¹⁸ applied peanut butter to intact skin on 38 children with a history (and previously reported inhalational reactions) and noted that although 10 patients developed erythema/pruritus in areas of contact (including 5 who developed similar erythema attributable to the soy butter placebo vehicle), no patient developed a systemic reaction. Moreover, no patient developed symptoms (including alterations of pulmonary function testing) from inhaling peanut butter masked with mint and tuna oil, further disproving that inhalation poses a risk. Similarly, Wainstein et al²¹ applied peanut butter to 281 children with sensitization to peanut butter and similarly noted that although 41% had urticaria at the site of contact, no patient had a systemic reaction. These studies indicate that although patients may experience local irritation in sites of allergen contact, this form of exposure is unlikely to trigger a systemic reaction.^{20,21}

Although the risk of a systemic reaction is only with ingestion of the allergen, appropriate avoidance measures must be implemented in the home to prevent unintentional ingestions or cross-contamination, particularly in young children, given the frequency of hand to mouth transfer.⁸ However, again data indicate peanut protein can be readily abated from surfaces and hands. Perry et al¹⁷ additionally evaluated the presences of residual peanut protein in routine household settings and found no peanut protein after adult hand washing with liquid soap or bar soap. Plain water and alcohol-based antibacterial sanitizer, however, left detectable protein after hand washing in a subset of individuals.¹⁷ Common cleaning agents and commercial wipes, except dishwashing liquid, effectively removed peanut allergen from tabletops.¹⁷ Brough et al¹⁸ evaluated environmental exposure after peanut consumption and found detectable peanut on hands and saliva 3 hours after ingestion; however, the use of hand washing or teeth brushing in removal of allergen was not evaluated.¹⁸ They additionally noted peanut being completely removed from granite tables after routine cleaning and found significantly reduced but still detectable levels ($<5 \mu\text{g}/\text{m}^3$) after cleaning of wooden table surfaces, pillows, and sofa covers (with the pillows and covers showing 1,000-fold reduction after machine washing).¹⁸

Thus, for families with food allergic children, washing hands before and after meals, wiping down surfaces, thoroughly cleaning utensils, and keeping unsafe food out of reach of young children are recommended.⁸ The decision of whether to keep an allergen in the home is individual, but evidence does not demonstrate that removal of the food from the home (or other environment, eg, schools) is necessary if appropriate avoidance measures can be implemented. More recent research can better frame the risk that small residual levels may pose, given that this was not tested in any of the aforementioned studies. Three studies^{22–24} of peanut threshold levels have found that less than 5% of patients objectively reacted to levels ranging from 1.5 to 1.95 mg of peanut protein, which would be an amount over a log-fold higher than what was detected by Brough et al.¹⁸ However, the allergist must be aware of these data to have an informed discussion with the family, given that the physician or family may believe that these scenarios pose a risk to the child. Given they do not, this may be a simple discussion-based intervention that could promote lower anxiety and enhanced QoL.

Question

Should any testing to tree nut have been performed in this child?

Myth Addressed

Tree nut avoidance is necessary for peanut allergic individuals.

Discussion

Peanuts are legumes, whereas tree nuts are drupaceous fruits. Although they share common allergenic structures that can elicit cross-reactivity, such as Bet v 1 homology, these items are phylogenically distinct. That said, there are cases of true tree nut allergy in peanut allergic individuals, although the exact rate is difficult to specify. Most data related to the risk of cross-reactivity between peanut and tree nut allergens are limited to cross-reactive sensitization through IgE inhibition studies and indicate that there is often serologic cross-recognition. However, the clinical significance of this is often in question, given that there are a paucity of studies that have investigated this through oral challenge. Food allergy QoL in the caregiver is inversely proportional to the number of foods avoided. Thus, it is imperative to not recommend unnecessary restriction and to use oral food challenge to evaluate the significance of unconfirmed sensitization. Recently, Couch et al²⁵ found that 96% of peanut allergic individuals within an academic clinic sample who were tree nut sensitized but who lack a history of symptomatic ingestion to tree nut were tolerant of tree nuts when actually challenged to these items. Specifically, among 63 peanut allergic individuals who underwent oral challenge to one of multiple tree nuts to which they were sensitized, 96% tolerated their tree nut challenge, including 100% who were sensitized to almond. For any single tree nut to which the individual was sensitized, a skin test wheal of 9 mm and an sIgE level of 11 KU/L represented a 50% negative predictive value for tolerance in an adjusted model in this specific clinical population.²⁵ Older data have suggested upward of 50% of peanut allergic individuals may be coallergic to tree nut, but the precise meaning of coallergy has been poorly defined.²⁶ This finding has led to a common practice of preemptive testing for tree nut sensitization among peanut allergic individuals and restriction of eating tree nuts to which one is sensitized based only on sensitization. Although ongoing studies into this issue from other research groups will better inform the risk, it appears that there are insufficient data to support routine testing to tree nut in peanut allergic individual because of the high likelihood that sensitization will be detected and the risk that unnecessary restriction will be recommended. However, when introducing tree nuts in a peanut allergic child, appropriate education must be given to prevent ingestion of products with peanut due to cross-contamination.

Question

The family has noted that peanut oil is listed in the ingredients of several food products and is wondering if these are safe for him to eat.

Myth Addressed

There is danger from ingestion of highly refined commercial peanut oil in a peanut allergic individual.

Discussion

Commercially available oils can be derived from common food allergens, such as peanut and soy, leading to confusion regarding their safety for allergic individuals.²⁷ In general, full refining of oils for commercial-grade food processing purposes leads to almost complete removal of protein; however, oils that are unrefined (expeller-pressed, cold-pressed, crude) may have detectable protein present.²⁸ Demonstrating this, Teuber et al²⁹ evaluated peanut and tree nut oils for allergenicity by examining for the presence of residual proteins that could bind IgE from sera of patients with the allergy, finding a greater amount of residual protein and greater IgE

binding in those with the least processing, although this did not directly assess clinical risk from ingestion. Hourihane et al³⁰ evaluated the tolerance to peanut oils based on processing by performing double-blind, crossover food challenges with crude and refined peanut oil in 60 peanut allergic individuals. None of the individuals reacted to refined oil, whereas 6 (10%) reacted to crude oil.³⁰ However, although evidence indicates that peanut allergic individuals can safely tolerate highly refined oils but not cold-pressed or expeller-pressed oils,^{8,30} it may be difficult for the consumer to determine which processing method of peanut oil has been used. Therefore, although most commercially available peanut oil is considered highly refined, it is recommended that patients inquire about the degree of refining and consider avoiding if not highly refined or it is unclear.

In regard to oils derived from other common allergens, sesame oil is often not refined and may contain protein; anaphylaxis to sesame seed oil has been reported³¹; thus, avoidance for sesame allergic individuals is typically recommended.³² Alternatively, evaluation of soy oil and soy lecithin, a fatty substance with little allergenicity often used as a food additive, demonstrates they are well tolerated among those with soybean allergy.³³ Similarly, sunflower oil, corn (maize) oil, and palm oil are typically considered nonallergenic.²⁸ Allergists must have knowledge on the allergenicity of oils to provide appropriate avoidance recommendations and prevent unintentional exposures. Labeling laws with soy are confusing, given that soy lecithin and oil are labeled under the Food Allergen Labeling and Consumer Protection Act (FALCPA) and may be the only source of soy in such products.

Question

The family is wondering if it they need to travel exclusively on airlines that don't serve peanuts.

Discussion

Although allergic reactions on commercial airlines have been reported, current literature is based on self-report of symptoms, which is subject to bias, so true prevalence is unknown.^{34–36} Sicherer et al³⁴ surveyed patients in the National Registry of Peanut and Tree Nut allergy and found that 62 of 3,704 individuals reported a reaction on an airplane, with reported ingestion exposures being associated with the most severe symptoms. Among the 14 patients who reported symptoms from inhalational exposure, the timing and exposure history was not convincing in 3, and in the remaining 11 participants, more than 25 passengers were eating peanuts at the time of the reaction in question.³⁴ Similarly, Comstock et al³⁶ recruited individuals with peanut, tree nut, and seed allergy and administered a survey that included assessment of in-flight reactions. In this predominantly adult cohort, 41 individuals reported an in-flight reaction, with 58% attributed to reported inhalational exposure, 9% to contact with the allergen, and 33% to ingestion exposure. Surprisingly, only 29% of all individuals and only 10.5% of those with an inhalational exposure told the flight attendant about their reaction.³⁶ In addition, just more than 50% treated their reactions, with most undertreating by using an oral antihistamine for symptoms of throat swelling and wheezing.³⁶ Greenhawt et al³⁵ reported similar findings with a more recent survey of participants in the Food Allergy & Anaphylaxis Network. Of the 150 participants who reported having an in-flight reaction, 15.7% reported reactions attributable to ingestion, with inhalational, skin, and unknown exposure accounting for 48.6%, 27.9%, and 7.8% of reactions, respectively. Surprisingly, although 33% of participants reported symptoms consistent with anaphylaxis, epinephrine was only used in 10%, highlighting the under treatment of reactions.³⁵

Greenhawt et al³⁷ additionally sought to identify potential risk-mitigating factors among individuals reporting in-flight peanut or tree nut reactions on international flights by distributing an online survey to members of the Food Allergy & Anaphylaxis Alliance. Among the 3,273 respondents, 349 cited in-flight reactions. Eight behaviors that were found to be risk mitigating include making any request of the airline, requesting a buffer zone, requesting an announcement that passengers not eat good that contained peanuts or tree nuts, requesting a peanut- or tree nut-free meal, wiping their tray table, bringing their own food from home, avoiding an airline-provided pillow, and avoiding use of an airline-provided blanket. They also emphasized the importance of having an epinephrine autoinjector readily available.³⁷

Because these studies are based on self-report of symptoms, they are subject to bias and the validity of the reported allergic reactions and its reported mechanism cannot be confirmed.^{34,36,37} Although there is a report of peanut protein being recovered from airline air filters, representing a cumulative exposure,³⁸ studies on inhalational and contact exposures to allergens do not support the notion of systemic reactions with casual contact.^{17,20,21} As well, it is unclear what particle denoted in an air filter represents because these particles could be pulled from circulation without passage through the cabin (Fig 1).³⁹ Therefore, it remains somewhat likely that the reported inhalational reactions were caused by unnoticed ingestion (peanut inadvertently consumed through casual hand to mouth contact of uncleaned residual levels on surfaces) or another source, such as anxiety-induced symptoms.³⁵ Overall, in-flight medical emergencies are rare, with allergic reactions contributing to a small portion of all events, and it appears that most peanut allergic passengers fly without event.^{40,41} Therefore, there appears to be no evidence to support that commercial air travel is dangerous or should be contraindicated for the peanut allergic patient. In addition, there should be no expectation that the allergic individual is at an elevated risk of reacting relative to any other situation. However, many patients and advocates do not share this view and consider air travel potentially risky.

Patients and families should be advised on appropriate avoidance behaviors that they themselves can self-manage, such as

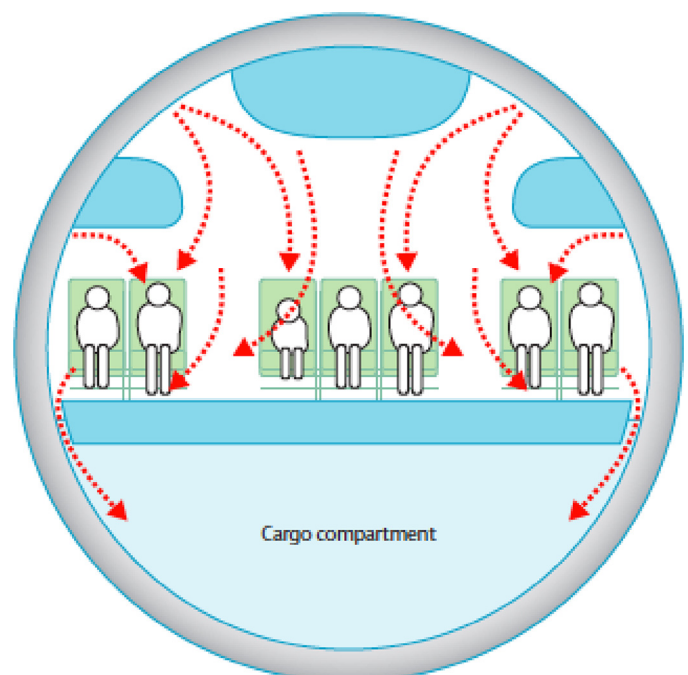


Figure 1. Model of air circulation in a passenger cabin.

bringing their own food and actions to minimize cross-contact, such as wiping down their tray table and inspecting the crevices around their seat, particularly for young children.⁸ The available data tend to indicate the risk in flying stems from inappropriate notification of a reaction occurring and then suboptimum medication choice in treating these reactions. Therefore, although the risk of reaction is low, all patients with a food allergy who fly should have emergency medications with them, including 2 epinephrine autoinjectors, and should ensure that epinephrine is used for treating severe symptoms.⁸ The decision to travel on a commercial airline that serves a culprit allergen is individual, but again the available evidence demonstrates that the presence of an allergen is of low risk, likely not to cause any problem as long as the allergen is not directly ingested. We believe that peanut or tree nut allergy should not serve as contraindication for travel in most circumstances, given a low likelihood of an event occurring and multiple risk-reducing behaviors that passengers can implement.

Case 2

An 11-month-old is brought to your office for evaluation of food allergy. She is breastfed, and her mother eats an unrestricted diet. She has been introduced to table foods, including fruits, vegetables, wheat, and egg. On her first ingestion of cow's milk-based yogurt she developed hives and vomiting. She was brought to the emergency department, where she is given epinephrine and an antihistamine, with prompt resolution of symptoms. She has otherwise never had cow's milk in any form. You have offered an oral food challenge to baked milk based on skin testing results but in the interim recommend avoidance of all forms of cow's milk.

Question

The parents are wondering what cow's milk substitute they can transition the patient to when she turns 1 year old next month. Specifically, the parents are wanting to give almond milk and are asking if that is appropriate.

Myth Addressed

Soy milk is a risk to children with cow's milk allergy (CMA), and other mammalian milks are an appropriate substitute for cow's milk in a child with CMA.

Discussion

Patients with food allergies are at a risk for nutritional deficiencies, particularly children with CMA.⁴² Common mistakes include recommending avoidance of foods without appropriate substitution or recommending substitutes that are not nutritionally or age appropriate.¹¹ On the basis of guidelines by the World Allergy Organization and European Society for Pediatric Gastroenterology Hematology and Nutrition, children with CMA who are not breastfed should use an appropriate substitute, typically until 2 years of age.^{43,44} Hypoallergenic formulas are commonly recommended, with options including extensively hydrolyzed casein-based formulas in the United States, because they are tolerated in more than 90% of children with CMA, or amino acid-based formulas.⁴⁵ However, both can be costly and less palatable.⁴⁵ Partially hydrolyzed whey formulas are sold in the United States but are not hypoallergenic, so these should not routinely be recommended for children with CMA.⁴⁵ Other available mammalian milks, such as goat's milk, have high cross-reactivity with cow's milk and thus are not appropriate substitutions.⁴⁶ Although mare milk may be better tolerated, it is not widely available so would similarly be inappropriate to recommend.^{26,46}

A number of alternative milk-type beverages are now available, but when selecting a fortified alternative beverage, the nutritional value must be taken into consideration. For example, milks derived from rice, almond, and potato are low in protein and fat and thus would not be appropriate substitutions without additional supplementation.⁴² Hemp milk has appropriate fat but low protein, whereas oat milk has more protein but is limited in fat; thus, both are also inappropriate substitutions.³² Outside hypoallergenic formulas, soy-derived formulas are a favorable nutritional substitute for cow's milk and are recommended as an optional substitute.^{43,44} Although children with CMA may be sensitized to soy, clinical coallergy is rare, and soy formula is considered a safe alternative. Soy formulas represent the best alternative choice besides eHFc or elemental formulas.⁴⁷ Although potential concerns have been raised with soy substitutes because of the presence of phytoestrogens, no identifiable risk has been supported by any available evidence.⁴⁵ Overall, the choice of a substitute formula is individual and should include consideration of patient (family) preference and cost. In this patient's case, transition to almond milk would not be an appropriate initial substitute given other superior choices from a nutritional standpoint, although there would be no *a priori* concern for transition to almond milk from an allergenic standpoint. The allergist should discuss nutritionally adequate substitutions with the family or refer the family to a registered dietitian, with expertise in infant nutrition, who could help advise and counsel the family.

Question

The parents express concern about reading nutrition labels and are wondering if they need to avoid foods that may be manufactured in a facility with milk.

Myth Addressed

There is a high risk from cross-contamination of products with precautionary labeling statements (eg, "may" or "might" contain, "made in a shared facility," "made on shared equipment").

Discussion

On the basis of FALCPA of 2004, major food allergens, including milk, egg, fish, crustacean shellfish, wheat, peanuts, tree nuts, and soybeans, must be listed on the label on food products subject to Food and Drug Administration regulation, including domestically manufactured and imported packaged foods.⁴⁸ The food must be listed in plain English on the ingredient list or in a separate "contains" statement. In addition, the type of tree nut, fish, or crustacean (but not mollusk) shellfish must be specifically listed.⁴⁸ Other foods allergens, such as seeds (eg, sesame), for labeling purposes under FALCPA are not considered major allergens. This is clinically relevant because major allergens must be identified even if they are minor ingredients or included in small quantities in item such as natural flavorings or spices. Seeds and sesame fall outside this, as do other allergens not considered to be major under FALCPA, and these potential allergens may be included in these vague ingredient terms without their specific mention so long as they are plant based (the technical definition of a spice) and used for flavoring purposes or not as a primary ingredient. These laws do not cover products regulated by the US Department of Agriculture, such as fresh fruits, vegetables, and meats. Similarly, they do not regulate PAL.^{48,49}

PAL is voluntary, and the wordings and definitions are not standardized.⁴⁹ Common wording formats include "may contain (allergen)," "manufactured on shared equipment with (allergen)," and "manufactured in the same facility with (allergen)."^{50,51} Hefle et al⁵⁰

examined the presence of peanut protein in 179 products with PAL, with 2 different lot numbers of each sample obtained, and reported that 13 of 179 (7%) had detectable peanut residue present in one or both lots tested.⁵⁰ Similarly, Ford et al⁵² assessed the presence of milk, egg, and/or peanut on advisory labeling and found detectable residues of allergenic foods in 5.3% of products with advisory labeling and 1.9% of products without labeling. On the basis of data from double-blinded, placebo-controlled food challenges to peanut,⁵³ Ford et al⁵² estimated that among products with peanut protein residue, only 20% of these products contained an amount of peanut that would elicit a reaction in the most sensitive 5% of the population (the ED₅, or eliciting dose), indicating an overall risk of less than 1%. More recent studies from Blom et al,²³ Ballmer-Weber et al,²² and Hourihane et al²⁴ have better defined a range of EDs (5%–50%) using population-level modeling, suggestive that the ED₅ at which the peanut allergic population would develop objective symptoms from exposure is between 1.5 and 1.95 mg of peanut protein. However, because a threshold level for clinical reactivity is not clearly defined, no firm conclusions can be drawn from this.

Individuals often ascribe a differing amount of risk based on the wording used in PAL, with consumers more likely to avoid products with a “may contain” statement as opposed to a “shared facility” or “shared equipment” statement.^{50,54} However, Hefle et al⁵⁰ detected peanut in 3.9% of products noting they “may contain,” 5.3% of products “made on shared equipment,” and 10.3% of “products made in a shared facility,” indicating actual risk cannot be identified based on which statement is used. Among products with PAL, Ford et al⁵² reported that 5.1% of products from smaller companies contained trace amounts of allergens compared with 0.75% of those from larger companies. Among food items, dark chocolates with PAL seem to have a greater risk of milk residue presence when compared with baked goods, granola bars, nonchocolate candy, cereals, frozen desserts, instant meals, and snack foods.⁵⁵

On the basis of the available data, the 2010 National Institute of Allergy and Infectious Diseases (NIAID) guidelines recommend avoidance of products with PAL for patients with food allergies.⁵ However, Turner et al⁵⁶ surveyed health care professionals on PAL and found that only 22% of allergists recommended total avoidance in all situations, with 71% of allergists recommending total avoidance if the patient had a prior reaction to ingestion of a small amount of the allergen in question. Moreover, the NIAID recommendations predated the 3 recent studies demonstrating an ED₅ above the levels noted to be contained in products with precautionary labeling, further obscuring whether such products truly need to be avoided. This finding highlights the need for further research and regulation of PAL, including additional studies that can better translate the risk and continue to refine the population-level eliciting dose models. Given that Hourihane et al²⁴ found that tolerance of a 1.5-mg peanut protein eliciting dose was associated with improved QoL, there could be considerable value to patients who could expand their diets to include these precautionary labeled foods. However, the key take-home point is that most of the residual contamination detected in the aforementioned studies is on the level of parts per million. Considering that 1 ppm would be equivalent to 1 mg of contaminated allergen per kilogram of the product, these are exceptionally minute quantities, well below the ED₅ denoted in multiple studies. Physicians therefore must become knowledgeable in the risks of ingesting foods with PAL to be able to have informed discussions with their patients.

Question

The patient attends day care and the parents are wondering if the day care should request a ban on cow's milk given their daughter's allergy.

Myth Addressed

Allergen bans are necessary to protect children in public environments, and such bans have evidence of being effective.

Discussion

Guidance in the management of food allergies in the school setting is a common question posed to the allergist. This is a well-founded concern given that allergic reactions in the school setting have been reported to occur in 16% to 18% of food allergic children,^{7,57} with a slight predominance of reactions in the preschool/day care setting likely reflecting the inability of young children to appropriately identify and avoid allergens.^{7,58,59} The Centers for Disease Control and Prevention published guidelines in 2013 titled *Voluntary Guidelines for Managing Food Allergies in Schools and Early Care and Education Programs*, which stress a coordinated approach among parents, school staff, and medical professionals.⁶⁰ A physician-provided Food Allergy Management and Prevention Plan that includes strategies needed to manage food allergies in a school setting is additionally recommended.⁶⁰

Although avoidance is essential for safety, decisions on placing blanket bans on foods must be made individually and carefully evaluated because commonly allergenic foods are likely staples in other children's diets.^{58,61} Although the theory of reducing exposure to a particular allergen in a school setting may make sense, there is no evidence to substantiate the effectiveness of such recommendations. In fact, recent evidence from a 5-year review of epinephrine use in Massachusetts schools noted no difference in use of epinephrine between schools allowing peanut and those not allowing peanut.⁶² Moreover, there is no evidence that these approaches are always desired by the families. Even if a school chooses to ban specific foods, there is no guarantee that such restrictions can be enforced or successfully implemented to ensure allergens will not enter the building. Therefore, measures such as an anaphylaxis management plan, available autoinjectable epinephrine, and rules incorporating actual evidence-based strategies, such as hand-washing and surface cleaning after food contact, are still necessary.⁶⁰ Overall, because the risk of a systemic reaction with skin or inhalational contact is low, avoidance measures should focus on prevention of ingestion and allergen abatement.⁶³ However, specific recommendations will depend on the age of the child and the availability of additional supervision.⁶¹ For example, younger children who are at risk of skin to mouth transfer of allergens and are unable to identify allergens may require additional supervision during meals.⁵⁸

Alternatives to banning foods include creating an allergen-safe zone in the cafeteria or classroom or food-free zones in buses, classrooms, and/or libraries, although again these approaches are not proven to be effective and are not necessarily desired by the families.⁶⁰ Allergen-free tables are generally not necessary for upper elementary school students who have comprehension of avoidance.⁵⁸ Overall, there needs to be an understanding that creating allergen-free zones may enhance social stigmatization and isolate the child; therefore, the risks and benefits of such actions need to be carefully weighed before they are implemented. Food service at schools is unavoidable, and for many low-income children who receive federally subsidized meals, this may include service of certain allergens. Moreover, there are ethical and practical considerations in fairly determining which allergens should or should not be permitted at school (eg, ban peanut but permit milk or egg). Under federal disability policy, the child's family can seek a section 504 plan, which legally entitles the child to fair and appropriate learning environment. This agreement is established between the school and the family and may involve allergist input regarding recommended policies. However, under disability law, a food allergic child

is not entitled to any specific protection per se (eg, such as a peanut-free class), just a safe learning environment, which can be rather subjectively interpreted. Therefore, in this patient's case, because cow's milk is likely a staple in other children's diets and possibly mandated to be served as part of a federally subsidized meal program, it would be preferable that the family work with the school to develop appropriate avoidance (and evidence-proven) avoidance and abatement measures in lieu of making a request for a ban of the food item.

Summary

Allergen avoidance is currently the standard of care in food allergy management.⁵ However, avoidance can be difficult because it requires the ability to correctly read ingredient labels on manufactured products, understanding the risks of casual contact with an allergen and use of appropriate practices to prevent cross-contact.⁸ Excessive avoidance behaviors are also of concern because this can contribute to the social isolation and nutritional deficiencies that have been demonstrated in food allergic individuals.^{11,15} Therefore, allergists must be able to counsel patients on appropriate avoidance behaviors to minimize the risk of unintentional ingestions while also promoting the social and nutritional well-being of the individual. It is thus essential for the allergist to understand the latest evidence regarding food allergy and the risk of environmental exposure and be able to differentiate myth from fact in best advising their patients.

There is often concern regarding the risk of casual contact with an allergen or with an allergen being present in an environment. However, available evidence indicates the risk to patients in these situations is very low. Specifically, for peanut, this allergen does not aerosolize and is readily abated from hands and surfaces, and systemic reactions are primarily attributable to ingestion of an allergen not from contact.⁸ Although unintentional ingestion can occur through cross-contact, particularly in younger children, this risk can be reduced by behaviors such as hand washing, cleaning utensils and surfaces thoroughly, and keeping free access to unsafe foods away from young children.^{8,17,18} This knowledge can be applied to situations of common concern, such as management of food allergies during airline travel or in the school setting, where the focus, in most cases, should be on avoidance behaviors to minimize unintentional ingestion and cross-contact, as opposed to recommending bans or complete avoidance of the situation.

In addition, patients must be counseled on correct interpretation of food ingredient labels in regard to the specific allergen avoided. For example, it is important to review that patients avoiding a major allergen do not need to avoid terms such as *spices* because all major allergens must be listed, even if they are only a minor ingredient.⁴⁸ In addition, because oils derived from allergens are common, patients should be counseled on whether it is safe to ingest these products dependent on the allergen in question.²⁷ For example, patients with peanut allergy may react to unrefined peanut oil but typically tolerate refined oil,³⁰ whereas patients with soy allergy generally tolerate soy oil and soy lecithin.³³ This appropriate guidance is necessary to prevent unintentional ingestions and unnecessary eliminations in the diet.^{11,42} However, once again, it is essential that the allergist understand the most up-to-date research in this area and differentiate myth from fact in best advising their patients. Given that QoL is heavily tied to the number of foods avoided and that there is some evidence that threshold levels can be established, care must be taken with this topic to not be overprescriptive with avoidance while balancing risk taking.

In recommending avoidance of a food, age and nutritionally appropriate substitutes must be provided to the family. This is a paramount responsibility for the allergist if any food elimination

is recommended, and in such situations, consultation with a registered dietician is highly recommended. In particular, with foods such as cow's milk, which is likely a staple in the diet, it is essential to counsel on the risk posed by nutritionally inferior substitutes, such as almond milk, for young children.^{11,32} Specific guidance will depend on the age of the child and other foods avoided. This guidance is often provided with the assistance of a dietician with appropriate expertise in infant nutrition, with recent NIAID guidelines stating that all children with food allergy receive nutrition counseling and close growth monitoring to prevent nutritional deficiencies.^{3,42}

Conclusion

Food allergy avoidance is problematic for families, with unintentional ingestions being a potential risk.^{6,7} Although strict avoidance has been a staple of past recommendations, many myths and misperceptions have resulted from this. These myths may result in detrimental or unnecessary advice being passed on to patients at a cost of their quality of life. Allergists must be able to provide appropriate advice to minimize unintentional ingestions while also preventing excessive elimination behaviors, which may have adverse nutritional and social consequences.^{15,42} Understanding the evidence and differentiating myth from fact are key skills necessary to manage effectively the food allergic patient. Specifically, allergists must be able to counsel on correct interpretation of food allergy labels, the risk with casual contact, and behaviors to limit the risk of cross-contamination with an allergen.¹⁵

References

- [1] Gupta RS, Springston EE, Warrier MR, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. *Pediatrics*. 2011;128:e9–e17.
- [2] Sicherer SH, Sampson HA. Food allergy. *J Allergy Clin Immunol*. 2010;125:S116–S125.
- [3] Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol*. 2010;126:S1–S58.
- [4] Jackson KD, Howie LD, Akinbami LJ. Trends in allergic conditions among children: United States, 1997–2011. *NCHS Data Brief*. 2013;1–8.
- [5] Sampson HA, Aceves S, Bock SA, et al. Food allergy: a practice parameter update-2014. *J Allergy Clin Immunol*. 2014;134:1016–1025, e43.
- [6] Fleischer DM, Perry TT, Atkins D, et al. Allergic reactions to foods in preschool-aged children in a prospective observational food allergy study. *Pediatrics*. 2012;130:e25–e32.
- [7] Sicherer SH, Burks AW, Sampson HA. Clinical features of acute allergic reactions to peanut and tree nuts in children. *Pediatrics*. 1998;102:e6.
- [8] Kim JS, Sicherer SH. Living with food allergy: allergen avoidance. *Pediatr Clin North Am*. 2011;58:459–470, xi.
- [9] Food Allergy Research & Education. Food allergy threshold survey results; 2013. <https://www.foodallergy.org/file/threshold-survey-results.pdf>. Accessed July 9, 2017.
- [10] Simons E, Weiss CC, Furlong TJ, Sicherer SH. Impact of ingredient labeling practices on food allergic consumers. *Ann Allergy Asthma Immunol*. 2005;95:426–428.
- [11] Mehta H, Groetch M, Wang J. Growth and nutritional concerns in children with food allergy. *Curr Opin Allergy Clin Immunol*. 2013;13:275–279.
- [12] Primeau MN, Kagan R, Joseph L, et al. The psychological burden of peanut allergy as perceived by adults with peanut allergy and the parents of peanut-allergic children. *Clin Exp Allergy*. 2000;30:1135–1143.
- [13] Greenhawt M. Food allergy quality of life. *Ann Allergy Asthma Immunol*. 2014;113:506–512.
- [14] DunnGalvin A, Dubois AE, Flokstra-de Blok BM, Hourihane JO. The effects of food allergy on quality of life. *Chem Immunol Allergy*. 2015;101:235–252.
- [15] Bollinger ME, Dahlquist LM, Mudd K, Sonntag C, Dillinger L, McKenna K. The impact of food allergy on the daily activities of children and their families. *Ann Allergy Asthma Immunol*. 2006;96:415–421.
- [16] Begin P, Nadeau KC. Diagnosis of food allergy. *Pediatr Ann*. 2013;42:102–109.
- [17] Perry TT, Conover-Walker MK, Pomes A, Chapman MD, Wood RA. Distribution of peanut allergen in the environment. *J Allergy Clin Immunol*. 2004;113:973–976.
- [18] Brough HA, Makinson K, Penagos M, et al. Distribution of peanut protein in the home environment. *J Allergy Clin Immunol*. 2013;132:623–629.
- [19] Roberts G, Golder N, Lack G. Bronchial challenges with aerosolized food in asthmatic, food-allergic children. *Allergy*. 2002;57:713–717.

- [20] Simonte SJ, Ma S, Mofidi S, Sicherer SH. Relevance of casual contact with peanut butter in children with peanut allergy. *J Allergy Clin Immunol*. 2003;112:180–182.
- [21] Wainstein BK, Kashef S, Ziegler M, Jelley D, Ziegler JB. Frequency and significance of immediate contact reactions to peanut in peanut-sensitive children. *Clin Exp Allergy*. 2007;37:839–845.
- [22] Ballmer-Weber BK, Fernandez-Rivas M, Beyer K, et al. How much is too much? threshold dose distributions for 5 food allergens. *J Allergy Clin Immunol*. 2015;135:964–971.
- [23] Blom WM, Vlieg-Boerstra BJ, Kruizinga AG, van der Heide S, Houben GF, Dubois AE. Threshold dose distributions for 5 major allergenic foods in children. *J Allergy Clin Immunol*. 2013;131:172–179.
- [24] Hourihane JO, Allen KJ, Shreffler WG, et al. Peanut Allergen Threshold Study (PATS): novel single-dose oral food challenge study to validate eliciting doses in children with peanut allergy. *J Allergy Clin Immunol*. 2017;139:1583–1590.
- [25] Couch C, Franxman T, Greenhawt M. Characteristics of tree nut challenges in tree nut allergic and tree nut sensitized individuals. *Ann Allergy Asthma Immunol*. 2017;118:591–596, e3.
- [26] Sicherer SH. Clinical implications of cross-reactive food allergens. *J Allergy Clin Immunol*. 2001;108:881–890.
- [27] Hidalgo FJ, Zamora R. Peptides and proteins in edible oils; stability, allergenicity and new processing trends. *Trends Food Sci Technol*. 2006;17:56–63.
- [28] Crevel RW, Kerkhoff MA, Koning MM. Allergenicity of refined vegetable oils. *Food Chem Toxicol*. 2000;38:385–393.
- [29] Teuber SS, Brown RL, Haapanen LA. Allergenicity of gourmet nut oils processed by different methods. *J Allergy Clin Immunol*. 1997;99:502–507.
- [30] Hourihane JO, Bedwani SJ, Dean TP, Warner JO. Randomised, double blind, crossover challenge study of allergenicity of peanut oils in subjects allergic to peanuts. *BMJ*. 1997;314:1084–1088.
- [31] Chiu JT, Haydik IB. Sesame seed oil anaphylaxis. *J Allergy Clin Immunol*. 1991;88:414–415.
- [32] Groetch M. Oops! frequently made mistakes in nutrition and avoidance strategies. Paper presented at: Jaffee Food Allergy Institute, Icahn School of Medicine at Mount Sinai; November 22, 2014; New York, NY.
- [33] Awazuwara H, Kawai H, Baba M, Matsui T, Komiya A. Antigenicity of the proteins in soy lecithin and soy oil in soybean allergy. *Clin Exp Allergy*. 1998;28:1559–1564.
- [34] Sicherer SH, Furlong TJ, DeSimone J, Sampson HA. Self-reported allergic reactions to peanut on commercial airliners. *J Allergy Clin Immunol*. 1999;104:186–189.
- [35] Greenhawt MJ, McMorris MS, Furlong TJ. Self-reported allergic reactions to peanut and tree nuts occurring on commercial airlines. *J Allergy Clin Immunol*. 2009;124:598–599.
- [36] Comstock SS, DeMera R, Vega LC, et al. Allergic reactions to peanuts, tree nuts, and seeds aboard commercial airliners. *Ann Allergy Asthma Immunol*. 2008;101:51–56.
- [37] Greenhawt M, MacGillivray F, Batty G, Said M, Weiss C. International study of risk-mitigating factors and in-flight allergic reactions to peanut and tree nut. *J Allergy Clin Immunol Pract*. 2013;1:186–194.
- [38] Jones RYSD, Susman GL, Yunginger JW. Recovery of peanut allergens from ventilation filters of commercial airlines (abstract). *J Allergy Clin Immunol*. 1996;97:423.
- [39] Mangili A, Gendreau MA. Transmission of infectious diseases during commercial air travel. *Lancet*. 2005;365:989–996.
- [40] Delaune EF III, Lucas RH, Illig P. In-flight medical events and aircraft diversions: one airline's experience. *Aviat Space Environ Med*. 2003;74:62–68.
- [41] DeJohn CA, Véronneau SJH, Wolbrink AM, et al. The Evaluation of In-flight Medical Care Aboard Selected U.S. Air Carriers: 1996 to 1997. Washington, DC: US Department of Transportation, Federal Aviation Administration Office of Aviation Medicine National Technical Information Service; 2000.
- [42] Groetch M, Nowak-Węgrzyn A. Practical approach to nutrition and dietary intervention in pediatric food allergy. *Pediatr Allergy Immunol*. 2013;24:212–221.
- [43] Fiocchi A, Schunemann HJ, Brozek J, et al. Diagnosis and Rationale for Action Against Cow's Milk Allergy (DRACMA): a summary report. *J Allergy Clin Immunol*. 2010;126:1119–1128, e12.
- [44] Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines. *J Pediatr Gastroenterol Nutr*. 2012;55:221–229.
- [45] Fiocchi A, Dahda L, Dupont C, Campoy C, Fierro V, Nieto A. Cow's milk allergy: towards an update of DRACMA guidelines. *World Allergy Organ J*. 2016;9:35.
- [46] Restani P, Beretta B, Fiocchi A, Ballabio C, Galli CL. Cross-reactivity between mammalian proteins. *Ann Allergy Asthma Immunol*. 2002;89:11–15.
- [47] Katz Y, Goldberg MR, Zadik-Mnuhin G, Leshno M, Heyman E. Cross-sensitization between milk proteins: reactivity to a "kosher" epitope? *Isr Med Assoc J*. 2008;10:85–88.
- [48] U.S. Food & Drug Administration. Food Allergen Labeling And Consumer Protection Act of 2004 Questions and Answers. <https://www.fda.gov/food/guidanceRegulation/GuidanceDocumentsRegulatoryInformation/Allergens/ucm106890.htm>. Accessed July 9, 2017. Published December 12, 2005. Updated July 18, 2006.
- [49] Zurzolo GA, de Courten M, Koplin J, Mathai ML, Allen KJ. Is advising food allergic patients to avoid food with precautionary allergen labelling out of date? *Curr Opin Allergy Clin Immunol*. 2016;16:272–277.
- [50] Hefle SL, Furlong TJ, Niemann L, Lemon-Mule H, Sicherer S, Taylor SL. Consumer attitudes and risks associated with packaged foods having advisory labeling regarding the presence of peanuts. *J Allergy Clin Immunol*. 2007;120:171–176.
- [51] Pieretti MM, Chung D, Pacenza R, Slotkin T, Sicherer SH. Audit of manufactured products: use of allergen advisory labels and identification of labeling ambiguities. *J Allergy Clin Immunol*. 2009;124:337–341.
- [52] Ford LS, Taylor SL, Pacenza R, Niemann LM, Lambrecht DM, Sicherer SH. Food allergen advisory labeling and product contamination with egg, milk, and peanut. *J Allergy Clin Immunol*. 2010;126:384–385.
- [53] Taylor SL, Hefle SL, Bindslev-Jensen C, et al. Factors affecting the determination of threshold doses for allergenic foods: how much is too much? *J Allergy Clin Immunol*. 2002;109:24–30.
- [54] Marchisotto MJ, Harada L, Kamdar O, et al. Food allergen labeling and purchasing habits in the United States and Canada. *J Allergy Clin Immunol Pract*. 2017;5:345–351, e2.
- [55] Crotty MP, Taylor SL. Risks associated with foods having advisory milk labeling. *J Allergy Clin Immunol*. 2010;125:935–937.
- [56] Turner PJ, Skypala LJ, Fox AT. Advice provided by health professionals regarding precautionary allergen labelling. *Pediatr Allergy Immunol*. 2014;25:290–292.
- [57] Nowak-Węgrzyn A, Conover-Walker MK, Wood RA. Food-allergic reactions in schools and preschools. *Arch Pediatr Adolesc Med*. 2001;155:790–795.
- [58] Young MC, Munoz-Furlong A, Sicherer SH. Management of food allergies in schools: a perspective for allergists. *J Allergy Clin Immunol*. 2009;124:175.e4–182.e4, quiz 83–84.
- [59] Ford LS, Turner PJ, Campbell DE. Recommendations for the management of food allergies in a preschool/childcare setting and prevention of anaphylaxis. *Expert Rev Clin Immunol*. 2014;10:867–874.
- [60] Centers for Disease Control and Prevention. Voluntary guidelines for managing food allergies in schools and early care and education programs. Washington, DC: US Dept of Health and Human Services; 2013. https://www.cdc.gov/healthyyouth/foodallergies/pdf/13_243135_A_Food_Allergy_Web_508.pdf. Accessed July 9, 2017.
- [61] Sicherer SH, Mahr T. Management of food allergy in the school setting. *Pediatrics*. 2010;126:1232–1239.
- [62] Bartnikas LM, Huffaker MF, Sheehan WJ, et al. Impact of school peanut-free policies on epinephrine administration. *J Allergy Clin Immunol*. 2017;140:465–473.
- [63] Egan M, Sicherer S. Doctor, my child is bullied: food allergy management in schools. *Curr Opin Allergy Clin Immunol*. 2016;16:291–296.