Published in final edited form as:
J Allergy Clin Immunol. 2009 August ; 124(2): 286–291.e6. doi:10.1016/j.jaci.2009.03.045.

Safety of a peanut oral immunotherapy protocol in peanut allergic children

Alison M. Hofmann, MD[1], **Amy M. Scurlock, MD**[2], **Stacie M. Jones, MD**[2], **Kricia P. Palmer, MD**[2], **Yuliya Lokhnygina, PhD**[3], **Pamela H. Steele, CPNP**[1], **Janet Kamilaris, RN**[1], and **A. Wesley Burks, MD**[1]

[1] Division of Allergy and Immunology, Department of Pediatrics, Duke University Medical Center, Durham, NC

[2] Division of Allergy and Immunology, Department of Pediatrics, University of Arkansas, Little Rock, Arkansas

[3] Department of Biostatistics and Bioinformatics, Duke University, Durham, NC

Abstract

Background—Oral immunotherapy offers a promising therapeutic option for peanut allergy. Given that during oral immunotherapy an allergic patient ingests an allergen that could potentially cause a serious reaction, safety of oral immunotherapy is of particular concern.

Objective—The purpose of this study is to examine safety during the initial escalation day, build-up phase, and home dosing phase in subjects enrolled in a peanut oral immunotherapy study.

Methods—Skin, upper respiratory, chest and abdominal symptoms were recorded with initial escalation day and build-up phase dosings. Subjects also maintained daily diaries detailing symptoms after each home dosing. A statistical analysis of this data was performed.

Results—Twenty of 28 patients completed all phases of the study. During the initial escalation day, upper respiratory (79%) and abdominal (68%) symptoms were the most likely symptoms experienced. The risk of mild wheezing during the initial escalation day was 18%. The probability of having any symptoms after a build-up phase dose was 46%, with a risk of 29% for upper respiratory symptoms and 24% for skin symptoms. The risk of reaction with any home dose was 3.5%. Upper respiratory (1.2%) and skin (1.1%) were the most likely symptoms after home doses. Treatment was given with 0.7% of home doses. Two subjects received epinephrine after one home dose each.

Conclusions—Subjects were more likely to have significant allergic symptoms during the initial escalation day when they were in a closely monitored setting than during other phases of the study. Allergic reactions with home doses were rare.

Keywords

peanut; food allergy; oral immunotherapy

Corresponding Author: A. Wesley Burks, MD, Division of Allergy and Immunology, Duke University Medical Center, Box 2644, Durham, NC 27710, Telephone: 919-681-2949, Fax: 919-668-3750, wesley.burks@duke.edu.

Clinical Implications: Peanut oral immunotherapy offers the promise of a novel therapy for peanut allergy and appears to be safe in peanut allergic children treated in a controlled setting by trained personnel.

INTRODUCTION

Peanut allergy is increasing in the United States. An estimate of the prevalence of peanut allergy in children is 0.8% in 2002 as compared to 0.4% in 1997 in a self-reported population survey. [1] Reactions to ingestion of peanuts in allergic patients include urticaria, angioedema, vomiting, diarrhea, wheezing, throat tightness and dyspnea.[2] Typically, peanut allergy is life-long and can lead to severe reactions and possibly death. Only approximately 20% of children outgrow their peanut allergy. [3,4]

Current management of peanut allergy includes avoidance and treatment with epinephrine and antihistamines in cases of accidental ingestion and anaphylaxis.[2] There is no cure for peanut allergy. In a landmark study, six patients were treated with standard injection immunotherapy with aqueous peanut during a rush and a maintenance phase.[5] Interestingly, these patients exhibited increased tolerance to higher peanut doses during food challenges and had decreased skin prick reactivity to peanuts post therapy. However, systemic reactions occurred frequently during immunotherapy (23% of rush injections and 39% of maintenance injections) leading the authors to conclude that the high rate of systemic reactions observed during standard immunotherapy with aqueous peanut make this form of treatment unacceptable.[5] Other researchers have modified the IgE binding epitopes of Ara h 1, 2, and 3, the major peanut allergens, to decrease IgE binding capacity while preserving T cell activation capabilities in hopes of using this as a safer immunotherapeutic agent in peanut allergic patients.[6] Investigators are also studying the use of anti-IgE in prevention of anaphylaxis in cases of accidental exposure in peanut allergic patients.[7]

Another potential treatment for peanut allergy is oral immunotherapy (OIT).[8,9] Patriarca and colleagues reported successful oral desensitization in 36 of 42 treatments (85%) to foods including milk, egg, codfish, apple and wheat. In their study, 11 of 36 patients (30.5%) reported mild side effects such as urticaria, vomiting, abdominal pain or worsening of asthma. Five patients were unable to successfully complete the desensitization secondary to severe side effects.[10] In a proof of concept study, 7 subjects who underwent an egg OIT protocol tolerated more egg protein in food challenges at study conclusion and 2 had evidence of oral tolerance to egg after discontinuation of the study.[11] In a randomized controlled trial of specific oral tolerance induction in children with severe cow's milk allergy, 36% of children developed complete tolerance to cow's milk allowing reintroduction into the diet and 54% developed partial tolerance to increased milk ingestion.[12]

OIT offers a promising therapeutic option for peanut allergy. In OIT protocols, allergic patients are desensitized to the allergic food which protects them against reactions from accidental ingestions. OIT also has the potential to induce tolerance so that an allergic food may be reintroduced into the diet on a regular basis without fear of reaction. Given that during OIT an allergic patient is given an allergen that could potentially cause a serious reaction, safety of OIT is a particular concern. The purpose of this study is to evaluate the safety of a peanut OIT protocol in a group of peanut allergic children.

METHODS

Patient Selection

Twenty eight peanut allergic patients age 1 to 16 years were recruited from the Duke Pediatric Allergy/Immunology Clinic or were referred from colleagues in the surrounding communities. Patients were confirmed to have peanut allergy by the presence of specific IgE to peanut (a positive skin prick test to peanut, defined as a wheal ≥ 3mm larger than the saline control, and a positive *in vitro* serum peanut IgE [CAP-FEIA] >15 Ku/L for children over 2 years of age and > 7 Ku/L for children 2 years and younger] and a history of significant clinical symptoms

within 60 minutes after the ingestion of peanuts. Patients were also accepted into the study if they had a positive skin prick test to peanut, an *in vitro* peanut IgE [CAP-FEIA] of ≥ 7 Ku/L and a clinical reaction to peanut ingestion within the past 6 months. Exclusion criteria were a history of severe, life-threatening anaphylaxis consisting of hypotension to peanut, severe or poorly controlled asthma, a medical history that would prevent a food challenge to peanut, inability to cooperate with challenge procedures or unavailability by telephone for follow-up. For the duration of the study, the patients were asked to continue a strict peanut elimination diet. The study was undertaken with the approval of the Duke University Institutional Review Board. The parents and patient were educated about the study and informed consent was obtained.

OIT Protocol

The OIT protocol consisted of three phases: (1) an initial escalation day, (2) a build-up phase, and (3) a home dosing phase. The goal of OIT was to achieve ingestion of a daily maintenance dose of 300 mg of peanut protein which is the equivalent of 1 peanut and is greater than the amount that might cause an accidental allergic reaction.[13]

Initial Escalation Day

On the initial escalation day, subjects were admitted to the Duke Clinical Research Unit (DCRU), an intravenous catheter was inserted, and diphenhydramine, epinephrine, and albuterol were made immediately available. Each subject first ingested 0.1 mg of peanut protein (Golden Peanut Co., Alpharetta Georgia) mixed in a food-vehicle. The dose was doubled every 30 minutes until a maximum dose of 50 mg of peanut protein (cumulative peanut protein=99 mg) was ingested. If the subject had a mild reaction to a dose, the next dose was determined at the discretion of the investigator: the investigator administered the last previously tolerated dose, waited an additional amount of time between doses, or repeated the current dose. If the subject tolerated this dose, the desensitization process resumed. If the subject continued to have symptoms or if the symptoms were moderate or severe, the desensitization process was discontinued and the highest tolerated dose was recorded. Symptoms were treated as medically indicated. Vital signs were recorded before each dose was given. Upon completion of the initial escalation day, the patient was observed for a minimum of 2 hours. The subject was then discharged home with self-injectable epinephrine after instructions were given to the parents regarding its use. The subject returned to the DCRU the following day for an observed ingestion of the maximum tolerated dose of peanut protein. This dose became the starting dose for home dosings.

Build-up Phase and Home Dosing Phase

The subject ingested the daily dose every day at home for a minimum of two weeks. If the home doses were well tolerated, the subject underwent an observed dosage escalation schedule whereby the daily dose was increased by 25 mg every two weeks at the DCRU until a 300 mg dose was reached. The 300 mg dose was ingested daily for a period of either 4 or 24 months (2 different groups). All initial escalation day protocols and build-up phase dose increases were performed by trained practitioners in the DCRU. Symptoms and treatments were recorded every 30 minutes for at least 2 hours after the last dose. If the patient experienced any allergic symptoms, blood pressure was measured. Parents of patients were also given a daily symptom and treatment diary to complete with each home dosing. Symptom categories in the diary included skin, upper respiratory, chest and abdominal. Parents were given an information sheet describing each category. (see Figure E1 in the Online Repository).

STATISTICAL ANALYSIS

Clinical characteristics for patients enrolled in the study were described using frequencies for categorical variables and means with ranges for continuous variables. Frequency of symptom occurrence during the initial escalation day was reported overall, by body system and by severity in each symptom category. It should be noted that frequency of symptom occurrence on a patient basis (number of patients with symptoms divided by total number of patients) during the initial escalation day estimates the risk (probability) of symptom occurrence among patients. For buildup and home dosing phases, frequency of symptom occurrence on a dose basis (number of doses associated with symptoms relative to total number of doses in the study) is not generally equal to the estimated risk of symptom occurrence associated with a dose, because of the correlation between symptom occurrence after doses administered to the same patient. Therefore, for buildup and home dosing phases, risk of symptom occurrence associated with any single dose was estimated (with 95% CI) using logistic regression adjusting for correlation between multiple doses within patients. Statistical analyses were performed using SAS software (version 8.2, SAS Institute, Cary, NC).

RESULTS

Twenty-eight patients were enrolled in the peanut OIT study. The mean age of the patients at enrollment was 4.8 years (range 1.1–9.4 years). Sixty-eight percent of the patients had asthma, 64% had atopic dermatitis, and 61% had allergic rhinitis. (see Table E1 in the Online Repository) All 28 patients completed the initial escalation day protocol. Three of the patients elected not to continue in the study after the initial escalation day for personal reasons. These 3 patients had reactions during the initial escalation day that were similar to the other 25 patients who continued in the study. Twenty of 28 patients had completed all 3 phases of the study at the time of data collection. Three patients were still in the build-up phase or on maintenance dosing. One patient dropped out during the build-up phase due to transportation difficulties. Another patient dropped out of the study during maintenance dosing secondary to documentation of eosinophilic esophagitis which resolved several weeks after peanut OIT was discontinued.

Symptoms during Initial Escalation Day

Twenty-six of 28 patients (93%) experienced some symptoms during the initial escalation day. The relative risk of respiratory symptoms was 79% with mild sneezing/itching and mild laryngeal symptoms reported most frequently. (see Table I and Table E2 in the Online Repository) Abdominal symptoms (68%) constituted the second most common symptom category noted during the initial escalation day. (see Figure 1) Symptoms in the skin category occurred with a frequency of 61%. Skin was the only symptom category in which patients had severe symptoms during the initial escalation day. (see Figure 1) Five patients experienced chest symptoms during the initial escalation day; all 5 had mild wheezing and 2 progressed to moderate wheezing. (see Figure 1) Forty percent of patients with chest symptoms during the initial escalation day also had a diagnosis of asthma. No changes in blood pressure were noted during the initial escalation day.

Symptoms during Build-up Phase

The total number of build-up phase doses was 301 for the 25 patients who continued in the study after the initial escalation day. The mean number of build-up phase dose increases was 12 per patient. Seven patients required dose decreases during the build-up phase due to reactions that occurred at home, missed home doses secondary to illness, or severity of reaction to a buildup phase dose. Six of these 7 were able to reach the 300 mg maintenance dose over time. One patient dropped out due to transportation issues.

The estimated risk of symptoms with a build-up phase dose was 46%. Upper respiratory symptoms were most likely (29%) followed by skin symptoms (24%). Abdominal symptoms (5.5%) and chest symptoms (1.7%) were less frequently recorded. (see Table I) In the upper respiratory category, the risks of mild sneezing/itching and mild laryngeal symptoms were 16.2% and 13.8% making them the most likely symptoms in this category. (see Figure 2 and Table E3 in the Online Repository) Only mild chest symptoms were experienced with build-up phase doses. There were no severe symptoms experienced in any of the 4 categories nor any changes in blood pressure noted during the buildup phase.

Symptoms during Home Dosing Phase

The total number of home dosings from study inception until August 2007 for all patients enrolled in this study was 10,184. The mean number of home dosings per patient was 391 with a range of 6 to 1024. Two patients dropped out of the study in either the maintenance phase or the build-up phase; any home dosings they took prior to dropping out were included in this analysis.

The estimated risk of experiencing any symptoms with a home dose was 3.5%. Upper respiratory symptoms and skin symptoms were the two most frequently recorded symptom categories with risks of 1.2% and 1.1%. (see Table I) One patient reported severe laryngeal symptoms with one home dose. Five minutes after the patient's home peanut dose, he developed cough, hoarseness and stridor with decreased peak flow. He was given diphenhydramine and albuterol and his symptoms resolved in 30 minutes. Because he had tolerated his previous home doses and was stable, he was allowed to take a decreased peanut dose at home the following day. He tolerated this dose without any symptoms and was advanced back to his original home peanut dose the next day. Most of the skin symptoms experienced with home doses were classified as mild with a 0.4% risk of mild urticaria/angioedema and a 0.4% risk of mild pruritus. (see Figure 3 and Table E4 in the Online Repository) One patient reported severe pruritus with 2 home doses. Abdominal symptoms (0.9%) were less likely to occur after home doses than upper respiratory (1.2%) and skin symptoms (1.1%). Eleven patients experienced chest symptoms during home dosings; 82% of these patients had asthma. There were no accidental ingestions of peanut reported during the home dosing phase.

Treatment during Peanut OIT

During the initial escalation day, 71% of patients required treatment for symptoms. The most frequent treatment was diphenhydramine with 50% of patients receiving this medication alone. Seven percent of patients were given both diphenhydramine and albuterol and 15% received epinephrine. (see Table II) Fewer patients received treatment during the buildup phase than during the initial escalation day. Four patients (16%) were given any medications for reactions during the buildup phase. Overall, treatment was given with 1.7% of buildup phase doses. No patient received epinephrine during the buildup phase. (see Table II) All patients were monitored in the DCRU until completely recovered to baseline. No patients were admitted to the hospital during the OIT study.

Treatment was given after 0.7% of home dosings. The most common treatment for symptoms experienced with home doses was diphenhydramine (0.4%) followed by albuterol and diphenhydramine (0.2%). Epinephrine was associated with 0.02% of home doses. Two patients received epinephrine after one home dose each. (see Table II) One patient received epinephrine at home after developing moderate laryngeal symptoms with ingestion of the daily peanut dose in the setting of fever. The patient was diagnosed with pneumonia the following day. Another patient developed severe pruritus, mild laryngeal symptoms, mild wheeze and mild nausea/pain after ingesting his daily peanut dose. The patient was given epinephrine in the local emergency room. Both patients were observed in the local emergency room until fully

recovered; neither patient was admitted to the hospital. Both patients had tolerated the home peanut dose without symptoms the day before. Of the 2 patients, the second one had been treated with epinephrine during the initial escalation day for moderate laryngeal symptoms, moderate pruritus and moderate emesis/diarrhea. He also was one of the four patients who received treatment during the buildup phase. After this reaction at home, the first patient stopped the study for 2 weeks. She then re-entered the study and completed a second initial escalation day, build-up phase and maintenance phase. The second patient underwent a dose reduction the next day at the DCRU and was able to eventually reach the maintenance dose.

DISCUSSION

Peanut allergy is increasing across industrialized countries and is usually lifelong.[2,14] The standard treatment for peanut allergy is to follow a strict elimination diet and to treat any reactions from accidental ingestions with epinephrine and antihistamines. However, peanut is difficult to avoid given its ubiquitous presence in the food supply. Therefore OIT offers a promising treatment for peanut allergy. In OIT protocols, the patient is given the allergic food in escalating doses in an attempt to increase tolerance. Because patients are given a food to which they may potentially react, the safety of OIT has been a concern. In this study, we show that a peanut OIT protocol consisting of an initial escalation day, a build-up phase and a home dosing phase is overall safe and well tolerated in patients without a history of severe life-threatening anaphylaxis to peanut ingestion or severe or poorly controlled asthma.

In this study, reactions were most frequently observed during the initial escalation day in which patients underwent an oral desensitization with peanut protein. Twenty-six of 28 patients had symptoms during the desensitization. However, the severity of symptoms varied widely across patients and only 4 of 28 patients received epinephrine for severe symptoms. Six of the 28 patients were able to tolerate the final 50 mg peanut dose of the modified rush desensitization. (see Table E5 in the Online Repository) There was no significant difference in peanut specific IgE levels between those who required epinephrine for severe reactions and those who tolerated the initial escalation day. It is likely that fewer patients would have reactions if the final dose of the initial escalation day was lower thereby extending the duration of the build-up phase.

Doses were better tolerated during the build-up phase than during the initial escalation day. The estimated probability of a reaction with a build-up phase dose was 46%. These reactions were usually mild in nature and there were no severe symptoms recorded during the build-up phase. Moderate symptoms were also less commonly experienced with build-up phase doses than during the initial escalation day. Peanut specific IgE levels were similar between those who had reactions and those who tolerated build-up phase doses

Home doses were rarely associated with any reactions. The estimated risk of a reaction with a home dose was quite low at 3.5%. When symptoms were recorded with home dosings, they were most commonly classified as mild with rare occurrences of more severe symptoms. Although 2 patients were treated with epinephrine for reactions after home dosings, they were both able to reach the maintenance dose of peanut and complete the study.

One interesting finding was the relationship between asthma and chest symptoms during the OIT protocol. Asthma was prevalent in this study population; 68% of the patients were asthmatics. Of those patients who experienced chest symptoms during the initial escalation phase or the build-up phase, 40% and 100% had asthma. Eighty-two percent of the patients who experienced chest symptoms with homes doses were asthmatics. Our experience suggests that having a diagnosis of asthma is associated with a higher rate of chest symptoms during OIT. Only 47% of the asthmatic children were on inhaled corticosteroid therapy during OIT. It is possible that placement of asthmatic children on adequate controller medications with

close monitoring of pulmonary function tests prior to and regularly during the OIT study could reduce the incidence of chest symptoms.

OIT has been studied as a treatment for other food allergies. However, OIT for peanut allergy has been described in the literature in only 2 case reports. In a Letter to the Editor, Mansfield describes an oral desensitization protocol using peanut kernels in a peanut allergic child.[15] After a rush desensitization followed by an 8 week buildup phase, the child was ingesting 2 whole peanuts twice a day and had tolerated an accidental exposure to peanut without symptoms. This child experienced wheezing and rash during the initial rush desensitization. Patriarca and colleagues report a rush desensitization procedure to peanut followed by a maintenance phase in a peanut allergic woman. Both the desensitization and maintenance phase were well tolerated without any side effects. After 6 months on therapy, skin prick tests which were initially positive were absent and peanut specific IgE had declined slightly. The woman was also able to tolerate peanut containing foods in her diet.[16]

Given the success of studies of OIT for milk and egg allergies and the rising prevalence of peanut allergy, there seems to be a void of studies related to peanut OIT. This may be due to several interesting features of peanut allergy. Although milk, egg, and peanut allergies are all IgE mediated, there are differences between these food allergies. Peanut allergy has been associated with a high risk of severe anaphylaxis as compared to egg allergy.[17, 18] Several studies have found that peanut is the most common cause of fatal food induced anaphylaxis.[18–20] Studies have also shown that reactions can occur at very low doses of peanut protein (0.1 mg).[14] The paucity of studies on peanut OIT may be related both to the high risk of anaphylaxis with peanut ingestion and the risk of reaction with very low doses of peanut.

In this study of peanut OIT, severe reactions requiring treatment were rare, much different than previous studies of peanut immunotherapy.[5] However, we caution that this was a select group of patients treated with peanut OIT in a controlled medical setting by personnel trained in food-induced anaphylaxis. Further studies are needed in larger populations of peanut allergic children to ensure safety of this protocol. Studies are underway to determine the efficacy of peanut OIT and duration of effect. In this study, none of the children had an accidental ingestion of peanut while on the 300 mg of peanut protein. The subjects did have a peanut challenge of 3900 mg at the conclusion of the original period of treatment and 93% tolerated this challenge without symptoms (Jones et al. Manuscript under consideration at JACI). Each of these subjects had allergic symptoms to peanut ingestion of 50 mg or less with the daily dosing early in the study.[21] The question remains whether peanut OIT will simply lead to desensitization or to true immune tolerance. If only desensitization is achieved, patients who are being treated with peanut OIT and who have an accidental ingestion will likely be protected from an allergic reaction. However, similar to drug desensitization, if peanut OIT only causes desensitization and is discontinued, the patient would be at risk for reactions if accidental ingestions occur. If immune tolerance is achieved by peanut OIT, then patients may be able to discontinue therapy and reintroduce peanut into their diet without fear of reaction. Even if peanut OIT only results in desensitization and not immune tolerance, it may offer protection for those who may have accidental peanut ingestions. Overall peanut OIT offers a promising therapy with a good safety profile for peanut allergic patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Declaration of all sources of funding: Food Allergy and Anaphylaxis Network, Gerber Foundation, Food Allergy Project, Dorothy and Frank Robins Family Foundation. The project described was supported by Grant Number 1 UL1

RR024128-01 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and NIH Roadmap for Medical Research, and its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR or NIH.

Abbreviations used

OIT

Oral Immunotherapy

DCRU

Duke Clinical Research Unit

References

1. Sicherer S, Munoz-Furlong A, Sampson HA. Prevalence of peanut and tree nut allergy in the United States determined by means of a random digit dial telephone survey: A 5-year follow-up study. J Allergy Clin Immunol 2003;112(6):1203–1207. [PubMed: 14657884]
2. Sicherer SH, Burks AW, Sampson HA. Clinical Features of Acute Allergic Reactions to Peanut and Tree Nuts in Children. Pediatrics 1998;102(1):e6. [PubMed: 9651458]
3. Fleischer DM. The natural history of peanut and tree nut allergy. Curre Allergy Asthma Rep 2007;7 (3):175–81.
4. Fleischer DM, Conover-Walker MK, Christie L, Burks AW, Wood RA. Peanut allergy: Recurrence and its management. J Allergy Clin Immunol 2004;114(5):1195–201. [PubMed: 15536431]
5. Nelson HS, Lahr J, Rule R, Bock A, Leung D. Treatment of analphylactic sensitivity to peanuts by immunotherapy with injections of aqueous peanut extract. J Allergy Clin Immunol 1997;99(6 Pt1): 744–751. [PubMed: 9215240]
6. King N, Helm R, Stanley JS, Vieths S, Luttkopf D, Hatahet L, et al. Allergenic characteristics of a modified peanut allergen. Mol Nutr Food Res 2005;49(10):963–7. [PubMed: 16189800]
7. Leung DY, Sampson HA, Yunginger JW, Burks AW Jr, Schneider LC, Wortel CH, et al. Avon Longitudinal Study of Parents and Children Study Team Effect of anti-IgE therapy in patients with peanut allergy. N Engl J Med 2003;348(11):986–93. [PubMed: 12637608]
8. Niggeman B, Staden U, Rolinck-Werninghaus C, Beyer K. Specific oral tolerance induction in food allergy. Allergy 2006 Jul;61(7):808–11. [PubMed: 16792577]
9. Meglio P, Bartone E, Plantamura M, Arabito E, Giampietro PG. A protocol for oral desensitization in children with IgE-mediated cow's milk allergy. Allergy 2004 Sep;59(9):980–7. [PubMed: 15291907]
10. Patriarca G, Nucera E, Pollastrini E, Roncallo C, De Pasquale T, Lombardo C, et al. Oral specific desensitization in food-allergic children. Dig Dis Sci 2007 Jul;52(7):1662–72. [PubMed: 17245630]
11. Buchanan AD, Green TD, Jones SM, Scurlock AM, Christie L, Althage KA, et al. Egg oral immunotherapy in nonanaphylactic children with egg allergy. J Allergy Clin Immunol 2007;119(1): 199–205. [PubMed: 17208602]
12. Longo G, Barbi E, Berti I, Meneghetti R, Pittalis A, Ronfani L, et al. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. J Allergy Clin Immunol 2008;121(2): 343–347. [PubMed: 18158176]
13. Nutrients in 1 Ounce of Tree Nuts and Peanuts. International Tree Nut Council Nutrition Research & Education Foundation. Oct. 2006 ttp://www.nuthealth.org/nutrition/nutrient1oz.html
14. Sicherer SH, Sampson HA. Peanut Allergy: Emerging concepts and approaches for an apparent epidemic. J Allergy Clin Immunol 2007;120(3):491–503. [PubMed: 17689596]
15. Mansfield L. Successful Oral Desensitization for Systemic Peanut Allergy. Ann Allergy Asthma Immunol 2006;97(2):266–7. [PubMed: 16937764]
16. Patriarca G, Nucera E, Pollastrini E, De Pasquale T, Lombardo C, Buonomo A, et al. Oral rush desensitization in peanut allergy: a case report. Dig Dis Sci 2006;51(3):471–3. [PubMed: 16614954]
17. Allen CW, Campbell DE, Kemp AS. Egg allergy: are all childhood food allergies the same? J Pediatr Child Health 2007;43(4):214–8.

18. Bock SA, Muñoz-Furlong A, Sampson HA. Further fatalities caused by anaphylactic reactions to food, 2001–2006. J Allergy Clin Immunol 2007;119(4):1016–8. [PubMed: 17306354]

19. Sampson HA, Mendelson LM, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. N Engl J Med 1992;327:380–384. [PubMed: 1294076]

20. Yunginger JW, Sweeney KG, Sturner WQ. Fatal food-induced anaphylaxis. JAMA 1988;260:1450–1452. [PubMed: 3404604]

21. Jones, et al. Manuscript under submission JACI. 2009

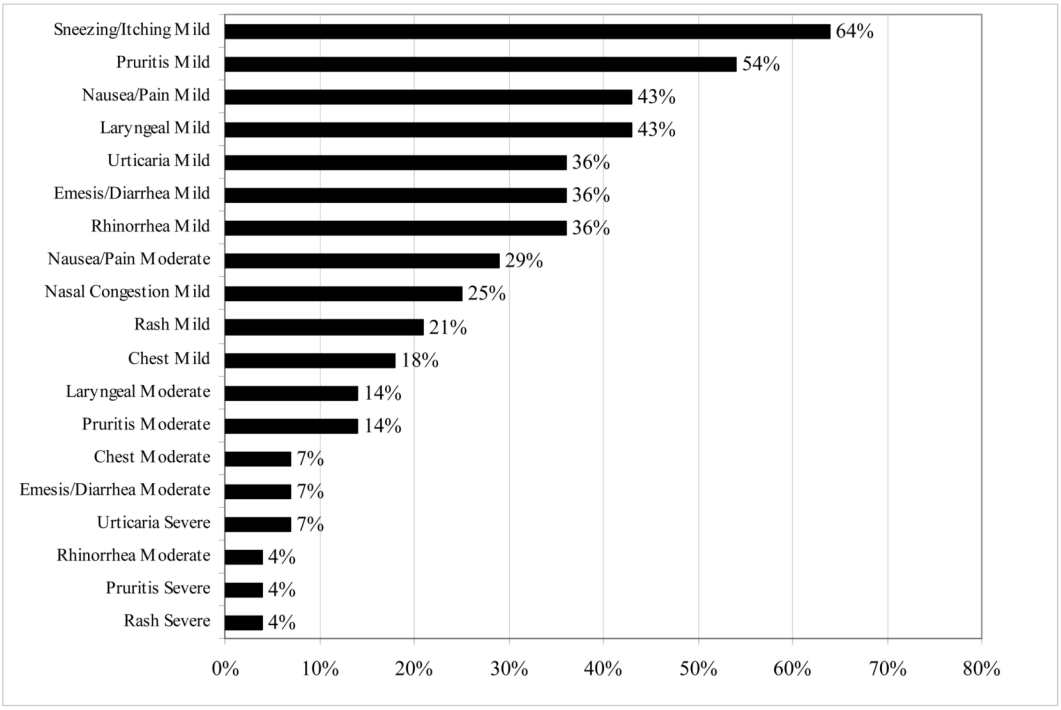

Figure 1.
Estimated Risk of Specific Symptoms during the Initial Escalation Day. Symptoms were recorded during the initial escalation day in four categories: upper respiratory, skin, abdominal, and chest.

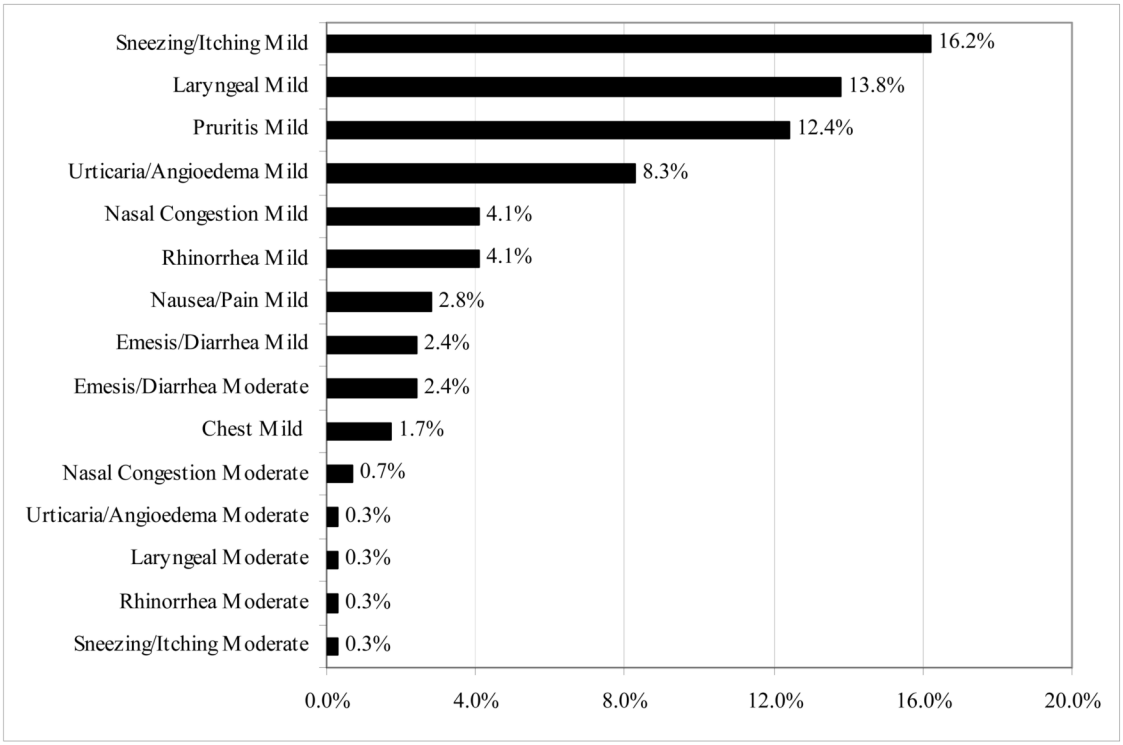

Figure 2.
Estimated Risk of Specific Symptoms During the Build-up Phase. Symptoms were recorded during the buildup phase in four categories: upper respiratory, skin, abdominal, and chest.

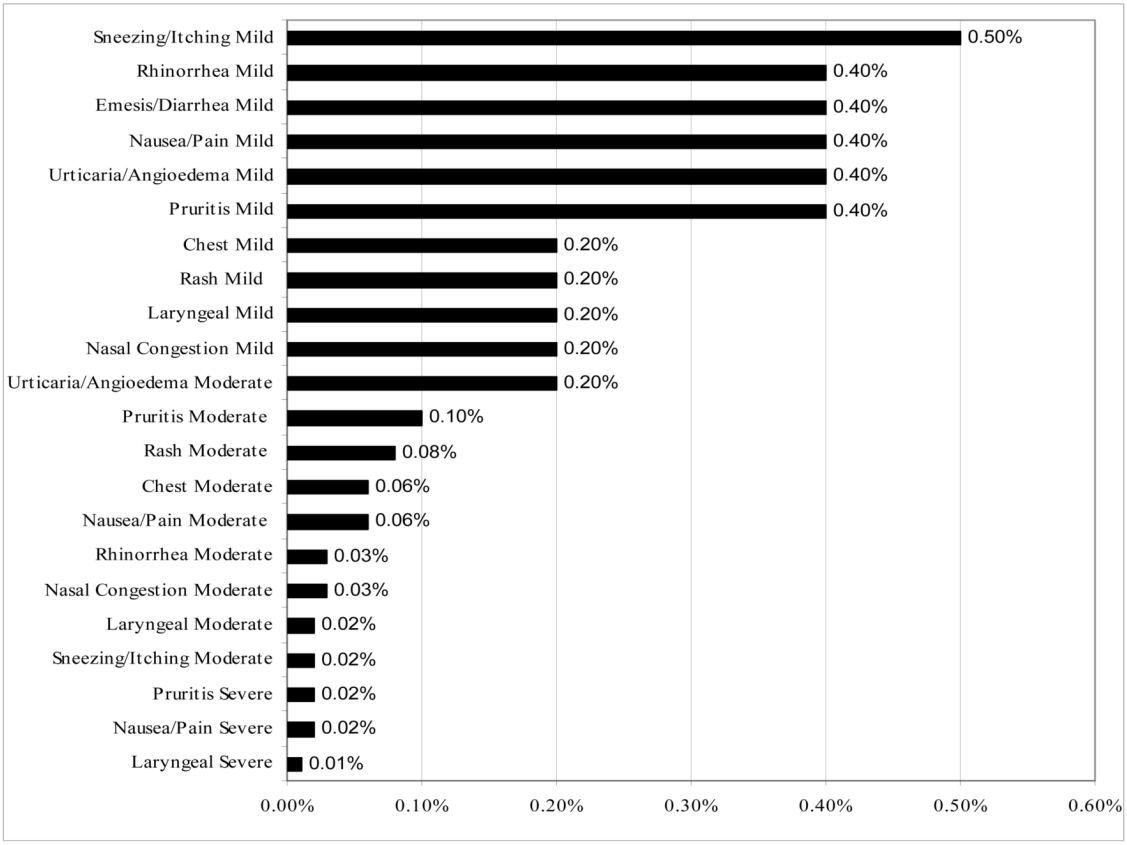

Figure 3.
Estimated Risk of Specific Symptoms During the Home Dosing Phase. Symptoms were recorded during the home dosing phase in four categories: upper respiratory, skin, abdominal, and chest.

Table I

Risk of Symptom Occurrence with 95% Confidence Intervals during the Initial Escalation Day, the Build-up Phase and the Home Dosing Phase

	Initial Escalation Day	Build-up Phase	Home Dosing
Any Symptom	93% (77%, 99%)	46% (37%, 56%)	3.5% (2.3%, 5.1%)
Upper Respiratory	79% (59%, 92%)	29% (20%, 41%)	1.2% (0.6%, 2.5%)
Skin	61% (41%, 79%)	24% (17%, 32%)	1.1% (0.7%, 1.8%)
Abdominal	68% (48%, 84%)	5.5% (3.2%, 9.2%)	0.9% (0.6%, 1.4%)
Chest	18% (6%, 37%)	1.7% (0.6%, 5.1%)	0.3% (0.1%, 0.4%)

Table II

Frequency of Treatment during the Initial Escalation Day, Build-up Phase and Home Dosing Phase of Peanut Oral Immunotherapy

Treatment	Percent of Initial Escalation Days	Percent of Build- up Doses	Percent of Home Doses
Any	71% (20/28)	1.7% (5/301))	0.7% (67/10,184)
Diphenhydramine Alone	50% (14/28)	1% (3/301)	0.4% (45/10,184)
Albuterol Alone	0%	0%	0.04% (4/10,184)
Diphenhydramine + Albuterol	7% (2/28)	0.7% (2/301)	0.2% (18/10,184)
Diphenhydramine + Epinephrine	11% (3/28)	0%	0%
Diphenhydramine + Albuterol +Epinephrine	4% (1/28)	0%	0.02% (2/10,184)