

Presentation of atopic disease in a large cohort of pediatric liver transplant recipients

Shroff P, Mehta RS, Chinen J, Karpen SJ, Davis CM. Presentation of atopic disease in a large cohort of pediatric liver transplant recipients.

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Abstract: Atopic disease occurs in solid organ transplant recipients with an increasingly recognized frequency. The time course for the development of these atopic diseases in liver transplantation has not been described. The objective was to characterize the atopic manifestations of children receiving chronic immunosuppression after orthotopic liver transplantation (OLT). Chart review and follow-up questionnaire were utilized for 176 OLT pediatric recipients at a single institution for manifestations of allergic disease. Atopic disease was present in 25 (14.2%) patients. Median age at transplant was 16 months with a median follow-up of 63 months. Food allergy and non-food related atopic symptoms presented at a median of 11.5 (IQR, 6–28) and 19 (IQR, 5–41) months post-transplantation, respectively. The median age at transplant of the non-atopic children was 72 months, higher than patients with atopy ($p < 0.001$). Food allergy and atopic skin disease symptoms were present in 40% and 56% of cases, respectively. Asthma, allergic rhinitis, or both were found in 66% of cases. The onset of symptoms of food allergy and eczema (median, 12 months post-transplantation) preceded symptoms of allergic rhinitis and asthma. (median of 27 and 30 months post-transplantation, respectively). Atopy occurs in ~14% of pediatric liver transplant recipients, with manifestations including food allergy, eczema, allergic rhinitis, and asthma.

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Immune dysregulation following solid organ transplantation has been associated with allergic disease (1). In select organ recipients, sensitization to allergens may be as high as 24% with 10% manifesting clinically relevant allergic disease (1). Specifically, there has been a suggestion of increased prevalence of food allergy in patients having received solid organ transplants of liver, heart, and small bowel (2). Much of the literature surrounding the allergic manifestations in post-transplant recipients presents in distinct populations, particularly liver transplant recipients and young children (3, 4).

Atopy is defined as the familial or personal tendency to develop IgE sensitization in response to environmental triggers (5, 6). This atopy is

critical to the development of food allergy, eczema, allergic rhinitis, and asthma (5, 6). The “atopic march” describes the temporal pattern of the diagnosis of eczema, allergic rhinitis, and asthma as a progression of disease which is influenced by genetic and environmental factors. This concept is supported by several cross-sectional and longitudinal studies, but the role of food allergy has not been clearly established (5–11). The progression of the atopic march has not been described in a liver transplantation cohort.

CNIs also appear to play a role in the development of atopy, although these agents are the primary means of reducing the incidence of organ rejection. CNIs have profound Th1 CD4+ helper cell immunosuppressive effects by repressing IL-2 production. This repression happens in the nucleus through blocking the translocation of NFAT. A shift to a Th2 CD4+ immune response has been proposed as a cause

Abbreviations: CIU, chronic idiopathic urticaria; CNIs, calcineurin inhibitors; GI, gastrointestinal; NFAT, nuclear factor of activated T cells; TCH, Texas Children’s Hospital.

of an allergic diathesis (12). Cyclosporine and tacrolimus are the two mainstay CNIs used currently in solid organ transplantation. Tacrolimus is up to 100-fold more potent than cyclosporine and has a greater potency of immune suppression to prevent rejection and is therefore a preferred CNI (13).

Not surprisingly, tacrolimus alone has been associated with allergic diseases in several transplant populations (1). Initially, 22% of 49 heart transplant recipients that received tacrolimus developed allergic disease with more than 50% of those being symptomatic (14). The use of tacrolimus in non-transplant conditions has been associated with elevated IgE (15). Furthermore, tacrolimus-based immunosuppression in pediatric liver transplant is associated with peripheral eosinophilia in up to 50% of patients and possibly eosinophilic gastroenteritis, which is associated with food allergy (16–18). Patients with IgE-mediated atopy on tacrolimus have demonstrated improvement with cyclosporine (19).

This study aimed to understand the difference of age in post-transplant liver recipients on the development of allergic diseases, including food allergy, eczema, allergic rhinitis, and asthma. The primary objective was to characterize specific food allergy as related to other atopic disease in liver organ transplantation patients receiving CNI in a single institution.

Methods

This study was approved by the Baylor College of Medicine and TCH Institutional Review Boards. This was a retrospective cohort study of patients from the TCH Liver Center.

Data collection

Chart review of liver transplant patients followed at TCH from January 1, 1995 to September 1, 2010 was performed.

Patients were included for review if the following criteria were met: Documented atopic condition based on post-transplant history (food allergy, atopic skin disease, asthma, allergic rhinitis, eosinophilic gastroenteritis, anaphylaxis, angioedema, or chronic diarrhea triggered by food ingestion) or worsening of disease after transplantation if atopic disease was present prior to transplantation. Atopic skin disease included atopic dermatitis or eczema, urticaria, and contact dermatitis where confirmed.

The following information was collected: demographic (current age/gender), age at transplant, indication and origin of transplant, follow-up time period, immunosuppressive regimen, symptoms of atopy including food allergy, atopic diagnoses, types of reactions and treatment (if documented), foods or triggers provoking allergy, specific IgE testing (if available), and history of atopy.

A telephone follow-up with questionnaire was conducted for the screened patients with atopy. This questionnaire

addressed specific atopic symptoms, foods causing exacerbation of atopic conditions, previous treatment, response to treatments, and previous testing. Specific food reactions included anaphylaxis, angioedema, eczema, GI intolerance (vomiting, diarrhea, difficulty swallowing) after ingestion of food, and urticaria. Data analysis was performed by chi-square, Kruskal–Wallis and Fisher's exact tests.

Results

Clinical features

The number of children having undergone solid organ liver transplant available for review was 176. All patients underwent orthotopic liver transplantation (Table 1). The majority of patients were transplanted for cholestatic liver disease, namely biliary atresia. Of these, atopy was recorded in 25 (14.2%). Median age at transplant was 16 months, and the follow-up period exceeded five yr (63 months). Median age of documentation of atopic symptoms was 19 months, with specific food allergy symptoms occurring earlier (11.5 months). All patients received CNIs, the majority of which were maintained on tacrolimus. Two patients who were initially treated with cyclosporine were switched to tacrolimus. Atopic symptoms began in these two patients after they were treated with

Table 1. Characteristics of 25/176 (14.2%) liver transplant recipients with atopy

Median age at transplant (months)	16 (3–127; IQR, 7–30) Mean, 26.6
Median follow-up period (months)	Median 63 (17–127; IQR, 42–110) Mean, 79.0
Type of transplant	Orthotopic liver transplant (100%)
Indication for transplant	Cholestatic liver disease (17/25 = 68%) Metabolic liver disease (6/25 = 24%)*
Sex (M:F)	12:13
Median time to first food allergy symptoms (months post-transplant)	11.5 (4–135; IQR, 6–28) Mean, 27.1
Median time to first symptoms of allergy/atopy (months post-transplant)	19 (1–135; IQR, 5–41) Mean, 29.5
Median peripheral eosinophilia (absolute)	561.2 (98.8–1672; IQR, 285–834.4) Mean, 623.4
Chronic immunosuppression with CNIs†	100%
Food allergy, % (n)	40 (10/25)
Other atopic disease (allergic skin disease, seasonal allergic rhinitis, asthma), % (n)	96 (24/25)
Atopic disease but no food allergy, % (n)	60 (15/25)

*Other (one patient was transplanted for cystic fibrosis and one patient for infantile hemangioendothelioma).

†All but two patients (cyclosporine) initially received tacrolimus.

Table 2. Manifestations of atopy in liver transplant recipient cohort

Atopic disease	Percentage (n)	Median age of presentation (months)
Food allergy	40 (10)	11.5
Eczema	56 (14)	12.0
Allergic rhinitis	64 (16)	27
Asthma	44 (11)	30
Other allergy*	36 (9)	NA

*Other atopy: hives without food allergy (4), drug allergy (1), ABPA (1), and allergic contact dermatitis (3).

tacrolimus for 1–3 months. Five patients were identified with symptoms of atopy prior to transplant. Two of these were excluded from analysis as they had no further development of present or new atopic symptoms. The median age at transplant of the non-atopic transplanted children in the cohort was 72 months, significantly higher than the patients with atopy (16 months; $p < 0.001$).

Atopic manifestations

Food allergy was present in 10 subjects (5.7% of the studied population). Atopic manifestations were not limited to food allergy, as food allergy was less frequent than allergic rhinitis, eczema, and asthma (see Table 2). The median of the onset of symptoms for food allergy, eczema, allergic rhinitis, and asthma was 11.5, 12, 27, and 30 months post-transplantation, respectively. The differences in the median ages for each atopic disease were not statistically significant ($p = 0.39$). The percentage of self-reported and test-proven food allergy was 5.7% and 3.9%, respectively. Furthermore, significant overlap existed among major atopic disorders (Fig. 1). Comparison of correlation of food allergy suggested a correlation of food allergy with eczema

Table 3. Comparison of food allergy with non-food allergy groups

	Food allergy % (n)	Non-food allergy % (n)	p-value
Atopic OLT patients	40 (10)	60 (15)	N/A
Allergic rhinitis	60 (6)	67 (10)	0.530
Asthma	30 (3)	53 (8)	0.231
Eczema	80 (8)	40 (6)	0.058*

*p-value determined by Fisher's exact test suggests correlation of eczema with food allergy but not with other atopy.

($p = 0.058$), but not with any other atopic disease ($p > 0.05$) (see Table 3). Egg, peanut, and milk were most common food allergens implicated as causative agents of food allergy.

Discussion

This study found reported food allergy symptoms in ~6% of children after liver transplantation with confirmatory specific IgE testing in ~4% (8/176). This is similar to frequencies reported in 2010 Food Allergy guidelines, although slightly elevated compared with those who received confirmatory testing in this study (20). These patients appear to have an older age of transplantation (median, 16 months) and later onset of symptoms of atopy (median, 19 months; food allergy of 15.5 months) than a large previously reported cohort (2) in which the age of transplant was recorded at 8.7 months with suspected first onset of symptoms of atopy at 6.0 months post transplant (2). This cohort appears to be starkly different by frequency of food allergy (6% vs. 22%), age ($p = 0.012$), and onset of symptoms ($p = 0.021$). This may suggest that later time to transplant may delay the time of onset of food allergy or altogether minimize increased risk of food allergy or atopy (4). This conclusion is supported by the observation that the median age at transplant of those who did not develop atopy in this cohort was 72 months. The contrast of allergy frequency in our cohort with previous reports might imply that delaying to transplant where clinically appropriate may protect against atopy and promote tolerance.

The correlation of food allergy with eczema found in this study is consistent with a prevalence of eczema in 35–70% of patients with food allergy (20). The median time of the appearance of symptoms of food allergy preceded allergic rhinitis and asthma, suggesting a role for the “atopic march” in these patients post-transplantation. This is consistent with recent data of children with cow's milk allergy diagnosed at seven months who were more likely to have

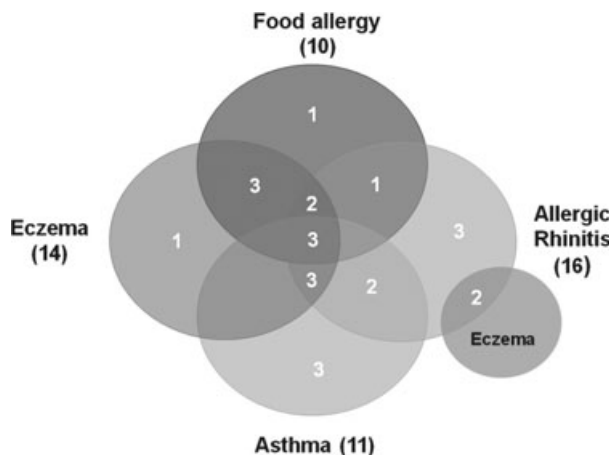


Fig. 1. Spectrum of atopic disease in liver transplant recipient cohort.

evidence of asthma at age 8 than those without food allergy or those with non-IgE-mediated cow's milk allergy (21, 22). Other cross-sectional data confirm the association between food allergy and asthma and allergic rhinitis (23) and a higher risk of developing eczema, allergic rhinitis, and asthma in food allergic infants (24).

Food allergy after transplantation was hypothesized to occur early on by transfer of donor hypersensitivity IgE or specific lymphocytes in several case reports; however, this finding has also been demonstrated in recipients in whom the donor had no evidence of food allergy (25, 26). Transplant-acquired food allergy, when the donor has not had food allergy, has been associated most strongly with tacrolimus predominantly in cases of transplanted livers but the heart as well (27–30). Milk protein sensitivity has been suggested in cases of tacrolimus-associated eosinophilic gastroenteritis and villous atrophy in select pediatric liver transplantation cases (31, 32). Studies implicating cyclosporine as a cause of food allergy following transplantation are less clear although cases have been reported (27). In a transplant setting, some of the earliest cases of non-rejection eosinophilic gastroenteritis were suggested with cyclosporine, although larger studies did not find an association with eosinophilia in pediatric liver transplant recipients (17, 33). Interestingly, cyclosporine has an important and efficacious role in treating many allergic diseases, including CIU in which at least a partial IgE-mediated mechanism has been suggested. In one large retrospective analysis of pediatric liver transplant recipients where 10% of patients developed angioedema as a result of tacrolimus, those who switched to cyclosporine were able to tolerate the food that initially caused their symptoms (34). In fact, the two patients in this cohort treated initially with cyclosporine had no evidence of atopic disease while on this therapy. However, given the overall improved efficacy and side effect profile of tacrolimus compared to cyclosporine, this is currently considered the principal CNI used in pediatric liver transplant recipients. How management plans, along with additional immunosuppressives, or tacrolimus dosages, weave into the development of atopic diseases remains to be determined.

There are some case reports of adult patients developing food allergy after solid organ transplantation (35–40). Five cases of food allergy have been reported in adults receiving liver transplantation with all cases involving development of peanut and/or tree nut [walnut (35) and cashew (37)] allergies. Two cases of peanut allergy were reported after lung transplantation

(39, 40). Interestingly, in two of the cases where a heart transplant was performed from the same peanut allergic donor of a liver transplant to a separate individual, the recipient of the liver developed peanut allergy while the heart transplant recipient did not develop allergic disease (38, 39). It is likely that the immunologic composition of the liver is important in the development of allergic disease in liver transplant recipients in comparison with other solid organ recipients.

Overall, this retrospective study found atopy present in ~14% of the pediatric liver transplant recipients cared for in one large center. This rate is similar to the rate of atopic dermatitis (~17%) (41) in general pediatric data, suggesting that this population should be evaluated for the development of allergic disease. The reported rate of atopic disease in children varies from ~6% to 64% in childhood populations (42), and the prevalence of allergic rhinitis and asthma in this liver transplant cohort falls within this range. The development of atopic disease may be a progression of the atopic march, characterized by increased IgE sensitization.

Of particular interest in this study is the review of a pediatric population having undergone transplantation. Records and documentation by the transplant service did not permit a similar evaluation of adult liver transplant recipients, so a matched comparison at our center was not possible. Some limitations exist with regard to our study, including the retrospective design which is limited by recall bias. As a result, prospective data regarding lack of atopy cannot be matched to the data reported in this study. In addition, no data regarding eosinophilic esophagitis could be obtained on these patients. However, the size of this center's cohort and the age at which transplantation and symptoms occurred provide different demographic characteristics than those previously reported and suggest the possibility of later onset of atopy being related to older age of transplantation (4). Atopic disease must be considered by clinicians in pediatric liver transplant patients, and food allergy is important, but not the only manifestation.

Author contributions

P. Shroff carried out data collection, data analysis/interpretation, drafting of the article, critical revision of the article, and approval of the article; R. S. Mehta collected the data; J. Chinen and S.J. Karpen carried out the concept/design, data analysis/interpretation, critical revision of the

article, approval of the article; and C.M. Davis was involved in concept/design, data analysis/interpretation, statistics, drafting of the article, critical revision of the article, approval of the article.

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References

1. DEHLINK E, GRUBER S, EIWEGER T, et al. Immunosuppressive therapy does not prevent the occurrence of immunoglobulin E-mediated allergies in children and adolescents with organ transplants. *Pediatrics* 2006; 118: e764–e770.
2. FRISCHMEYER-GUERRERIO PA, WISNIEWSKI J, WOOD RA, NOWAK-WEGRZYN A. Manifestations and long-term outcome of food allergy in children after solid organ transplantation. *J Allergy Clin Immunol* 2008; 122: 1031–1033.
3. LEVY Y, DAVIDOVITS M, CLEPER R, SHAPIRO R. New-onset post-transplantation food allergy in children – is it attributable only to the immunosuppressive protocol? *Pediatr Transplant* 2009; 13: 63–69.
4. OZBEK OY, OZCAY F, AVCI Z, HABERAL A, HABERAL M. Food allergy after liver transplantation in children: A prospective study. *Pediatr Allergy Immunol* 2009; 20: 741–747.
5. ZHENG T, YU J, OH MH, ZHU Z. The atopic march: Progression from atopic dermatitis to allergic rhinitis and asthma. *Allergy Asthma Immunol Res* 2011; 3: 67–73.
6. ASHER MI, MONTEFORT S, BJÖRKSTÉN B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006; 368: 733–743.
7. MARTINEZ FD, WRIGHT AL, TAUSSIG LM, HOLBERG CJ, HALONEN M, MORGAN WJ. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med* 1995; 332: 133–138.
8. KULIG M, BERGMANN R, KLETTKE U, WAHN V, TACKE U, WAHN U. Natural course of sensitization to food and inhalant allergens during the first 6 years of life. *J Allergy Clin Immunol* 1999; 103: 1173–1179.
9. GUSTAFSSON D, SJÖBERG O, FOUCARD T. Development of allergies and asthma in infants and young children with atopic dermatitis – A prospective follow-up to 7 years of age. *Allergy* 2000; 55: 240–245.
10. VAN DER HULST AE, KLIP H, BRAND PL. Risk of developing asthma in young children with atopic eczema: A systematic review. *J Allergy Clin Immunol* 2007; 120: 565–569.
11. KAPOOR R, MENON C, HOFFSTAD O, BILKER W, LECLERC P, MARGOLIS DJ. The prevalence of atopic triad in children with physician-confirmed atopic dermatitis. *J Am Acad Dermatol* 2008; 58: 68–73.
12. NOWAK-WEGRZYN AH, SICHERER SH, CONOVER-WALKER MK, WOOD RA. Food allergy after pediatric organ transplantation with tacrolimus immunosuppression. *J Allergy Clin Immunol* 2001; 108: 146–147.
13. MARTIN-MUNOZ MF, LETRAN CAMACHO A, DE LUCAS LAGUNA R. Topical treatment tacrolimus and food allergy. *Br J Dermatol* 2005; 153: 842–843.
14. ASANTE-KORANG A, BOYLE GJ, WEBBER SA, MILLER SA, FRICKER FJ. Experience of FK506 immune suppression in pediatric heart transplantation: A study of long-term adverse effects. *J Heart Lung Transplant* 1996; 15: 415–422.
15. KAWAMURA N, FURUTA H, TAME A, et al. Extremely high serum level of IgE during immunosuppressive therapy: Paradoxical effect of cyclosporine A and tacrolimus. *Int Arch Allergy Immunol* 1997; 112: 422–424.
16. GRANOT E, YAKOBOVICH E, BARDENSTEIN R. Tacrolimus immunosuppression – An association with asymptomatic eosinophilia and elevated total and specific IgE levels. *Pediatr Transplant* 2006; 10: 690–693.
17. ROMERO R, ABRAMOWSKY CR, PILLEN T, SMALLWOOD GA, HEFFRON TG. Peripheral eosinophilia and eosinophilic gastroenteritis after pediatric liver transplantation. *Pediatr Transplant* 2003; 7: 484–488.
18. ERWIN EA, JAMES HR, GUTEKUNST HM, RUSSO JM, KELLEHER KJ, PLATTS-MILLS TA. Serum IgE measurement and detection of food allergy in pediatric patients with eosinophilic esophagitis. *Ann Allergy Asthma Immunol* 2010; 104: 496–502.
19. MAAROF G, KRZYSIEK R, DECLINE JL, COHEN J, HABES D, JACQUEMIN E. Management of post-liver transplant-associated IgE-mediated food allergy in children. *J Allergy Clin Immunol* 2011; 127: 1296–1298.
20. 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(6 Suppl): S1–S58.
21. MALMBERG LP, SAARINEN KM, PELKONEN AS, SAVILAHTI E, MÄKELÄ MJ. Cow's milk allergy as a predictor of bronchial hyperresponsiveness and airway inflammation at school age. *Clin Exp Allergy* 2010; 40: 1491–1497.
22. ALLEN KJ, DHARMAGE SC. The role of food allergy in the atopic march. *Clin Exp Allergy* 2010; 40: 1439–1441.
23. PÉNARD-MORAND C, RAHERISON C, KOPFERSCHMITT C, et al. Prevalence of food allergy and its relationship to asthma and allergic rhinitis in schoolchildren. *Allergy* 2005; 60: 1165–1171.
24. KUSUNOKI T, MORIMOTO T, NISHIKOMORI R, HEIKE T, FUJII T, NAKAHATA T. Allergic status of schoolchildren with food allergy to eggs, milk or wheat in infancy. *Pediatr Allergy Immunol* 2009; 20: 642–647.
25. LEGENDRE C, CAILLAT-ZUCMAN S, SAMUEL D, et al. Transfer of symptomatic peanut allergy to the recipient of a combined liver-and-kidney transplant. *N Engl J Med* 1997; 337: 822–824.
26. CASTELLS M, BOYCE J. Transfer of peanut allergy by a liver allograft. *N Engl J Med* 1998; 338: 202–203.
27. ARIKAN C, KILIC M, TOKAT Y, AYDOĞDU S. Allergic disease after pediatric liver transplantation with systemic tacrolimus and cyclosporine as therapy. *Transpl Proc* 2003; 35: 3039–3041.
28. LACAILE F, LAURENT J, BOUSQUET J. Life-threatening food allergy in a child treated with FK506. *J Pediatr Gastroenterol Nutr* 1997; 25: 228–229.
29. GABE SM, BJARNASON I, TOLOU-GHAMARI Z, et al. The effect of tacrolimus (FK506) on intestinal barrier function and cellular energy production in humans. *Gastroenterology* 1998; 115: 67–74.
30. OZDEMIR O, ARREY-MENSAH A, SORESENSEN RU. Development of multiple food allergies in children taking tacrolimus after heart and liver transplantation. *Pediatr Transplant* 2006; 10: 380–383.
31. SAEED SA, INTEGLIA MJ, PLESKOW RG, et al. Tacrolimus-associated eosinophilic gastroenterocolitis in pediatric liver transplant recipients: Role of potential food allergies in pathogenesis. *Pediatr Transplant* 2006; 10: 730–735.
32. BLANCHARD SS, GERREK M, CZINN S, et al. Food protein sensitivity with partial villous atrophy after pediatric liver transplantation with tacrolimus immunosuppression. *Pediatr Transplant* 2006; 10: 529–532.
33. DHAWAN A, SEEMAYER TA, PINSINSKI C, GROSS TG, SHAW BW JR, MACK DR. Posttransplant eosinophilic gastroenteritis in children. *Liver Transpl Surg* 1997; 3: 591–593.

34. LYKAVIERIS P, FRAUGER E, HABES D, BERNARD O, DEBRAY D. Angioedema in pediatric liver transplant recipients under tacrolimus immunosuppression. *Transplantation* 2003; 75: 152–155.
35. VAGEFI PA, BLAZICK E, HAMILOS D, ADES A, COSIMI AB, HERTL M. Transference of food allergy after adult liver transplantation. *Transplantation* 2009; 87: 1426.
36. DEWACHTER P, VÉZINET C, NICAISE-ROLAND P, et al. Passive transient transfer of peanut allergy by liver transplantation. *Am J Transplant* 2011; 11: 1531–1534.
37. PHAN TG, STRASSER SI, KOOREY D, et al. Passive transfer of nut allergy after liver transplantation. *Arch Intern Med* 2003; 163: 237–239.
38. TROTTER JF, EVERSON GT, BOCK SA, WACHS M, BAK T, KAM I. Transference of peanut allergy through liver transplantation. *Liver Transpl* 2001; 7: 1088–1089.
39. SCHULLER A, BARNIG C, MATAU C, et al. Transfer of peanut allergy following lung transplantation: A case report. *Transplant Proc* 2011; 43: 4032–4035.
40. KHALID I, ZORATTI E, STAGNER L, BETENSLEY AD, NEMEH H, ALLENSPACH L. Transfer of peanut allergy from the donor to a lung transplant recipient. *J Heart Lung Transplant* 2008; 27: 1162–1164.
41. BOGUNIEWICZ M. Atopic dermatitis: Beyond the itch that rashes. *Immunol Allergy Clin North Am*. 2005; 25: 333–351, vii.
42. RONCHETTI R, JESENAK M, RENNEROVA Z, BARRETO M, RONCHETTI F, VILLA MP. Relationship between atopic asthma and the population prevalence rates for asthma or atopy in children: Atopic and nonatopic asthma in epidemiology. *Allergy Asthma Proc* 2009; 30: 55–63.