Food Allergy—Lessons From Asia

Bee Wah Lee,*,** Lynette Pei-Chi Shek,*,** Irvin Francis A. Gerez,** Shu E Soh,* and Hugo P. van Bever*,**

Objective: This is a review on published data available on food allergy in East Asia and a discussion on the insights that it offers.

Methods: PubMed searches were made for terms food allergy and anaphylaxis, in combination with Asia.

Results: There is a paucity of population-based prevalence studies on food allergy in Asia. Certain unique food allergens, such as buckwheat, chestnuts, chickpeas, bird’s nest, and royal jelly, which are consumed extensively by certain Asian populations have resulted in clinical food allergy of little importance in other populations. Crustacean shellfish is of importance in this region relative to other common food allergens. The high consumption of these foods and possibly coupled with cross-reactive tropomyosins from dominant inhalant dust mite and cockroach allergens in this region may explain this phenomenon. In contrast, the prevalence of peanut allergy is relatively low in this region. The reasons for this difference are not apparent. However, this may be a reflection of the general reduced propensity in this region to allergic diseases as seen with asthma.

Conclusions: Further research on food allergy in Asia is warranted because it offers unique opportunities to further our understanding on the influence of population and environment.

Key Words: food allergy, Asia, shellfish allergy, peanut allergy, buckwheat, bird’s nest, chickpeas, royal jelly

(WAO Journal 2008;129–133)

The allergy epidemic has resulted in a global rise in prevalence of allergic diseases such as asthma, allergic rhinitis, and eczema in the recent decades. This increase is highest in affluent communities adopting a westernized lifestyle, with the western populations documenting the highest prevalence.1 Similar trends have been observed for food allergy, particularly peanut allergy,2 but these are less well documented globally. The reason, at least in part, may be related to the inherent difficulties ascertaining a population’s prevalence of true food allergy. Self-reported food allergy notoriously overestimates the true prevalence, probably because of subjective bias. Nonetheless, such observations between populations are useful starting points for understanding differences in the patterns of food allergy and possibly their underlying mechanisms. The objective of this article is to review the data available on food allergy (immunoglobulin E [IgE] mediated) in East Asia and discuss the insights that it might offer.

METHODS

PubMed searches were made for food allergy and Asia. In addition, a search was also made for food allergy and the respective East Asian countries, China, Japan, Korea, India, Indonesia, Malaysia, Singapore, Philippines, Thailand, and Vietnam. Similarly, these regions were searched in combination with the term anaphylaxis.

POPULATION STUDIES

There are few population-based studies on food allergy in Asia. The epidemiology of food allergy in Asia has been reviewed recently.3 Population prevalence studies based on self-reported questionnaires targeted at children younger than 12 years ranged from 4% in Singapore4 and rural China5 to as high as 12% in Seoul, Korea,6 and Japan.7 This wide range in prevalence mirrors those reported in a recent meta-analysis obtained from surveys on populations elsewhere (3%–35%),8 and it was concluded that these differences were related to survey methodologies rather than a true difference. The authors recommended that standardized methods, including specific IgE measurements with standardized allergen extracts, and if possible challenge testing, are necessary to obtain more accurate estimates of prevalence. It therefore seems that comparing the true prevalence of food allergies across populations will still require considerable research effort.

FOOD ALLERGENS UNIQUE TO ASIA

It has been observed that certain specific foods consumed mainly in the Asian region have resulted in allergies that are unique to their respective populations. Allergy to edible bird’s nest from swiftlets has been described in the Chinese population in Singapore,9,10 Malaysia,11 and Hong Kong (G. W. K. Wong, MD, oral communication, 2006). It is the most common cause of anaphylaxis in Singapore children.12 This food is a popular Chinese delicacy believed to have health benefits. A salivary protein with homology to the ovomucoid inhibitor has been identified as the major allergen.13,14 Similarly, royal jelly, another food supplement very popular among the Chinese, has also been reported to trigger asthma and anaphylaxis in Hong Kong15 and ethnic Chinese in Australia.16

Buckwheat causing anaphylaxis has been observed in Japan, Korea, and China.17,18 In a national survey in Japan, it has been ranked fourth as a cause of immediate hypersensitivity.19

Received for publication November 7, 2007; accepted April 10, 2008.
From the *Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore; and **Children’s Medical Institute, National University Hospital, Singapore.
Reprints: Bee Wah Lee, Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, 5 Lowe Kent Ridge Rd, Singapore 119074. E-mail: pacleebw@nus.edu.sg
Supported by the National Medical Research Council Singapore (grant R-178-000-131-112).
Copyright © 2008 by World Allergy Organization

WAO Journal • July 2008

129
FISH ALLERGENS

The fish from tropical waters consumed in Asia are quite different from temperate fish. Consumption practices are also quite different. Fish is a weaning food among many populations in Asia. This contrasts with the western diet, where fish is regarded as a highly allergenic food. Fish allergy affects up to 3% of children in Scandinavian populations, and until very recently, the American Academy of Pediatrics had recommended that fish be avoided until the age of 3 years. There is an impression that fish allergy in this part of the world is less common than the western world, but this has not been substantiated by a systematic study. Of the temperate fish, the major allergen of cod, Gad c 1, belonging to the protein family of parvalbumins, has been the most extensively studied. Evaluation of other temperate fish has shown that parvalbumin constitutes the major cross-reactive fish allergen of these fish. The evaluation of 4 species of tropical fish (threadfin, pomfret, Indian anchovy, and tengiri) commonly consumed in Singapore and often used as weaning foods in infants has also shown that parvalbumin is the major allergen of these tropical fish. These parvalbumins are cross-reactive with Gad c 1, which was also clinically evident because most fish-allergic children in this study had clinical reactions to more than 1 fish. Only one of the 10 children evaluated was monosensitized and could tolerate consuming other fish without a clinical reaction. Hence, the allergenicity of tropical fish is comparable with cod. The reason(s) that fish allergy is not highly prevalent in tropical Asia despite high consumption and exposure in early life is not obvious, although it is tempting to postulate that paradoxically, early large exposure rather than conventional strict avoidance has induced immune tolerance.

PEANUT ALLERGY

Peanut allergy is recognized as an important food allergy because it is known to cause severe life-threatening reactions, is long-lasting, and is increasingly common in some populations. The prevalence of peanut allergy was 0.3%, or about a third of those who had peanut allergy were recorded. Similarly, a study from Hong Kong reported crustacean shellfish as the most common food trigger in 89% of cases, but there was no mention of peanut allergy because it is known to cause severe life-threatening anaphylaxis from Thailand (adults and children), where no severe peanut allergy resulting in anaphylaxis was very uncommon, with no documented cases in children and only 2 adult patients (2.7%). These data are corroborated by a study on anaphylaxis from Thailand (adults and children), where no cases of peanut allergy were recorded. Similarly, a study from Hong Kong reported crustacean shellfish as the most common food trigger in 89% of cases, but there was no mention of peanut allergy. The data from Asia contrast markedly with those from other temperate regions.

TABLE 1. Prevalence of Peanut Allergy in Various Population-Based Surveys

| Country       | Prevalence%, 95% Confidence Interval | No. Surveyed, Response Rate | Age of Population, yrs | Study Year | Reference                          |
|---------------|--------------------------------------|-----------------------------|------------------------|------------|------------------------------------|
| United States | 0.4*                                 | 2998                        | <18                    | 1997       | Sicherer et al30                   |
|               | 0.8*                                 | 2948                        | <18                    | 2002       | Sicherer et al31                   |
| United Kingdom| 1.2**                                | 1218/1456                   | 4                      | 1993–1994  | Tariq et al32                      |
|               | 1.5**                                | 1273/2878                   | 3–4                    | 1997–1999  | Grundy et al33                     |
|               | 1.8** (1.1–2.7)                      | 957                         | 4–5                    | 2003–2005  | Hourihane et al34                  |
| Canada        | 1.5** (1.2–1.9)                      | 4339/7768                   | 7                      | 2000–2005  | Kagan et al35                      |
| France        | 1                                    | 33,110/44,000               | <0–60                  | 1997       | Kanny 200136                       |
| Singapore     | 0.3, 0.014**                         | 6765/8072                   | 14–15                  | 2005–2006  | Gerez et al30                      |

*Based on nationwide telephone survey with standardized questionnaire.
**Taking into account SPTs, for Singapore study only done in a subcohort.
the United States,39 United Kingdom,40 and Australia,41 where hospitalization and fatalities caused by peanut allergy are well documented. This apparent low prevalence rate of peanut allergy in Asian populations is not likely caused by lack of exposure. Sensitization to peanuts is not uncommon among the atopic population here. In a hospital-based study of children older than 3 years attending a hospital-based allergy clinic in Singapore, sensitization to peanuts rates 27.3% and is ranked third most common after egg and shellfish,42 and in a separate study, the rate was 12% in those younger than 3 years.43 Relatively high rates of sensitization have also been recorded among allergic Hong Kong (31% in atopic eczema)44 and Taiwanese children (36% in atopic eczema).45

The data presented here strongly support the notion that the low prevalence of peanut allergy in Asian populations compared with that in North America and the United Kingdom is true and not just conjecture. In view of the relatively high peanut sensitization among the atopic subjects in these populations, this low prevalence of allergy in Asia is more likely caused by immune tolerance rather than the lack of exposure. Resolving the reasons for this difference between populations would provide important insights into possible public health measures that could prevent further escalation of the peanut allergy epidemic of the West. Speculation on environmental and genetic differences has been discussed in detail in a recent review article by Sicherer and Sampson.2 The reason regarding the method of cooking and the allergenicity of roasted peanuts compared with boiled peanuts46 is often mentioned reason, although roasted peanut such as peanut butter is also widely available in Asia. Environmental rather than genetic factors are likely to play an important role in these differences in the prevalence of peanut allergy between geographic regions because the data from the United States suggest that peanut allergy prevalences of all ethnicities are similar.31

CRUSTACEAN SHELLFISH ALLERGY

In contrast to the low prevalence of peanut allergy in Asia, crustacean shellfish seems to be an important cause of food allergy. In terms of severity, hospital-based studies on anaphylaxis show that crustacean shellfish are one of the most important food triggers in adults and children in Singapore42,10,12 and Thailand,37 and adults in Hong Kong.38 Interestingly, this phenomenon seems to be reversed in western populations, with less severe crustacean shellfish allergy in comparison with peanut allergy. Only a few or no cases of crustacean shellfish—induced anaphylaxis were reported in hospital-based surveys in children in the United Kingdom,47 Italy,48 and children and adults in Australia.49 Instead, peanut-triggered anaphylaxis predominates in these populations. In addition, registries recording fatalities caused by anaphylaxis in the United Kingdom and United States40 also show that although peanuts and tree nut are important triggers, there was only 1 case triggered by crustacean seafood in the United Kingdom registry. It therefore seems that there is a reversal of importance between these food allergens—the importance of peanut in the West and crustacean shellfish in Asia.

Based on population surveys, the prevalence of crustacean shellfish allergy in the United States for all ages is 2%, and 0.1% for the 0- to 5-year and 0.8% for the 6- to 17-year age group.50 Slightly lower prevalence rates were found in Denmark. This study involved a birth cohort and their family members, which showed the absence of shellfish allergy in children (up to 21 years) and a prevalence of 0.3% in adults.51 Like peanut allergy, there have been no published studies on population surveys in any Asian population. However, a survey conducted in Singapore schoolchildren aged 14 to 15 years presented as an abstract showed that the positive responses for convincing shellfish allergy are comparatively high (3.95% or about 5 times that of US children),52 although most had mild symptoms (L.P.C.S., unpublished data, 2007).

Like fish, crustacean shellfish is a major component of the East Asian diet. However, unlike fish allergy, this increased exposure may explain the high prevalence of shellfish allergy in this region. Sensitization to shrimp has been observed in our atopic population from an early age. The sensitization rate was reported to be 3.6% in atopic children younger than 1 year, and 10.6% in those between 1 and 3 years.43 Because exposure to fish and peanuts has not resulted in a high prevalence of allergy to these food allergens in Asia, it is tempting to speculate on an alternative hypothesis for the high prevalence of shellfish allergy.

The high prevalence of inhalant dust mite and cockroach allergies in tropical and subtropical Asia may contribute to cross-reacting allergens through the panallergen tropomyosin.53 This protein is a major allergen in shrimp and shellfish allergy. If confirmed, this would be akin to the pollen-food syndrome observed in the temperate climates,54 and the cross-reacting tropomyosin allergens may be responsible for the mild form of shellfish allergy, very much like the described oral allergy syndrome. This hypothesis is supported by the correlation of sensitization to shrimp and cockroach allergens in Singapore children,42 as well as population studies on unexposed Jews who observed Kosher dietary rules, which showed that sensitization to shrimps was related to cross-reacting tropomyosin in house-dust mites.55 Furthermore, in a study of 17 house dust mite allergic (HDM) patients receiving immunotherapy, 3 developed IgE against shrimp, and 2 of these having IgE against tropomyosin had oral allergy symptoms after ingesting shrimp.56

CONCLUDING REMARKS

The data on food allergy in Asia have provided insight into the relative importance of certain food allergens in this region. Foods such as buckwheat, chestnut, chickpea, bird’s nest, and royal jelly, which are consumed extensively within certain Asian populations, have resulted in clinical food allergy that is of little or no importance in other populations. Crustacean shellfish also seems to be of importance relative to other common food allergens. Whether high consumption of shellfish coupled with cross-reactive tropomyosins from inhalant dust mite and cockroach allergens (inhalant food/oral allergy syndrome) is responsible for these observations deserves further evaluation. In contrast, peanut allergy and anaphylaxis triggered by peanuts is relatively low in this region. This may reflect the relatively generally reduced propensity to allergic diseases in these populations, as is seen with asthma.57 However, unlike the rising trends in asthma in the urbanized
Asian communities, similar increases in peanut allergy are not yet apparent. Although the reasons for this are not obvious, the possibility that the threshold of developing inhalant allergies is lower than that for food allergies may be a consideration, as there is efficient induction of immune tolerance via the gastrointestinal tract.  

REFERENCES

1. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISACA. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Lancet. 1998;351:1225–1232.
2. Sicherer SH, Sampson HA. Peanut allergy: emerging concepts and approaches for an apparent epidemic. J Allergy Clin Immunol. 2007;120:491–503; [quiz 504–495].
3. Shek LP, Lee BW. Food allergy in Asia. Curr Opin Allergy Clin Immunol. 2006;6:197–201.
4. Lee BW, Chew FT, Goh DYT. Changing prevalence of childhood allergic diseases in Singapore. Paper presented at: the 5th West-Pacific Allergy Symposium & 7th Korea-Japan Joint Allergy Symposium, Seoul, Korea, 11–14 June, 1997.
5. Wang Z. An allergy prevalence survey in population of 10,144 people. Zhonghua Liu Xing Bing Xue Za Zhi. 1990;11:100–102.
6. Lee SI, Shin MH, Lee HB, Lee JS, Son BK, Koh YY, et al. Prevalences of symptoms of asthma and other allergic diseases in Korean children: a nationwide questionnaire survey. J Korean Med Sci. 2001;16:155–164.
7. Ikura Y, Imai Y, Imai T, Akasawa A, Fujita K, Hoshiyama K, et al. Frequency of immediate-type food allergy in children in Japan. Int Arch Allergy Immunol. 1999;118:251–252.
8. Rona RJ, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E, et al. The prevalence of food allergy: a meta-analysis. J Allergy Clin Immunol. 2007;120:638–646.
9. Goh DL, Chew FT, Chua KY, Chay OM, Lee BW. Edible “bird’s nest”-induced anaphylaxis: an under-recognized entity? J Pediatr. 2000;137:277–279.
10. Thong BY, Cheng YK, Leong KP, Tang CY, Chng HH. Immediate food hypersensitivity among adults attending a clinical immunology/allergy centre in Singapore. Singapore Med J. 2007;48:236–240.
11. de Bruyne J, Lee B. Anaphylaxis in the Asia Pacific. Allergy Clin Immunol Int. J World Allergy Org. 2004;16:137–141.
12. Goh DL, Lau NY, Chew FT, Shek LP, Lee BW. Pattern of food-induced anaphylaxis in children of an Asian community. Allergy. 1999;54:84–86.
13. Goh DL, Chua KY, Chew FT, Liang RC, Seow TK, Ou KL, et al. Immunological characterization of edible bird’s nest allergens. J Allergy Clin Immunol. 2001;107:1082–1087.
14. Ou K, Seow TK, Liang RC, Lee BW, Goh DL, Chua KY, Chung MC. Identification of a serine protease inhibitor homologous in bird’s nest by an integrated proteomics approach. Electrophoresis. 2001;22:3589–3595.
15. Leung R, Lam CW, Ho A, Chan JK, Choy D, Lai CK. Allergic sensitisation to common environmental allergens in adult asthmatics in Hong Kong. Hong Kong Med J. 1997;3:211–217.
16. Leung R, Ho A, Chan J, Choy D, Lai CK. Royal jelly consumption and hyperactivity in the community. Clin Exp Allergy. 1997;27:333–336.
17. Wielandger G, Norback D, Wang Z, Zhang Z, Mi Y, Lin R. Buckwheat allergy and reports on asthma and atopic disorders in Tuyuqian City, Northern China. Asian Pac J Allergy Immunol. 2000;18:147–152.
18. Lee SY, Lee KS, Hong CH, Lee KY. Three cases of childhood nocturnal asthma due to buckwheat allergy. Allergy. 2001;56:763–766.
19. Sohn MH, Lee SY, Kim KE. Prediction of buckwheat allergy using specific IgE concentrations in children. Allergy. 2003;58:1308–1310.
20. Imai T, Ikura Y. The national survey of immediate type of food allergy. Aruyuji. 2003;52:1006–1013.
21. Niphadkar PV, Patil SP, Bapat MM. Chickpea-induced anaphylaxis. Allergy. 1997;52:115–116.
22. Patil SP, Niphadkar PV, Bapat MM. Chickpea: a major food allergen in the Indian subcontinent and its clinical and immunochoolchemical correlation. Ann Allergy Asthma Immunol. 2001;87:140–145.
23. Lee SK, Yoon SH, Kim SH, Choi JH, Park HS. Chestnut as a food allergen: identification of major allergens. J Korean Med Sci. 2005;20:573–578.
24. Kajosaari M. Food allergy in Finnish children aged 1 to 6 years. Acta Paediatr Scand. 1982;7:815–819.
25. Greer FR, Sicherer SH, Burks AW. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. Pediatrics. 2008;121:183–191.
26. Elsayed S, Bennich H. The primary structure of allergen M from cod. Scand J Immunol. 1975;4:203–208.
27. Poulsen HK, Hansen TK, Norgaard A, Vestergaard H, Stahl Skov P, Bindsløv-Jensen C. Allergens from fish and egg. Allergy. 2001;56(suppl 67):39–42.
28. Hansen TK, Bindsløv-Jensen C, Skov PS, Poulsen HK. Codfish allergy in adults: IgE cross-reactivity among fish species. Ann Allergy Asthma Immunol. 1997;78:187–194.
29. Lim D, Noh K, Yi F, Chua KY, Goh DL, Shek LP, et al. Parvalbumin—the major tropical fish allergen. Pediatr Allergy Immunol. 2007. In press.
30. Gerez I, Soh J, Soh S, Morales E, Ng PZ, et al. Prevalence of peanut and tree-nut allergy in Singapore teenagers—estimates from a questionnaire survey, allergy testing and challenges. Paper presented at: World Allergy Congress, 2007; Bangkok, Thailand.
31. Sicherer SH, 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;112:1203–1207.
32. Tariq SM, Stevens M, Matthews S, Ridout S, Twiselton R, Hide DW. Cohort study of peanut and tree nut sensitisation by age of 4 years. BMJ. 1996;313:514–517.
33. Grundy J, Matthews S, Bateman B, Dean T, Arshad SH. Rising prevalence of allergy to peanut in children: data from 2 sequential cohorts. J Allergy Clin Immunol. 2002;110:784–789.
34. Hourihane JO, Alken R, Briggs R, Gudgeon LA, Grimshaw KE, DunnGalvin A, Roberts SR. The impact of government advice to pregnant mothers regarding peanut avoidance on the prevalence of peanut allergy in United Kingdom children at school entry. J Allergy Clin Immunol. 2007;119:1197–1202.
35. Kagan RS, Joseph L, Dufresne C, Gray-Donald K, Turnball E, Pierre YS, Clarke AE. Prevalence of peanut allergy in primary-school children in Montreal, Canada. J Allergy Clin Immunol. 2003;112:1223–1228.
36. Kanny G, Moneret-Vautrin DA, Flabbee J, Beauaudin E, Morisset M, Thevenin F. Population study of food allergy in France. J Allergy Clin Immunol. 2001;108:133–140.
37. Jirapongsananuruk O, Bunsawansong W, Piyaphananet N, Visitsunthorn N, Thongnarm T, Vichyanond P. Features of patients with anaphylaxis admitted to a university hospital. Ann Allergy Asthma Immunol. 2007;98:157–162.
38. Smit DV, Cameron PA, Raimer TH. Anaphylaxis presentations to an emergency department in Hong Kong: incidence and predictors of biphasic reactions. J Emerg Med. 2005;28:381–388.
39. Bock SA, Munoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. J Allergy Clin Immunol. 2001;107:191–193.
40. Pumphrey RS, Gowland MH. Further fatal allergic reactions to food in the United Kingdom, 1999–2006. J Allergy Clin Immunol. 2007;119:1018–1019.
41. Hill DJ, Hosking CS, Heine RG. Clinical spectrum of food allergy in children in Australia and South-East Asia: identification and targets for treatment. Ann Med. 1999;31:272–281.
42. Chiang WC, Kidon M, Liew WK, Goh A, Tang JP, Chay OM. The changing face of food hypersensitivity in an Asian community. Clin Exp Allergy. 2007;37:1055–1061.
43. Khoo J, Shek L, Khor ES, Wang DY, Lee BW. Pattern of sensitization to common environmental allergens amongst atopic Singapore children in the first 3 years of life. Asian Pac J Allergy Immunol. 2001;19:225–229.
44. Hon KL, Leung TF, Lam MC, Wong KY, Chow CM, Ko WS, et al. Eczema exacerbation and food atopy beyond infancy: how should we advise Chinese parents about dietary history, eczema severity, and skin prick testing? Adv Ther. 2007;24:223–230.
45. Lo YC, Yang YH, Chiang BL. Food-specific immunoglobulin E among children with atopic dermatitis: a retrospective study. *J Microbiol Immunol Infect*. 2005;38:338–342.

46. Beyer K, Morrow E, Li XM, Bardina L, Bannon GA, Burks AW, Sampson HA. Effects of cooking methods on peanut allergenicity. *J Allergy Clin Immunol*. 2001;107:1077–1081.

47. Colver AF, Nevantaus H, Macdougall CE, Cant AJ. Severe food-allergic reactions in children across the UK and Ireland, 1998-2000. *Acta Paediatr*. 2005;94:689–695.

48. Novembre E, Cianferoni A, Bernardini R, Muggnaini A, Caffarelli C, Cavagni G, et al. Anaphylaxis in children: clinical and allergologic features. *Pediatrics*. 1998;101:E8.

49. Braganza SC, Acworth JP, McKinnon DR, Peake JE, Brown AF. Paediatric emergency department anaphylaxis: different patterns from adults. *Arch Dis Child*. 2006;91:159–163.

50. Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of seafood allergy in the United States determined by a random telephone survey. *J Allergy Clin Immunol*. 2004;114:159–165.

51. Osterballe M, Hansen TK, Mortz CG, Host A, Bindslev-Jensen C. The prevalence of food hypersensitivity in an unselected population of children and adults. *Pediatr Allergy Immunol*. 2005;16:567–573.

52. Shek L, Soh JY, Ng PZ, Morales EA, Ma S, Lee BW. Prevalence of peanut and shellfish allergy in Singapore children estimated from a questionnaire survey [Abstract]. *J Allergy Clin Immunol*. 2007;119:S118.

53. Crespo IF, Rodriguez J. Food allergy in adulthood. *Allergy*. 2003;58:98–113.

54. Egger M, Mutschlechner S, Wopfner N, Gadermaier G, Briza P, Ferreira F. Pollen-food syndromes associated with weed pollinosis: an update from the molecular point of view. *Allergy*. 2006;61:461–476.

55. Fernandes J, Reshef A, Patton L, Ayuso R, Reese G, Lehrer SB. Immunoglobulin E antibody reactivity to the major shrimp allergen, tropomyosin, in unexposed Orthodox Jews. *Clin Exp Allergy*. 2003;33:956–961.

56. van Ree R, Antonicelli L, Akkerdaas JH, Garritani MS, Aalberse RC, Bonifazi F. Possible induction of food allergy during mite immunotherapy. *Allergy*. 1996;51:108–113.

57. Asher MI, Montefort S, Bjorksten 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.

58. Husby S, Mestecky J, Moldoveanu Z, Holland S, Elson CO. Oral tolerance in humans. T cell but not B cell tolerance after antigen feeding. *J Immunol*. 1994;152:4663–4670.

59. Sicherer SH, Munoz-Furlong A, Burks AW, Sampson HA. Prevalence of peanut and tree nut allergy in the US determined by a random digit dial telephone survey. *J Allergy Clin Immunol*. 1999;103:559–562.