Asia Pac Allergy. 2020 Jan;10(1):e6
https://doi.org/10.5415/apallergy.2020.10.e6
pISSN 2233-8276·eISSN 2233-8268

Asia Pacific allergy

Educational & Teaching Material

Case Report

A 5-year retrospective review of children with peanut allergy in the largest paediatric hospital in Singapore

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Received: Nov 29, 2019
Accepted: Jan 23, 2020

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ABSTRACT

Background: The prevalence of peanut allergy (PA) among children has increased significantly over the past decade. Even though the prevalence of PA in Singapore is considered low, peanut is the top trigger for food-induced anaphylaxis in Singaporean children.
Objective: To describe the demographic characteristics and clinical features of children with PA.
Methods: This is a 5-year retrospective review of children diagnosed with PA based on clinical history coupled with a positive skin prick test to peanut or positive oral food challenge results.
Results: There were 269 patients (53.9% males) with a clinical diagnosis of PA. The median age at first allergic presentation for the PA group was 24 months old, with interquartile range of 13–39 months. The most common form of peanut introduced was roasted peanut. The rate of peanut anaphylaxis was 7.1%. Concomitant tree nut sensitization was found in 32.3% of this cohort, predominantly to cashew nut. Majority of them have a personal history of atopy – 75.8% with eczema, 63.6% with allergic rhinitis, and 19.7% with asthma.
Conclusion: This is the first large review of peanut-allergic children in Singapore. Prospective population-based studies are needed to establish the true prevalence and risk factors associated with the development of this potentially life-threatening condition.

Keywords: Peanut allergy; Children; Singapore; Asia

INTRODUCTION

The prevalence of peanut allergy (PA) among children has risen significantly over the past decade [1, 2]. However, in Asia, the prevalence of PA has remained relatively low in comparison to Western countries—0.22% in Korea, 0.1%–0.3% in Singapore, 0.43% in the Philippines versus 1.50% in the UK, 1.40% in the US, and 3% in Australia [3-7]. The reason for this difference is unknown but hypotheses include early exposure to peanut and differences in the methods of peanut preparation [3, 8]. In Asia, peanuts are traditionally consumed as boiled, braised, fried or roasted whole nuts. Peanuts may be crushed into powder, made into sauce or spread and incorporated as a culinary ingredient in many dishes. The Asian cooking method of boiling and frying peanuts results in lower allergenicity compared with the Western method of roasting [9].

Conflict of Interest
The authors have no financial conflicts of interest.

Author Contributions
Conceptualization: May Ping Lee, Kok Wee Chong. Data curation: May Ping Lee, Kok Wee Chong. Formal analysis: Seyed Ehsan Saffari. Funding acquisition: May Ping Lee. Methodology: May Ping Lee, Kok Wee Chong. Project administration: May Ping Lee, Kok Wee Chong. Visualization: May Ping Lee, Kok Wee Chong. Writing - original draft: May Ping Lee. Writing - review & editing: Kok Wee Chong, Wenyin Loh, Si Hui Goh, Anne Goh, Wen Chin Chiang.

To date, published data on the demographic and clinical profile of children with PA in Singapore is scarce. Even though the prevalence of PA in Singapore had been reported to be low [4], there is evidence of an increasing trend [10] and a change in the pattern of food anaphylaxis. Within 2 decades, peanut anaphylaxis had risen from a rare entity to the commonest trigger of food anaphylaxis in Singapore [11]. Hence, this retrospective study aims to describe the demographic and clinical characteristics of PA in Singaporean children. Peanut skin prick test (SPT) wheal size and peanut-specific IgE of this cohort have been published separately [12].

MATERIALS AND METHODS

Children ≤ 16 years old who had a positive SPT to peanut between 2012 to 2016 were identified from our departmental electronic database at KK Women's and Children's Hospital, the largest tertiary paediatric hospital in Singapore. Clinical documents were reviewed. Data on demographic characteristics, age at initial presentation, clinical reactions to peanut, personal or family history of atopy and associations with tree nuts (almond, brazil nut, cashew nut, hazelnut, pecan, walnut, and pistachio) were collected.

Diagnosis of PA was made based on a history of clinical reaction within 2 hours of peanut exposure (either by ingestion or contact) with evidence of peanut sensitization (either positive SPT and/or positive IgE), or a positive oral food challenge (OFC) to peanut. A group of children whom had positive SPT but tolerant to regular peanut ingestion, was identified for comparison (peanut tolerant [PT] group).

SPT was performed using Stallergenes Greer Laboratories (Lenoir, NC, USA) commercial extracts and Duotip-Test II (Lincoln Diagnostics Inc., Decatur, IL, USA) disposable skin applicator. Positive SPT was defined as mean wheal diameter of ≥3 mm in comparison to the negative control. Positive peanut-specific IgE (ImmunoCAP, Thermo Fisher, Uppsala, Sweden) was defined as ≥0.35 kU/L.

OFC using peanut butter or roasted peanuts was performed at the Allergy Outpatient Specialist Clinic in our unit following the recommendations set out by the PRACTALL Consensus Report [13]. The diagnosis of anaphylaxis was in accordance to the definition by the World Allergy Organization [14].

Data were extracted for statistical analysis using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Baseline demographic and clinical features were compared between PA and PT groups using 2-sided 2 independent sample *t* test and chi-square/Fisher exact test for continuous and categorical variables, respectively. The association between demographics, atopic history and the measures of SPT wheal size and food-specific IgE concentrations with the risk of PA were tested using univariate and multivariable logistic regression analysis.

The study is approved by SingHealth Centralised Institutional Review Board (reference number: 2016/2346).

RESULTS

A total of 269 patients were diagnosed as PA and 59 patients as PT. Their demographics is shown in **Table 1**. The ethnic distribution of the PA group was Chinese (68.4%), Malay (12.6%), Indian (4.1%), and other races (14.9%) with Caucasians making up 4.5%. Rhinitis was a more common comorbidity in the PA group compared to the PT group (odds ratio [OR], 2.52; 95% confidence interval [CI], 1.42–4.47) (**Table 2**).

The median age of peanut introduction and first allergic presentation for the PA group were both 24 months old, with interquartile range (IQR) of 15–41.8 months and 13–39 months respectively. The age of peanut introduction for the PT group could not be analysed as they

Table 1. Demographic and clinical characteristics of peanut allergy and peanut tolerant groups

Variable	Peanut allergy (PA) (n = 269)	Peanut tolerant (PT) (n = 59)	*p* value†
Demographics			
Male sex	145 (53.9)*	37 (62.7)	0.218
Age (yr)	3.9 ± 3.2	3.7 ± 3.3	0.633
Race, Chinese	184 (68.4)	39 (66.1)	0.732
History of atopy			
Rhinitis‖	171 (63.6)	24 (40.7)	<0.01
Atopic dermatitis‖	204 (75.8)	47 (79.7)	0.530
Asthma¶	53 (19.7)	9 (15.3)	0.429
Drug allergy‖	14 (5.2)	4 (6.8)	0.630
Urticaria/angioedema‖	27 (10.1)	9 (15.3)	0.250
Tree nut sensitisation	87 (32.3)	15 (25.4)	0.299
Other food allergies**	149 (55.4)	26 (44.1)	0.114
Investigation results			
SPT wheal size (mm)	10.2 ± 5.5	5.2 ± 3.3	<0.01
IgE to peanut (kU/L)	22.8 ± 30.7	7.6 ± 19.3	<0.05

Values are presented as number (%) or mean ± standard deviation.
SPT, skin prick test.
†Comparing the 2 groups (PA and PT); 2-sided 2 independent sample *t* test for continuous variables and chi-square/Fisher exact test for categorical variables. ‖Parental report of patient's history of rhinitis, atopic dermatitis, drug allergy and urticaria/angioedema. ¶Physician-diagnosed asthma. **Clinical diagnosis of food allergy based on clinical history and positive SPT/IgE.

Table 2. Univariate and multivariable analysis of demographics, atopic history, and investigation parameters with peanut allergy

Variable	Unadjusted OR (95% CI)*	*p* value	Adjusted OR (95% CI)†	*p* value
Demographics				
Male sex	0.70 (0.39–1.25)	0.228	0.68 (0.38–1.23)	0.200
Age (yr)	1.57 (0.89–2.78)	0.122	1.18 (0.64–2.18)	0.598
Race, Chinese	1.12 (0.62–2.03)	0.709	1.03 (0.56–1.88)	0.936
History of atopy				
Rhinitis‡	2.52 (1.42–4.47)	<0.01	2.39 (1.30–4.38)	<0.01
Atopic dermatitis‡	0.82 (0.41–1.63)	0.575	0.80 (0.40–1.62)	0.541
Asthma§	1.31 (0.61–2.81)	0.482	0.90 (0.40–2.02)	0.792
Drug allergy‡	0.70 (0.23–2.16)	0.534	0.45 (0.14–1.46)	0.182
Urticaria/angioedema‡	0.61 (0.27–1.36)	0.223	0.67 (0.29–1.53)	0.345
Tree nut sensitisation‖	1.38 (0.73–2.60)	0.324	1.33 (0.70–2.54)	0.378
Other food allergies‖	1.57 (0.89–2.76)	0.118	1.57 (0.87–2.84)	0.132
Investigation results				
SPT wheal size (mm)¶	4.68 (2.32–9.41)	<0.01	1.32 (1.20–1.45)	<0.01
IgE to peanut (kU/L)¶	1.96 (0.63–6.11)	0.244	1.09 (1.02–1.17)	<0.05

OR, odds ratio; CI, confidence interval; SPT, skin prick test.
*Odds ratio (OR) using univariate logistic regression analysis. †Odds ratio using multivariable logistic regression analysis; adjusted for age and rhinitis. ‡Parental report of patient's history of rhinitis, atopic dermatitis, drug allergy, and urticaria/angioedema. §Physician-diagnosed asthma. ‖Clinical diagnosis of food allergy based on clinical history and positive SPT/IgE. ¶Odds ratio is reported for the risk of SPT ≥ 3 mm, and serum IgE ≥ 0.35 kU/L.

https://doi.org/10.5415/apallergy.2020.10.e6

Table 3. Clinical manifestation of children with peanut allergy (n = 269)

Clinical manifestation	No. (%)
Mucocutaneous	233 (86.6)
Eye angioedema	70 (26.0)
Lip angioedema	42 (15.6)
Urticaria	84 (31.2)
Maculopapular rash	4 (1.5)
Rash: not specified	109 (40.5)
Respiratory	215 (80.0)
Sneezing	179 (66.5)
Runny nose	65 (24.2)
Cough	16 (5.9)
Stridor/voice hoarseness	4 (1.5)
Wheeze	20 (7.4)
Dyspnoea	20 (7.4)
Gastrointestinal	51 (18.9)
Vomiting	50 (18.6)
Abdominal pain	7 (2.6)
Diarrhoea	1 (0.4)
Cardiovascular	3 (1.1)
Drowsiness/lethargy	3 (1.1)
Anaphylaxis	19 (7.1)

were not routinely documented. In the PA group, the commonest form of peanut that was first introduced was roasted peanut such as peanut butter, peanut kernel, peanut snack, peanut sauce, or crushed peanut topping (80.3%). This was followed by boiled peanut such as peanut soup or porridge (6.3%). In 36 PA children (13.4%), the form of peanut that was introduced was not specified.

The onset of symptoms was within 1 hour of exposure in 93.3% of the PA group and the commonest clinical features were mucocutaneous signs (86.6%) (**Table 3**). The rate of peanut anaphylaxis in our study population was 7.1%. There was no reported mortality in these patients who develop anaphylaxis in this study.

Amongst the PA group, 32.3% were also sensitized to tree nuts; predominantly to cashew nut (17.1%), followed by almond (15.6%), hazelnut (15.6%), and walnut (14.1%). With regards to atopic tendencies, 75.8% had eczema, 63.6% had allergic rhinitis, and 19.7% had physician-diagnosed asthma. About half of the children (44.6%) with PA had other food allergies, of which 29% were allergic to egg, 13% to cow's milk and 2.6% to soy. Family history of atopy was present in 45% of PA children, including a family history of PA in 3.3%.

DISCUSSION

Singapore is a multiethnic country with a total population of 5.64 million, comprising of Chinese (74.1%), Malays (13.4%), Indians (9.2%), and Others (3.3%) [15]. In the PA cohort, there was a higher percentage patient of "other" ethnicity (14.9%) with the majority (57.5%) originating from the Philippines and Indonesia, whilst 42.5% of them were Eurasians or Caucasians. A population-based questionnaire survey by Shek et al. [16] reported a higher prevalence of PA in Singapore expatriate children (1.2%) versus local Singaporean children (0.47%–0.64%), albeit a relatively small number. At the same time, there is also evidence of increasing prevalence of food allergy in rapidly developing countries such as Thailand [17] and China [18]. Hence we postulate that a rising trend of PA in Singapore could be a result

of a true rising incidence or in part, contributed by a larger migrant population from high prevalence regions [15].

It is noteworthy that the median age at presentation of PA in our study was 24 months old compared to the median age of 12 to 14 months reported in Western countries [19, 20]. This is possibly due to delayed peanut introduction in our cohort whose mean age was 30.4 ± 22.4 months. A recent local study by Tham et al. [4] (GUSTO Cohort) demonstrated similar pattern of late introduction of peanut (beyond 1 year old) at a mean age of 19 ± 7.87 months. Delay in peanut introduction has been attributed to multiple reasons including fear of choking, concerns of possible PA, lack of knowledge on the types of peanut-containing food suitable for young children or the perception that peanut butter is too sweet for toddlers. This is of particular concern as delayed introduction of peanut in a subset of atopic patients with moderate to severe atopic dermatitis has been shown to contribute to the rising rates of PA [21, 22]. Furthermore, it is noted that the most common form of peanut introduced in this cohort was roasted peanut compared to the more traditional practice of giving boiled peanut in soups/porridge as one of the first weaning foods [11]. Both the shift in age of peanut introduction as well as the increased consumption of roasted peanuts highlighted the "Westernisation" of diet and lifestyle in parts of Asia such as Singapore, which may have an impact on the incidence of PA.

The most common clinical feature of peanut-allergic reaction in our cohort was mucocutaneous signs (86.6%), similar to that in the Western countries (58.2%–89%) [19, 23]. However, the rate of anaphylaxis in our study is significantly lower (7.1%) in comparison to the West (US – 23.7% to 34.9%) [19, 24]. Even though, the rate of peanut anaphylaxis was low in our cohort, a study by Liew et al. [11] showed that there is a recent change in the pattern of food anaphylaxis in Singapore. Peanut, which used to be a nonexistent food trigger 2 decades ago, is currently the top trigger for food-induced anaphylaxis in Singaporean children (19%). This is similar to the findings reported in Korea, the US, the UK, and Australia [3, 11, 25-27].

Many studies have shown the association between tree nut allergy and PA [28, 29]. A study in the US by Anagnostou [28] showed high cross-sensitization of 80% to tree nut in peanut-allergic children, mainly to cashew nut and walnut (50% and 49%, respectively). Another US study conducted by Maloney et al. [30] also showed a high proportion of peanut-allergic children (86%) with cross-sensitization to tree nut, and 34% with cross-allergy, mainly to walnut and almond. A retrospective cohort study in the UK showed 23.4% of children with PA had cross-reactivity to tree nuts and 7.4% of them had concomitant tree nut allergy, predominantly to almond [31]. Several studies have shown an *in vitro* cross-reactivity between peanut and tree nut IgE binding epitopes which could explain the association between peanut and tree nut allergy, but whether this translates to clinical cross-reactivity remains controversial [24, 32, 33]. In our study cohort, 32.3% of children with PA were also sensitized to tree nuts, predominantly to cashew nut (17.1%). While an OFC would have been necessary to confirm allergy, most subjects in this cohort did not proceed to OFC. The rate of tree nut cross-sensitization in our cohort of children with PA appears to be much lower than in the US. This may be related to the low prevalence of tree nut allergy in Singapore (0.3%), in comparison to the West (1.1% US, 1.14%–1.7% Canada, 0.5%–1.3% Europe, and 2.3% Australia) [16, 34].

In vitro cross-reactivity between peanut, soy and other legumes was previously reported [35]. However, recent studies have demonstrated that this is unlikely to translate into clinical cross-reactivity and thus, it is not recommended for children with PA to routinely eliminate legumes

https://doi.org/10.5415/apallergy.2020.10.e6

in their diet [36, 37]. A study in the US by Bock and Atkins [37] showed that the prevalence of *in vivo* cross-reactivity between peanut and soy allergy in children was low (3%). Similar rate was seen in our study cohort, where 2.6% of children with PA had concomitant soy allergy.

Eczema is a strong predictor for the development of food allergy [38]. The presence of Filaggrin gene mutation in patients with eczema leads to epithelial barrier dysfunction, which ultimately results in allergen sensitization and the development of PA [39, 40]. Overall, the prevalence of eczema in Singaporean children was high (>20%) and similar rates were reported in other Asian countries [4, 41-44]. In our study, 75.8% of our patients with PA had underlying eczema. The absence of statistically significant association between eczema and PA in our cohort (adjusted OR, 0.80; 95% CI, 0.40–1.62; $p = 0.541$) is likely due to the fact that the comparison was made with atopic children.

Instead, we found an association between allergic rhinitis and PA (adjusted OR, 2.39; 95% CI, 1.30-4.38; $p = <0.01$). Wang et al. [45] reported a high prevalence rate of allergic rhinitis in Singaporean children with 25.5% in 6- to 7-year-olds and 42.1% in 12- to 15-year-olds. Although the overall high prevalence of allergic rhinitis in our population may have confounded the finding of an association between allergic rhinitis and PA, the coexistence of primary food allergies and allergic rhinitis in children has been described in a few cohort studies [46-48]. In a prospective longitudinal birth cohort study in Sweden, it concluded that 40% of children with food allergies in infancy had allergic rhinitis by the time they were 8 years old [46]. In a retrospective cohort study by Hill et al. [48], 35% of paediatric patients with established food allergies went on to develop allergic rhinitis (adjusted OR, 2.72; 95% CI, 2.45–3.03).

This is the first largest study in this region to evaluate the demographic pattern and clinical manifestations of PA in children. Our study findings suggest that changing dietary practices with regards to peanut introduction may have an impact on the prevalence of PA in Singapore and this warrants further investigation with prospective population-based studies. Limitations of this study include its retrospective design, and the limited use of OFCs to confirm PA in the majority of patients.

In conclusion, PA is an important cause of food-induced anaphylaxis and possibly underestimated health burden in developing countries including Singapore. In particular, the paucity of data from South East Asian countries necessitates prospective population-based studies to establish the true prevalence and the risk factors associated with the development of PA in the region.

ACKNOWLEDGEMENTS

We thank our allergy specialist nurses, Ms. Lim Hwee Hoon and Ms. Ding Xiao Mei, and our SPT laboratory technicians for their consistent hard work and excellent patient care.

REFERENCES

1. Sicherer SH, Sampson HA. Peanut allergy: emerging concepts and approaches for an apparent epidemic. J Allergy Clin Immunol 2007;120:491-503.
PUBMED | CROSSREF

2. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR Jr, Beck LA, Block J, Byrd-Bredbenner C, Chan ES, Eichenfield LF, Fleischer DM, Fuchs GJ 3rd, Furuta GT, Greenhawt MJ, Gupta RS, Habich M, Jones SM, Keaton K, Muraro A, Plaut M, Rosenwasser LJ, Rotrosen D, Sampson HA, Schneider LC, Sicherer SH, Sidbury R, Spergel J, Stukus DR, Venter C, Boyce JA. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. J Allergy Clin Immunol 2017;139:29-44.
PUBMED | CROSSREF
3. Kim M, Lee JY, Jeon HY, Yang HK, Lee KJ, Han Y, Kim YH, Kim J, Ahn K. Prevalence of Immediate-Type Food Allergy in Korean Schoolchildren in 2015: A Nationwide, Population-based Study. Allergy Asthma Immunol Res 2017;9:410-6.
PUBMED | CROSSREF
4. Tham EH, Lee BW, Chan YH, Loo EXL, Toh JY, Goh A, Teoh OH, Yap F, Tan KH, Godfrey KM, Chong MFF, Van Bever HPS, Chong YS, Shek LP. Low food allergy prevalence despite delayed introduction of allergenic foods-data from the GUSTO Cohort. J Allergy Clin Immunol Pract 2018;6:466-75.e1.
PUBMED | CROSSREF
5. Koplin JJ, Wake M, Dharmage SC, Matheson M, Tang ML, Gurrin LC, Dwyer T, Peters RL, Prescott S, Ponsonby AL, Lowe AJ, Allen KJ; HealthNuts study group. Cohort Profile: The HealthNuts Study: Population prevalence and environmental/genetic predictors of food allergy. Int J Epidemiol 2015;44:1161-71.
PUBMED | CROSSREF
6. Venter C, Maslin K, Patil V, Kurukulaaratchy R, Grundy J, Glasbey G, Twiselton R, Dean T, Arshad SH. The prevalence, natural history and time trends of peanut allergy over the first 10 years of life in two cohorts born in the same geographical location 12 years apart. Pediatr Allergy Immunol 2016;27:804-11.
PUBMED | CROSSREF
7. Sicherer SH, Muñoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. J Allergy Clin Immunol 2010;125:1322-6.
PUBMED | CROSSREF
8. Lee AJ, Thalayasingam M, Lee BW. Food allergy in Asia: how does it compare? Asia Pac Allergy 2013;3:3-14.
PUBMED | CROSSREF
9. 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;107:1077-81.
PUBMED | CROSSREF
10. Chiang WC, Kidon MI, Liew WK, Goh A, Tang JP, Chay OM. The changing face of food hypersensitivity in an Asian community. Clin Exp Allergy 2007;37:1055-61.
PUBMED | CROSSREF
11. Liew WK, Chiang WC, Goh AE, Lim HH, Chay OM, Chang S, Tan JH, Shih E, Kidon M. Paediatric anaphylaxis in a Singaporean children cohort: changing food allergy triggers over time. Asia Pac Allergy 2013;3:29-34.
PUBMED | CROSSREF
12. Chong KW, Saffari SE, Chan N, Seah R, Tan CH, Goh SH, Goh A, Loh W. Predictive value of peanut skin prick test, specific IgE in peanut-sensitized children in Singapore. Asia Pac Allergy 2019;9:e21.
PUBMED | CROSSREF
13. Sampson HA, Gerth van Wijk R, Bindslev-Jensen C, Sicherer S, Teuber SS, Burks AW, Dubois AE, Beyer K, Eigenmann PA, Spergel JM, Werfel T, Chinchilli VM. Standardizing double-blind, placebo-controlled oral food challenges: American Academy of Allergy, Asthma & Immunology-European Academy of Allergy and Clinical Immunology PRACTALL consensus report. J Allergy Clin Immunol 2012;130:1260-74.
PUBMED | CROSSREF
14. Simons FE, Ardusso LR, Bilò MB, Cardona V, Ebisawa M, El-Gamal YM, Lieberman P, Lockey RF, Muraro A, Roberts G, Sanchez-Borges M, Sheikh A, Shek LP, Wallace DV, Worm M. International consensus on (ICON) anaphylaxis. World Allergy Organ J 2014;7:9.
PUBMED | CROSSREF
15. Singapore Department of Statistics. Singapore census of population 2010. Statistical release 1: demographic characteristics, education, language and religion. Singapore: Singapore Department of Statistics; 2011.
16. Shek LP, Cabrera-Morales EA, Soh SE, Gerez I, Ng PZ, Yi FC, Ma S, Lee BW. A population-based questionnaire survey on the prevalence of peanut, tree nut, and shellfish allergy in 2 Asian populations. J Allergy Clin Immunol 2010;126:324-31, 331.e1-7.
PUBMED | CROSSREF
17. Lao-araya M, Trakultivakorn M. Prevalence of food allergy among preschool children in northern Thailand. Pediatr Int 2012;54:238-43.
PUBMED | CROSSREF

18. Hu Y, Chen J, Li H. Comparison of food allergy prevalence among Chinese infants in Chongqing, 2009 versus 1999. Pediatr Int 2010;52:820-4.
PUBMED | CROSSREF

19. Leickly FE, Kloepfer KM, Slaven JE, Vitalpur G. Peanut allergy: an epidemiologic analysis of a large database. J Pediatr 2018;192:223-8.e1.
PUBMED | CROSSREF

20. Sicherer SH, Furlong TJ, Muñoz-Furlong A, Burks AW, Sampson HA. A voluntary registry for peanut and tree nut allergy: characteristics of the first 5149 registrants. J Allergy Clin Immunol 2001;108:128-32.
PUBMED | CROSSREF

21. Du Toit G, Katz Y, Sasieni P, Mesher D, Maleki SJ, Fisher HR, Fox AT, Turcanu V, Amir T, Zadik-Mnuhin G, Cohen A, Livne I, Lack G. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. J Allergy Clin Immunol 2008;122:984-91.
PUBMED | CROSSREF

22. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, Brough HA, Phippard D, Basting M, Feeney M, Turcanu V, Sever ML, Gomez Lorenzo M, Plaut M, Lack G; LEAP Study Team. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med 2015;372:803-13.
PUBMED | CROSSREF

23. Al-Muhsen S, Clarke AE, Kagan RS. Peanut allergy: an overview. CMAJ 2003;168:1279-85.
PUBMED

24. Yang L, Clements S, Joks R. A retrospective study of peanut and tree nut allergy: Sensitization and correlations with clinical manifestations. Allergy Rhinol (Providence) 2015;6:39-43.
PUBMED | CROSSREF

25. Cianferoni A, Muraro A. Food-induced anaphylaxis. Immunol Allergy Clin North Am 2012;32:165-95.
PUBMED | CROSSREF

26. de Silva IL, Mehr SS, Tey D, Tang ML. Paediatric anaphylaxis: a 5 year retrospective review. Allergy 2008;63:1071-6.
PUBMED | CROSSREF

27. Silva R, Gomes E, Cunha L, Falcão H. Anaphylaxis in children: a nine years retrospective study (2001-2009). Allergol Immunopathol (Madr) 2012;40:31-6.
PUBMED | CROSSREF

28. Anagnostou A. Insights into tree nut and sesame consumption from a cohort of 80 peanut-allergic children. Pediatr Allergy Immunol 2019;30:389-92.
PUBMED | CROSSREF

29. de Leon MP, Glaspole IN, Drew AC, Rolland JM, O'Hehir RE, Suphioglu C. Immunological analysis of allergenic cross-reactivity between peanut and tree nuts. Clin Exp Allergy 2003;33:1273-80.
PUBMED | CROSSREF

30. Maloney JM, Rudengren M, Ahlstedt S, Bock SA, Sampson HA. The use of serum-specific IgE measurements for the diagnosis of peanut, tree nut, and seed allergy. J Allergy Clin Immunol 2008;122:145-51.
PUBMED | CROSSREF

31. Ball H, Luyt D, Bravin K, Kirk K. Single nut or total nut avoidance in nut allergic children: outcome of nut challenges to guide exclusion diets. Pediatr Allergy Immunol 2011;22:808-12.
PUBMED | CROSSREF

32. de Leon MP, Drew AC, Glaspole IN, Suphioglu C, O'Hehir RE, Rolland JM. IgE cross-reactivity between the major peanut allergen Ara h 2 and tree nut allergens. Mol Immunol 2007;44:463-71.
PUBMED | CROSSREF

33. Barre A, Sordet C, Culerrier R, Rancé F, Didier A, Rougé P. Vicilin allergens of peanut and tree nuts (walnut, hazelnut and cashew nut) share structurally related IgE-binding epitopes. Mol Immunol 2008;45:1231-40.
PUBMED | CROSSREF

34. Chitta S, Lian BX, Rao R, Loh W, Goh A, Chong KW. Cashew nut allergy in Singaporean children. Asia Pac Allergy 2018;8:e29.
PUBMED | CROSSREF

35. Barnett D, Bonham B, Howden ME. Allergenic cross-reactions among legume foods--an in vitro study. J Allergy Clin Immunol 1987;79:433-8.
PUBMED | CROSSREF

36. Sicherer SH, Sampson HA, Burks AW. Peanut and soy allergy: a clinical and therapeutic dilemma. Allergy 2000;55:515-21.
PUBMED | CROSSREF

37. Bock SA, Atkins FM. The natural history of peanut allergy. J Allergy Clin Immunol 1989;83:900-4.
PUBMED | CROSSREF

38. Lack G, Fox D, Northstone K, Golding J; Avon Longitudinal Study of Parents and Children Study Team. Factors associated with the development of peanut allergy in childhood. N Engl J Med 2003;348:977-85.
PUBMED | CROSSREF

39. Brown SJ, Asai Y, Cordell HJ, Campbell LE, Zhao Y, Liao H, Northstone K, Henderson J, Alizadehfar R, Ben-Shoshan M, Morgan K, Roberts G, Masthoff LJ, Pasmans SG, van den Akker PC, Wijmenga C, Hourihane JO, Palmer CN, Lack G, Clarke A, Hull PR, Irvine AD, McLean WH. Loss-of-function variants in the filaggrin gene are a significant risk factor for peanut allergy. J Allergy Clin Immunol 2011;127:661-7.
PUBMED | CROSSREF

40. Asai Y, Greenwood C, Hull PR, Alizadehfar R, Ben-Shoshan M, Brown SJ, Campbell L, Michel DL, Bussières J, Rousseau F, Fujiwara TM, Morgan K, Irvine AD, McLean WH, Clarke A. Filaggrin gene mutation associations with peanut allergy persist despite variations in peanut allergy diagnostic criteria or asthma status. J Allergy Clin Immunol 2013;132:239-42.
PUBMED | CROSSREF

41. Tay YK, Kong KH, Khoo L, Goh CL, Giam YC. The prevalence and descriptive epidemiology of atopic dermatitis in Singapore school children. Br J Dermatol 2002;146:101-6.
PUBMED | CROSSREF

42. Loo EX, Shek LP, Goh A, Teoh OH, Chan YH, Soh SE, Saw SM, Kwek K, Gluckman PD, Godfrey KM, Chong YS, Lee BW, Van Bever HP. Atopic dermatitis in early life: evidence for at least three phenotypes? Results from the GUSTO Study. Int Arch Allergy Immunol 2015;166:273-9.
PUBMED | CROSSREF

43. Guo MM, Tseng WN, Ou CY, Hsu TY, Kuo HC, Yang KD. Predictive factors of persistent infantile atopic dermatitis up to 6 years old in Taiwan: a prospective birth cohort study. Allergy 2015;70:1477-84.
PUBMED | CROSSREF

44. Park YM, Lee SY, Kim WK, Han MY, Kim J, Chae Y, Hahm MI, Lee KJ, Kwon HJ, Park KS, Park JS, Ahn K. Risk factors of atopic dermatitis in Korean schoolchildren: 2010 international study of asthma and allergies in childhood. Asian Pac J Allergy Immunol 2016;34:65-72.
PUBMED

45. Wang XS, Tan TN, Shek LP, Chng SY, Hia CP, Ong NB, Ma S, Lee BW, Goh DY. The prevalence of asthma and allergies in Singapore; data from two ISAAC surveys seven years apart. Arch Dis Child 2004;89:423-6.
PUBMED | CROSSREF

46. Goksör E, Loid P, Alm B, Åberg N, Wennergren G. The allergic march comprises the coexistence of related patterns of allergic disease not just the progressive development of one disease. Acta Paediatr 2016;105:1472-9.
PUBMED | CROSSREF

47. Alduraywish SA, Lodge CJ, Campbell B, Allen KJ, Erbas B, Lowe AJ, Dharmage SC. The march from early life food sensitization to allergic disease: a systematic review and meta-analyses of birth cohort studies. Allergy 2016;71:77-89.
PUBMED | CROSSREF

48. Hill DA, Grundmeier RW, Ram G, Spergel JM. The epidemiologic characteristics of healthcare provider-diagnosed eczema, asthma, allergic rhinitis, and food allergy in children: a retrospective cohort study. BMC Pediatr 2016;16:133.
PUBMED | CROSSREF