

Are peanut allergies a concern for using peanut-based formulated foods in developing countries?

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Abstract

Background. Peanut allergy is relatively common among children in developed countries and may have severe outcomes, including anaphylaxis. However, few data about peanut allergy in developing countries are available. Meanwhile, formulated foods with peanuts as a major ingredient are being promoted to prevent and control malnutrition in developing countries.

Objective. The objectives of the paper are to review the existing epidemiologic data about peanut allergy, to determine whether the prevalence of peanut allergy is lower in developing countries, and to explore the possible reasons for onset of peanut allergy.

Methods. Publications relevant to peanut allergy were searched via Pubmed, and prevalence and etiological factors of peanut allergy were reviewed.

Results. Data about peanut allergy were scarce in most developing countries. The existing data support the conclusion that peanut allergy is not as common in developing countries as in developed countries and may not be a major concern for programs promoting formulated food containing peanuts for control of malnutrition. However, plans for treatment of individuals with peanut allergy could be incorporated into these formulated food supplementation programs. A few risk factors (late introduction of peanuts to children, peanut processing technology, non-oral peanut exposure, and maternal peanut exposure during pregnancy and lactation) have been hypothesized to be associated with peanut allergy. However, more conclusive data are needed to verify or disprove these hypotheses.

Conclusions. Peanut allergy is not as common in developing countries as in developed countries and may not be a major concern for programs promoting formulated food containing peanuts for control of malnutrition.

However, more research about prevalence of peanut allergy is warranted in developing countries.

Key words: Developing countries, formulated food, peanut allergy

Introduction

Peanut allergy is an IgE-mediated food allergy that is quite common in some developed countries (e.g., the United Kingdom, Australia, and the United States). Around 1% of children under 5 years of age are affected by the disease in these countries [1]. Peanut allergy can result in anaphylactic reactions that are potentially life-threatening; thus, special attention should be paid to peanut allergy when peanut consumption is promoted at scale. However, few epidemiologic data are available about peanut allergy in developing countries.

With the increasing use of formulated foods containing peanuts (e.g. Plumpy'nut, Nutributter) for the treatment and prevention of malnutrition, concerns have been raised about large-scale use of peanut-based formulated foods and risks associated with peanut allergy. To prevent and control malnutrition, supplying formulated foods is one of the most important strategies, and milk, eggs, soybeans, and peanuts are among the key potential ingredients. However, other potential replacements for peanuts (i.e., milk, eggs, and soybeans) have similar or even stronger allergenicity, so substituting these products does not necessarily reduce risk [2]. The purpose of this paper is to review the current evidence regarding the epidemiology of peanut allergy, especially in developing countries.

To elucidate intake of peanuts globally, data on per capita peanut consumption are shown in **figure 1**. The figure shows that peanut consumption per capita per year is highest in North America, lowest in Europe, and moderate in Africa, Asia and the Pacific region, and Central America and the Caribbean. By contrast, peanut oil consumption is highest in Africa, lowest in

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Central America and the Caribbean, and moderate in Asia and the Pacific, North America, and Europe (fig. 2) (The data were extracted from Food Balance Data Sheet 2003, from FAO website [3]).

Definition of peanut allergy and peanut sensitization

Reported peanut allergy is usually determined by a clinical history of allergic symptoms and the temporal association between peanut intake and these symptoms. Diagnosis of peanut allergy is based on general symptoms of the skin, gastrointestinal tract, and respiratory tract, the medical history of the temporal association between peanut consumption and the symptoms (generally seconds or minutes, but can be up to 2 hours), and evidence of peanut-specific IgE [1]. The gold standard for diagnosis is the double-blind, placebo-controlled food challenge test.

Peanut sensitization is determined by the peanut-specific skinprick test and/or serum peanut-specific IgE (peanut-sIgE) [4]. The majority of subjects with low positive peanut-specific IgE do not have peanut allergy [4, 5], just as most food sensitization may not lead to food allergy in most circumstances [6]. Thus, the positive predictive value of the skinprick test is usually low [7, 8]. The peanut sensitization test could be used more as a screening tool for peanut allergy rather than a diagnostic test confirming peanut allergy [4].

Sources searched and search strategy for the review

Publications relevant to peanut allergy were searched by PubMed with specific key words on 14 July 2009 and updated on 14 December 2009. All titles and abstracts were assessed for their relevance to peanut

allergy. The phrase ((“Peanut Hypersensitivity”[MAJR]) AND “Humans”[MeSH Terms]) AND (“Child, Preschool”[MeSH Terms] OR “Infant”[MeSH Terms]) was used for the search. Only publications written in English were reviewed. The references were extracted from the search results based on the following criteria for inclusion: population-based studies with estimation of the prevalence of peanut allergy, etiologic studies of peanut allergy, reviews of peanut allergy, and case report studies. Ninety-three papers were found, of which 27 met these criteria. The phrase (“Food Hypersensitivity”[MAJR] AND “Humans”[MeSH Terms]) AND (“Africa”[All Fields] OR “Asia”[All Fields] OR “America”[All Fields]) AND (“arachis hypogaea”[MeSH Terms] OR (“arachis”[All Fields] AND “hypogaea”[All Fields]) OR “arachis hypogaea”[All Fields] OR “peanut”[All Fields]) was used to identify all potential peanut allergy studies in developing countries. Five additional papers met the criteria.

Epidemiology

Age distribution

The mean age for the diagnosis of peanut allergy based on clinical characteristics was 14 months in children [1], and the median age of first peanut reaction was 14 to 24 months in the United States [9–11]. A study in the United Kingdom also found that the median age of onset of peanut allergy symptoms was about 24 months [12]. The mean and median ages of first reaction were 12 and 15.1 months, respectively, in a population study in Australia. Later onset was associated with increased risk of anaphylaxis [13]. Peanut allergy developed before 6 months of age in 4.4% of these patients, before 24 months in about 68%, and before 72 months in about 90% [13]. In a study in France, the first symptoms of 46% of peanut allergy cases appeared before 1 year

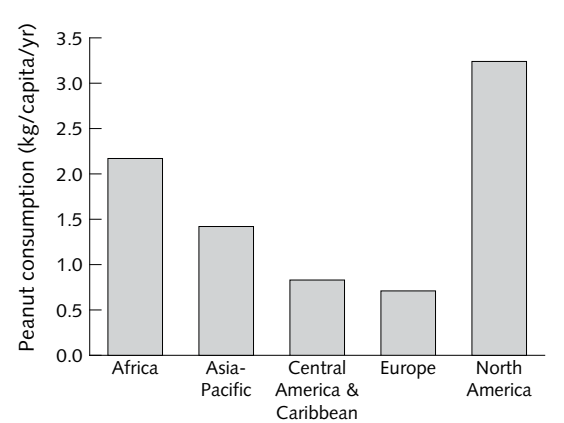


FIG. 1. Peanut consumption in 2003 in the world

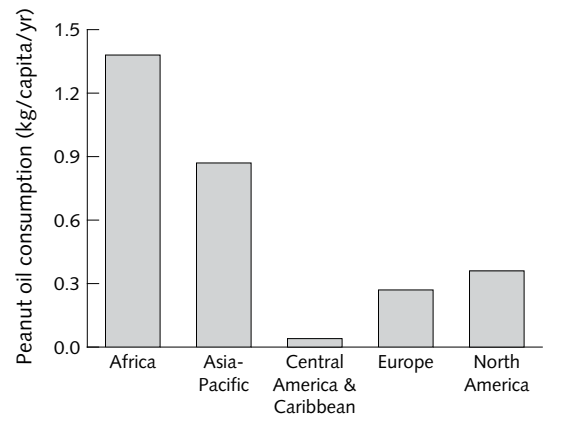


FIG. 2. Peanut oil consumption in 2003 in the world

of age, 7% had symptoms before 6 months of age, and 80% of all cases occurred by 3 years of age [14]. The peak age for diagnosis of food allergy was 18 months in a Denmark study [6]. Most peanut allergy occurred by 72 months of age.

Geographic distribution

Most of the prevalence data about peanut allergies are reported from studies in North America, Western Europe, and Australia (**table 1**). A recent study in Canada among children with a mean age of about 7 years found that the prevalence of peanut allergy was 1.63% [21]. A study in the United States showed that the prevalence of peanut allergy was 0.8% for children under 18 years of age [23]. The prevalence of peanut allergy was 1% for 3- to 4-year-old children [19], 1.8% for 4- to 5-year-old children [18], and 1.85% for 4- to 18-year-old children [16] in the United Kingdom and 1.15% to 2.1% for children under 6 years of age in Australia [13, 15].

The rates of peanut allergy are not consistent across Europe [24]. The prevalence of peanut allergy among

young adults with a mean age of 22 years in Denmark was about 0.6% [25]. The estimated prevalence of peanut allergy was 0.3% to 0.75% in France [26]. Peanut is not a very common allergenic food in the eastern Black Sea region of Turkey [27]. In Spain, peanut allergy is also not a common food allergy [28].

The occurrence of peanut allergy may differ between Asian and Western populations [29]. Although prevalence data on peanut allergy are not available for most Asian countries, available data on the occurrence of peanut allergy also differed across countries in Asia (peanut hypersensitivity was low in Malaysia, Japan, and the Philippines and relatively high in Indonesia) [30, 31]. Peanut ranked only sixth among common food allergens in Asia [31]. A survey in China found that the prevalence of peanut sensitization, defined by skinprick test wheal diameter at least 3 mm greater than the saline control, was about 12.3% for 11- to 17-year-olds [7], which was much higher than the 3.3% reported in the United Kingdom [19]. However, the prevalence of self-reported peanut allergy was only about 0.3% for these Chinese populations ($n = 2,118$). Only one of the seven subjects who reported peanut allergy had peanut

TABLE 1. Prevalence of peanut allergy and/or peanut sensitization across the world

Region	Country	Year	Age	Peanut allergy (%)	Peanut sensitization (%)	Reference
Asia Pacific	Australia	2005	5 yr	2.1 ^a	—	Kljakovic [15]
	Australia	2004	0–72 mo	1.15 ^b	1.53 ^c	Mullins [13]
	Australia	2001	0–72 mo	0.73 ^b	0.84 ^c	Mullins [13]
Western Asia and Middle East	Israel	2004	4–18 yr	0.17 ^d	—	Du Toit [16]
Europe	Denmark	2002	22 yr	0.6 ^d	—	Osterballe [17]
	UK	2004	4–18 yr	1.85 ^e	—	Du Toit [16]
	UK	2003	4–5 yr	1.8 ^f	2.8	Hourihane [18]
	UK	1998	3–4 yr	1 ^g	3.3	Grundy [19]
	UK	1995	4–5 yr	0.5 ^h	1.1	Tariq [20]
North America	Canada	2005	7.1–7.6 yr	1.63 ⁱ	—	Ben-Shoshan [21]
	Canada	2000	7.4 yr	1.50 ⁱ	—	Kagan [22]
	USA	2002	0–5 yr	0.8 ^j	—	Sicherer [23]
	USA	1997	0–5 yr	0.4 ^j	—	Sicherer [23]

a. Parent-reported allergic reaction to peanut with confirmed skinprick test (SPT) or elevated serum peanut-specific IgE.

b. Peanut allergy was diagnosed as a history of acute allergic reaction within 2 hours of peanut exposure and a positive SPT.

c. Peanut sensitization was diagnosed as a positive SPT, which was defined as a wheal size at least 3 mm greater than negative control.

d. Self-reported peanut allergy confirmed by SPT and double-blinded, placebo-controlled, peanut challenge test (DBPCCT).

e. History of allergic reaction (at least one of the symptoms: itchy rash, wheezing, vomiting, diarrhea, and swelling) within 2 hours of peanut ingestion, confirmed by positive SPT or peanut-specific IgE or both, or oral peanut challenge test.

f. SPT, peanut-specific IgE, and DBPCCT.

g. Parent-reported allergic reaction to peanut with confirmed SPT and open food challenge test.

h. Parent-reported allergic reaction to peanut with confirmed SPT and peanut-specific IgE.

i. Parent-reported allergic reaction to peanut with confirmed SPT or elevated serum peanut-specific IgE or DBPCCT.

j. History of allergic reaction (skin with hives or angioedema; respiratory tract with trouble breathing, wheezing, or throat tightness; and gastrointestinal tract with vomiting or diarrhea) occurring within 2 hours of peanut ingestion.

sensitization, as assessed by the peanut allergen-specific skinprick test (mean wheal diameter > 3 mm), and four of the seven subjects had allergic symptoms. Thus, the prevalence of actual peanut allergy appears to be less than the reported prevalence of peanut allergy (0.3%). Peanut was one of the leading causes of adverse food reactions for 2- to 7-year-old children in Hong Kong, and peanut allergy was less common among those born in mainland China than those born in Hong Kong [32]. About 0.52% of these children had parent-reported and doctor-diagnosed adverse peanut reactions. In Israel, the incidence of peanut allergy is also quite low (~ 0.17%) for 4- to 18-year-old children [16]. Overall, peanut allergy is relatively rare in Asia, although data for many parts of Asia are lacking [33].

No data on the prevalence of peanut allergy are available for Africa. Some cases of peanut sensitization diagnosed using peanut-specific IgE concentration (> 0.35 kU/L) have been reported in South Africa [34]. However, in Nigeria, food intolerance was a relatively minor risk factor for atopic dermatitis (an allergic disease that can increase the risk of other allergic diseases) [35]. About 3.5% of atopic dermatitis patients in the Nigerian study had food intolerance, mainly for eggs, crayfish, and artificial milk. In a cross-sectional study in Mozambique, seafood, meat, and fruits or vegetables were common reasons for self-reported food allergy, and peanut was not reported as a reason for self-reported food allergy [36].

When peanut-based foods (such as Plumpy'nut and Nutributter, both of which contain peanut butter, milk powder, vegetable oil, and micronutrients) are used in research settings, children are first given a test dose to assess food intolerance. In published studies on a total of 1,262 children in Africa who consumed peanut-based supplements for at least 2 months, no cases of peanut allergy were observed. The children in these studies ranged in age from 6 to 60 months (personal communication, Drs. Kathryn Dewey and Ken Maleta).

Plumpy'nut has been widely used for treatment of severe acute malnutrition in more than 1 million children in Africa (e.g., Niger, Malawi, and Congo) during the last 10 years. No peanut allergy has been reported in these populations, although underreporting cannot be ruled out (personal communication, Dr. André Briend).

Epidemiologic trends

Several studies suggest that the incidence of peanut allergy has risen during the past several decades in some developed countries. For example, in Australia, the estimated minimum prevalence of peanut allergy for children by 72 months of age increased from 0.73% in 2001 to 1.15% in 2007 [13]. Self-reported peanut allergy increased from 0.4% in 1997 to 0.8%

in 2002 among children less than 18 years old in the United States [23]. The prevalence of self-reported peanut allergy verified by the open food challenge test increased from 0.5% in 1989 to 1.0% in 1994 in the United Kingdom, but this change was not statistically significant. The overall prevalence of peanut allergy among 3- to 4-year-old children in the United Kingdom was 1.5% [19]. However, an increasing prevalence of peanut allergy has not been conclusively documented in other studies. For example, in one study in Canada, the prevalence of peanut allergy among 5- to 9-year-old children was 1.64% in 2007, versus 1.34% in 2002. The difference between these two surveys was not statistically significant [21].

Theories about reasons for different levels of peanut allergy

It is well accepted that allergic diseases are becoming more common in general, which may be due to cleaner environments. The "hygiene hypothesis" posits that lower exposure to infectious agents during childhood (related to smaller family size and greater affluence) increases susceptibility to allergic diseases [37, 38]. This may partially explain the differences in prevalence rates of peanut allergy between developing and developed countries. On the other hand, protein-energy malnutrition could result in weak immunologic function and lower the risk of allergic response [39], which may partially explain why no peanut allergy cases have been reported when Plumpy'nut is used widely for treating severely malnourished children (personal communication, Dr. André Briend).

A recent study compared the occurrence of peanut allergy among Jewish children with similar genetic backgrounds (Ashkenazi or Sephardic ancestry) living in the United Kingdom and in Israel [16]. The prevalence of peanut allergy among 4- to 18-year-old children was significantly higher in the United Kingdom (1.85%) than in Israel (0.17%). In this study, peanuts were introduced by 9 months of age to 69% of Israeli infants, compared with only 10% of UK infants, and the amount consumed was greater for the children in Israel (monthly median consumption, 7.1 g) than in the United Kingdom (monthly median consumption, 0 g during the first year. The authors suggested that avoidance of peanut consumption in early life could increase the risk of peanut allergy [16]. Thus, early exposure to peanuts could decrease the occurrence of peanut allergy [40], and delayed introduction of peanuts may not prevent it [41].

Another hypothesis for varying prevalence rates of peanut allergy is that peanut processing procedures could be related to the degree of allergenicity [42]. Roasting peanuts can induce the Maillard reaction, which is a chemical reaction between an amino acid

in proteins and an aldehyde or ketone group in sugar in carbohydrates, producing insoluble glycol-protein and related end products, which could become antigens and cause immunologic reactions [42]. The difference in the prevalence of peanut allergy between the United States and China could be due to different peanut processing procedures [42]. In China, peanuts are usually boiled or fried or used as peanut oil. In the United States, by contrast, peanuts are usually roasted by using dry heat [42]. The temperature used for roasting is high [43]. Moreover, peanut oil is commonly used for cooking in China, and small amounts of peanut antigens in the oil could be introduced into the diet during early childhood.

Nonoral peanut exposure could be another risk factor for peanut allergy. A recent case-control study found that household peanut consumption (peanut consumption by all family members during the first year of the subject's life) was associated with greater risks of peanut allergy [44]. Another nested case-control study by the same group showed that infants' epicutaneous exposure to creams containing peanut oil in the first 6 months of life may be related to an increased risk of peanut allergy, diagnosed by using clinical history, the skinprick test, and the double-blinded, placebo-controlled, food challenge test [45]. Low doses of peanut antigens, which were detected in refined peanut oil and can produce a positive skinprick test in peanut allergy patients, could pass through the skin barrier into the circulation and cause peanut allergy. By contrast, peanut protein when ingested is usually digested into single amino acids, which are absorbed from the gastrointestinal tract. In the United States, skin care products containing peanut oil either are not widely available or the peanut antigen level of peanut oil-containing cream is too low to cause peanut allergy [46, 47], so exposure to skin creams does not explain the relatively high rates of peanut allergy in the United States. Other factors may explain the similarity in allergy prevalence between the United Kingdom and the United States, such as environmental peanut exposure, maternal history of allergic diseases, or other food allergies among children.

Another hypothesis is that maternal peanut exposure

during pregnancy and/or lactation is related to peanut allergy in the child, but the evidence is not convincing. In one study, peanut-specific IgE was not detectable in the cord blood, a finding that supports the assumption that peanut IgE antibody cannot cross the placenta to cause peanut allergy [45]. Another study found that peanut consumption during pregnancy was marginally associated with peanut allergy (OR, 3.97; 95% CI, 0.73 to 24; $p = .063$) [34], but this finding was not replicated in other studies [44, 45]. The major peanut antigens (Ara h1 and Ara h2) have been detected in breastmilk [48]. Breastfeeding was associated with an increased risk of peanut allergy in crude analysis in a few studies [18, 19, 44, 45]. However, the association became nonsignificant after controlling for other covariates in most of these studies [18, 44, 45]. An intervention trial that included peanut avoidance during the 3rd trimester of pregnancy, lactation, and infancy did not significantly prevent peanut allergy during the 7-year follow-up [49].

Summary

Data about peanut allergy are scarce for most developing countries. Based on the experience of using Plumpy'nut and Nutributter in Africa, peanut allergy does not appear to be a major concern in that region.

Early consumption of peanuts by infants (i.e., starting from 6 months of age) may decrease the risk of peanut allergy, but further research is needed.

There are several hypotheses regarding risk factors for peanut allergy (e.g., peanut processing technology, nonoral peanut exposure, and maternal peanut exposure during pregnancy and lactation), but additional evidence is needed to confirm or refute these hypotheses.

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References

1. Burks AW. Peanut allergy. *Lancet* 2008;371:1538–46.
2. Rona RJ, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E, Sigurdardottir ST, Lindner T, Goldhahn K, Dahlstrom J, McBride D, Madsen C. The prevalence of food allergy: a meta-analysis. *J Allergy Clin Immunol* 2007;120:638–46.
3. FAO. Food Balance Sheets. Available at: <http://faostat.fao.org/site/368/default.aspx#ancor> Accessed 2 September 2009.
4. Du Toit G, Santos A, Roberts G, Fox AT, Smith P, Lack G. The diagnosis of IgE-mediated food allergy in childhood. *Pediatr Allergy Immunol* 2009;20:309–19.
5. Sampson HA, Albergo R. Comparison of results of skin tests, RAST, and double-blind, placebo-controlled food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 1984;74:26–33.
6. Eller E, Kjaer HF, Host A, Andersen KE, Bindslev-Jensen C. Food allergy and food sensitization in early childhood: results from the DARC cohort. *Allergy* 2009.
7. Kim JS, Ouyang F, Pongracic JA, Fang Y, Wang B, Liu X, Xing H, Caruso D, Zhang S, Xu X, Wang X. Dissociation between the prevalence of atopy and allergic disease in

- rural China among children and adults. *J Allergy Clin Immunol* 2008;122:929–35 e4.
8. Skripak JM, Wood RA. Peanut and tree nut allergy in childhood. *Pediatr Allergy Immunol* 2008;19:368–73.
 9. Green TD, LaBelle VS, Steele PH, Kim EH, Lee LA, Mankad VS, Williams LW, Anstrom KJ, Burks AW. Clinical characteristics of peanut-allergic children: recent changes. *Pediatrics* 2007;120:1304–10.
 10. Sicherer SH, Furlong TJ, Munoz-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.
 11. Sicherer SH, Burks AW, Sampson HA. Clinical features of acute allergic reactions to peanut and tree nuts in children. *Pediatrics* 1998;102:e6.
 12. Roberts G, Lack G. Diagnosing peanut allergy with skin prick and specific IgE testing. *J Allergy Clin Immunol* 2005;115:1291–6.
 13. Mullins RJ, Dear KB, Tang ML. Characteristics of childhood peanut allergy in the Australian Capital Territory, 1995 to 2007. *J Allergy Clin Immunol* 2009;123:689–93.
 14. Moneret-Vautrin DA, Rance F, Kanny G, Olsewski A, Gueant JL, Dutau G, Guerin L. Food allergy to peanuts in France—evaluation of 142 observations. *Clin Exp Allergy* 1998;28:1113–9.
 15. Kljakovic M, Gatenby P, Hawkins C, Attewell RG, Ciszek K, Kratochvil G, Moreira A, Ponsonby AL. The parent-reported prevalence and management of peanut and nut allergy in school children in the Australian Capital Territory. *J Paediatr Child Health* 2009;45:98–103.
 16. Du Toit G, Katz Y, Sasieni P, Meshier 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.
 17. 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;16:567–73.
 18. Hourihane JO, Aiken 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;119:1197–202.
 19. 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;110:784–9.
 20. 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;313:514–7.
 21. Ben-Shoshan M, Kagan RS, Alizadehfard R, Joseph L, Turnbull E, St Pierre Y, Clarke AE. Is the prevalence of peanut allergy increasing? A 5-year follow-up study in children in Montreal. *J Allergy Clin Immunol* 2009;123:783–8.
 22. Kagan RS, Joseph L, Dufresne C, Gray-Donald K, Turnbull E, Pierre YS, Clarke AE. Prevalence of peanut allergy in primary-school children in Montreal, Canada. *J Allergy Clin Immunol* 2003;112:1223–8.
 23. 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;112:1203–7.
 24. Boulay A, Houghton J, Gancheva V, Sterk Y, Strada A, Schlegel-Zawadzka M, Sora B, Sala R, van Ree R, Rowe G. A EuroPrevall review of factors affecting incidence of peanut allergy: priorities for research and policy. *Allergy* 2008;63:797–809.
 25. Osterballe M, Mortz CG, Hansen TK, Andersen KE, Bindslev-Jensen C. The prevalence of food hypersensitivity in young adults. *Pediatr Allergy Immunol* 2009;20:686–92.
 26. Morisset M, Moneret-Vautrin DA, Kanny G. Prevalence of peanut sensitization in a population of 4,737 subjects—an Allergo-Vigilance Network enquiry carried out in 2002. *Eur Ann Allergy Clin Immunol* 2005;37:54–7.
 27. Orhan F, Karakas T, Cakir M, Aksoy A, Baki A, Gedik Y. Prevalence of immunoglobulin E-mediated food allergy in 6–9-year-old urban schoolchildren in the eastern Black Sea region of Turkey. *Clin Exp Allergy* 2009;39:1027–35.
 28. Crespo JF, Pascual C, Burks AW, Helm RM, Esteban MM. Frequency of food allergy in a pediatric population from Spain. *Pediatr Allergy Immunol* 1995;6:39–43.
 29. Tham EH, Tay SY, Lim DL, Shek LP, Goh AE, Giam YC, Chng HH, Lee BW. Epinephrine auto-injector prescriptions as a reflection of the pattern of anaphylaxis in an Asian population. *Allergy Asthma Proc* 2008;29:211–5.
 30. 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;31:272–81.
 31. Hill D, Hosking C, Zhie C, Leung R, Baratwidjaja K, Iikura Y, Iyngkaran N, Gonzalez-Andaya A, Wah L, Hsieh K. The frequency of food allergy in Australia and Asia. *Environ Toxicol Pharmacol* 1997;4:101–10.
 32. Leung TF, Yung E, Wong YS, Lam CW, Wong GW. Parent-reported adverse food reactions in Hong Kong Chinese pre-schoolers: epidemiology, clinical spectrum and risk factors. *Pediatr Allergy Immunol* 2009;20:339–46.
 33. Shek LP, Lee BW. Food allergy in Asia. *Curr Opin Allergy Clin Immunol* 2006;6:197–201.
 34. Frank L, Marian A, Visser M, Weinberg E, Potter PC. Exposure to peanuts in utero and in infancy and the development of sensitization to peanut allergens in young children. *Pediatr Allergy Immunol* 1999;10:27–32.
 35. Nnoruka EN. Current epidemiology of atopic dermatitis in south-eastern Nigeria. *Int J Dermatol* 2004;43:739–44.
 36. Lunet N, Falcao H, Sousa M, Bay N, Barros H. Self-reported food and drug allergy in Maputo, Mozambique. *Public Health* 2005;119:587–9.
 37. Strachan DP. Family size, infection and atopy: the first decade of the “hygiene hypothesis”. *Thorax* 2000;55 Suppl 1:S2–10.
 38. Bloomfield SF, Stanwell-Smith R, Crevel RW, Pickup J. Too clean, or not too clean: the hygiene hypothesis and home hygiene. *Clin Exp Allergy* 2006;36:402–25.
 39. Abbassy AS, el-Din MK, Hassan AI, Aref GH, Hammad SA, el A, II, el-Din AA. Studies of cell-mediated immunity and allergy in protein energy malnutrition. II. Immediate hypersensitivity. *J Trop Med Hyg* 1974;77:18–21.

40. Wennergren G. What if it is the other way around? Early introduction of peanut and fish seems to be better than avoidance. *Acta Paediatr* 2009;98:1085–7.
41. Snijders BE, Thijs C, van Ree R, van den Brandt PA. Age at first introduction of cow milk products and other food products in relation to infant atopic manifestations in the first 2 years of life: the KOALA Birth Cohort Study. *Pediatrics* 2008;122:e115–22.
42. Nowak-Węgrzyn A, Fiocchi A. Rare, medium, or well done? The effect of heating and food matrix on food protein allergenicity. *Curr Opin Allergy Clin Immunol* 2009;9:234–7.
43. Crespo JF, James JM, Fernandez-Rodriguez C, Rodriguez J. Food allergy: nuts and tree nuts. *Br J Nutr* 2006;96:S95–S102.
44. Fox AT, Sasieni P, du Toit G, Syed H, Lack G. Household peanut consumption as a risk factor for the development of peanut allergy. *J Allergy Clin Immunol* 2009;123:417–23.
45. Lack G, Fox D, Northstone K, Golding J. Factors associated with the development of peanut allergy in childhood. *N Engl J Med* 2003;348:977–85.
46. Wilkin JK, Pappas EG, DeCamp WH. Peanut allergy. *N Engl J Med* 2003;349:301–3; author reply 301–3.
47. Roth JS. Peanut allergy. *N Engl J Med* 2003;349:301–3; author reply 301–3.
48. Vadas P, Wai Y, Burks W, Perelman B. Detection of peanut allergens in breast milk of lactating women. *JAMA* 2001;285:1746–8.
49. Zeiger RS, Heller S. The development and prediction of atopy in high-risk children: follow-up at age seven years in a prospective randomized study of combined maternal and infant food allergen avoidance. *J Allergy Clin Immunol* 1995;95:1179–90.