

Rising prevalence of allergy to peanut in children: Data from 2 sequential cohorts

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Background: Allergy to peanut is common. However, it is not known whether the prevalence of sensitization and clinical allergy to peanut is increasing.

Objective: We sought to determine any change in the prevalence of peanut sensitization and reactivity in early childhood in 2 sequential cohorts in the same geographic area 6 years apart.

Methods: Of 2878 children born between September 1, 1994, and August 31, 1996, living on the Isle of Wight, 1273 completed questionnaires, and 1246 had skin prick tests at the age of 3 to 4 years. Those with positive skin prick test responses to peanut were subjected to oral peanut challenges, unless there was a history of immediate systemic reaction. These data were compared with information on sensitization and clinical allergy to peanut available from a previous cohort born in 1989 in the same geographic area.

Results: There was a 2-fold increase in reported peanut allergy (0.5% [6/1218] to 1.0% [13/1273]), but the difference was nonsignificant ($P = .2$). Peanut sensitization increased 3-fold, with 41 (3.3%) of 1246 children sensitized in 1994 to 1996 compared with 11 (1.1%) of 981 sensitized 6 years ago ($P = .001$). Of 41 sensitized children in the current study, 10 reported a convincing clinical reaction to peanut, and 8 had positive oral challenge results, giving an overall estimate of peanut allergy of 1.5% (18/1246).

Conclusions: Sensitization to peanut had increased between 1989 and 1994 to 1996. There was a strong but statistically nonsignificant trend for increase in reported peanut allergy. (*J Allergy Clin Immunol* 2002;110:784-9.)

Key words: Peanut, allergy, sensitization, prevalence, oral challenge, cohort

Allergy to peanuts is common and can be a potentially serious form of food allergy.^{1,2} During the last decade, there has been mounting concern over the avoidable morbidity and mortality associated with peanut allergy.^{3,4} The prevalence of self-reported peanut allergy is estimated to be around 0.5% to 1.0% of the unselected popula-

Abbreviation used
SPT: Skin prick test

tion in both adults and children.⁴⁻⁶ Perceived food allergy is said to be higher than can be confirmed by means of oral challenge.⁷ Studies using oral challenges to confirm the presence of peanut allergy are few.^{8,9} Thus far, no study has reported prevalence of this condition in an unselected population confirmed by oral challenge.

There is now a general consensus that allergic disorders are increasing in prevalence, at least in the Western world. Most convincing data comes from prevalence studies in the same population by using the same methodology at different time points (eg, for asthma and allergic rhinitis).^{10,11} It has also been suggested that the incidence of peanut allergy has increased in recent years,^{12,13} but others have argued against such an increase.⁶

The diagnosis of nut allergy has a major effect on the quality of life of individuals and their families.¹⁴ Oral challenges are currently required to make a firm diagnosis, but these are cumbersome to perform, and there is a slight risk of a serious reaction. Skin prick test (SPT) wheal size or level of specific IgE to peanut correlate with challenge outcome.^{8,15} Attempts have been made to find a level with a high sensitivity and specificity for the likelihood of a positive reaction, thus obviating the need for oral challenge.^{16,17}

Tariq et al¹⁸ suggested that 1.1% of children are sensitized to peanut by the age of 4 years and that approximately half of these (0.5%) have some allergic symptoms when ingesting peanuts, whereas the remainder have no physical reaction. These prevalence figures were taken from a birth cohort of children born in 1989 on the Isle of Wight. A more recent study of children aged 3 to 4 years from the same geographic location has given us the opportunity to identify any change in the prevalence of peanut allergy and to improve our understanding of the relationship of sensitization to clinical reactivity proved by means of oral challenge.

METHODS

Parents of all children ($n = 2878$) born between September 1, 1994, and August 31, 1996, and registered with a general practitioner on the Isle of Wight were approached just after the child's third birthday as part of a study that examined the effect of artificial food additives on behavior and allergy. Approval for the study was

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obtained from the local research ethics committee. Parents of 1273 (44%) children (mean age, 3.2 years [SD 7.6]) agreed to participate and completed a questionnaire seeking information on past and current atopic symptoms (asthma, wheeze, hay fever, and eczema) on the basis of the standardized International Study of Asthma and Allergy in Children questionnaire.¹⁹ In addition, specific questions were asked relating to food allergy, including peanut allergy, and any anaphylactic reactions. Every child was offered an SPT to a battery of food and aeroallergens (ALK, Horsholm, Denmark), including house dust mite, grass pollen mix, cat, milk, egg, and peanut. Histamine dihydrochloride, (10 mg/mL) and physiologic saline were used as positive and negative controls. A mean wheal diameter at least 3 mm larger than that produced by saline after 15 minutes was taken as a positive result. Atopy was defined as having a positive response to at least one allergen.

All children with a positive SPT response to peanut who had not previously had a convincing adverse reaction or had never knowingly eaten peanut were invited for an open challenge to peanut. The challenges were performed on the children's ward, where facilities for full resuscitation were available. The children were told not to take antihistamines for at least 48 hours before the challenge.

In the first stage (labial challenge) the inside of the child's lip was rubbed with a peanut for 10 seconds. The child was observed for 15 minutes for any symptoms. If no reaction was observed, an oral challenge (stage 2) was performed. The child was given increasing amounts of peanut butter spread on bread or a flapjack biscuit that contained peanut at 15-minute intervals. The child was offered a portion containing 0.25 g of peanut, then 0.5 g, 1 g, 2 g, and 4.25 g (in total, 8 g). At every stage of the challenge, observations of pulse and blood pressure were recorded. If the child had a positive reaction, the procedure was immediately stopped, and the appropriate medication was given. No child had life-threatening symptoms requiring adrenaline, but several were given an antihistamine. All children stayed for at least 1 hour after the challenge for observation, regardless of the outcome.

Data on sensitization to peanut and reported peanut allergy prevalence were compared with data from a whole-population birth cohort that was established on the Isle of Wight, United Kingdom, in 1989. Of 1536 children born between January 1, 1989, and February 28, 1990, informed consent was obtained for 1456 subjects. Children were enrolled at birth and subsequently seen at the ages of 1, 2, and 4 years. At 4 years of age, clinical review of allergic symptoms was conducted on 1218 (84%) children, and SPTs to common allergens were performed on 981 (67%) children.¹⁸

Data were double entered into SPSS software (version 10.0; SPSS Inc, Chicago, Ill). Data that did not conform to normality despite log transformation were analyzed with a nonparametric test (Mann-Whitney *U* test). Differences in proportions between groups were tested by means of χ^2 analysis (2-sided Fisher exact test).

RESULTS

In the current study SPTs were performed on 1246 children (98% of those who consented, $n = 1273$) and 43% of the whole-population cohort ($n = 2878$). Forty-one (3.3%) children had a positive SPT response to peanut (Fig 1). Children sensitized to peanut were highly atopic; half of them had a history of asthma, and nearly all of them had had eczema (Table I). They were also commonly sensitized to other allergens (Table II). However, 7 (17.1%) of 41 children had positive responses to peanut only, although none of these 7 reacted adversely on peanut challenge. Interestingly, 88% of peanut-sensitized children were breast-fed for at least 1 month com-

pared with 69% of those who were not so sensitized (odds ratio, 3.3; 95% CI, 1.3-8.4; $P < .01$).

A comparable population of 4-year-old children born in 1989 on the Isle of Wight had a prevalence of peanut sensitization of 1.1% compared with 3.3% in this population born 5 to 6 years later ($P = .001$, Table III). However, there was no increase in overall atopy. Nineteen percent of 4-year-old children had a positive SPT response and were classed as atopic in 1993, whereas only 15% of 3-year-old children met the same criteria 6 years later (odds ratio, 0.73; 95% CI, 0.60-0.88; $P = .001$). There was a 2-fold increase in reported peanut allergy, with 6 (0.5%) of 1218 children from the 1989 cohort, from when questionnaire information was available, reporting peanut allergy compared with 13 (1.0%) of 1273 children from the 1994 to 1996 cohort (Table III). However, this failed to reach statistical significance ($P = .2$).

Of the 41 children who had a positive SPT response to peanut, 10 children reported a convincing clinical reaction to peanut occurring at home, with a range of symptoms including angioedema, urticaria, wheezing, rhinorrhoea, vomiting, and abdominal discomfort. A diagnosis of peanut allergy was accepted in these children, and oral challenges were not performed. Five children had eaten peanuts without any adverse effects and hence did not undergo the challenge procedure. Of the remaining 26 children, 24 had an oral challenge to peanut, and 8 challenge results were considered positive (Fig 1). Overall, 18 (1.5%) of 1246 children were considered to have symptomatic allergy to peanut.

There was a direct relationship between the likelihood of a positive reaction to peanut and skin test wheal size (Fig 2). None of the 7 children with wheal sizes of less than 3 mm reacted to peanut on exposure. The median SPT sizes for those who did or did not clinically react to peanut were 9.0 and 3.25 mm, respectively ($P \leq .001$, Mann-Whitney *U* test).

DISCUSSION

Studies from the United States⁴ and the United Kingdom⁶ have estimated the prevalence of peanut allergy to be around 0.5% to 1% of the population. However, these studies were questionnaire surveys and are likely to overestimate the prevalence because self-reported food allergies are generally higher than can be proved with oral challenge.⁷ Moreover, there is a risk of bias because those with peanut allergy are more likely to agree to participate in any questionnaire surveys. Our previous whole-population birth cohort study¹⁸ revealed a point prevalence of sensitization to peanut in 4-year-old children of 1.1% (11/981). Information gathered from questionnaires suggested a prevalence of clinical allergy to peanut of 0.5% (46% of those who were sensitized), although oral challenges were not performed.

This more recent cohort study has given us the opportunity to study any change in the prevalence of sensitization in the intervening 6 years and to perform open peanut challenges to confirm diagnosis, where necessary. From

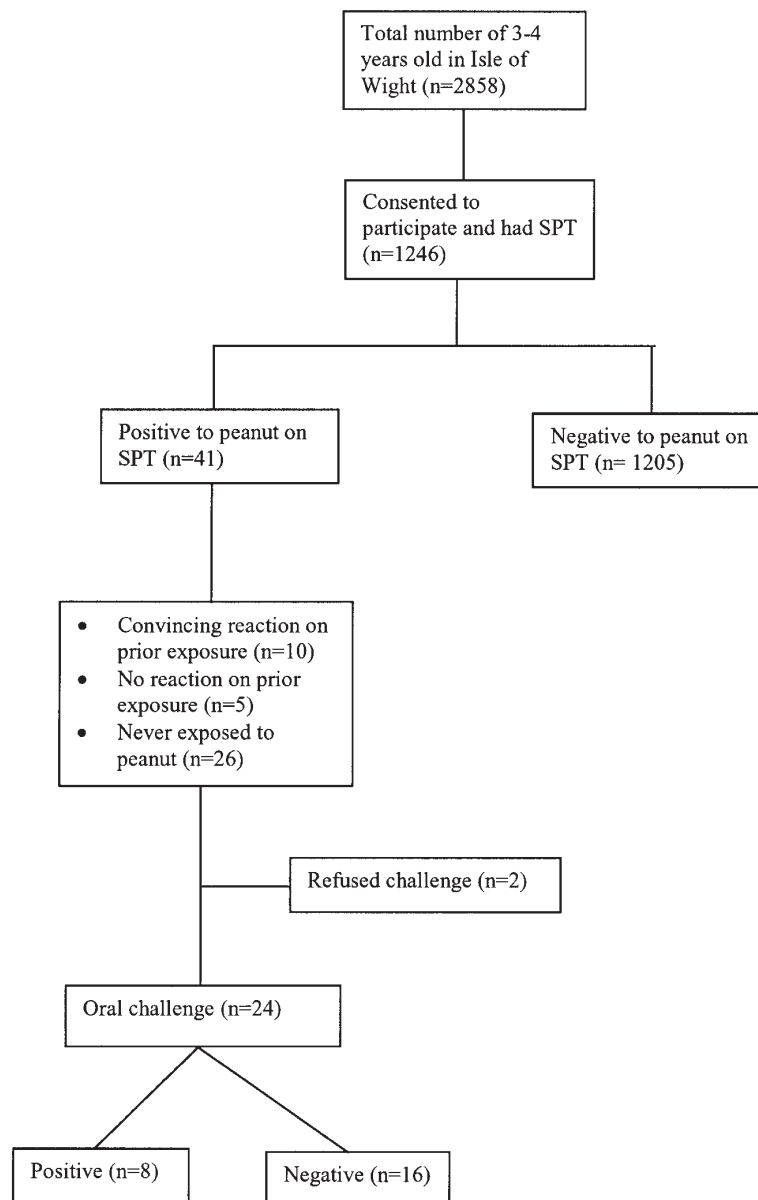


FIG 1. Flow diagram of children recruited to the study.

TABLE I. Comparison of allergic morbidity according to the International Study of Asthma and Allergy in Children questionnaire

Allergic disorders	Not sensitized to peanut (n = 1191),* % (n)	Sensitized to peanut (n = 40),* % (n)	OR (95% CI)	P value
Ever asthma	18.4 (219)	50.0 (20)	4.4 (2.4-8.4)	<.001
Current wheeze	33.0 (393)	47.5 (19)	1.84 (1.0-3.5)	.06
Ever hay fever	8.6 (103)	30.0 (12)	4.5 (2.2-9.2)	<.001
Ever eczema	44.1 (525)	90.0 (36)	11.5 (4.1-32.4)	<.001

OR, Odds ratio.

*Questionnaire information was incomplete for 14 of 1205 children not sensitized to peanut and for 1 of 41 peanut-sensitized children.

new data, it appears that sensitization levels to peanut have increased from 1.1% to 3.3% in this period, and reported symptomatic allergy has increased from 0.5% to 1.0%. Sampson¹³ suggested, in 1996, that the incidence

of peanut allergy had doubled over the previous 10 years. However, Emmett et al⁶ argued against such an increase. Evidence from our latest cohort shows a substantial increase in the number of children with peanut allergy.

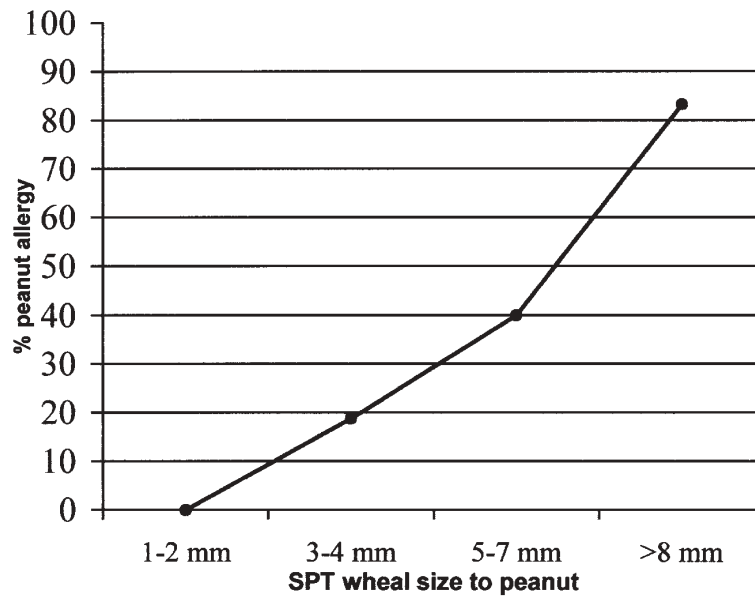


FIG 2. Relationship of SPT size to peanut allergy (history of an immediate reaction or outcome of oral peanut challenge).

TABLE II. Level of atopic sensitization in 3- to 4-year-old children who were or were not sensitized to peanut

Skin test positivity*	Not sensitized to peanut (n = 1200),† % (n)	Sensitized to peanut (n = 41), % (n)	OR (95% CI)	P value
House dust mite	8.8 (106)	58.5 (24)	14.6 (7.6-28.0)	<.001
Grass pollen	3.7 (44)	46.3 (19)	22.7 (11.4-44.9)	<.001
Cat	4.3 (51)	36.6 (15)	13.0 (6.5-26.0)	<.001
Egg	0.3 (4)	32.5 (13)	144.0 (44.1-470.3)	<.001
Milk	0.4 (5)	10.0 (4)	26.5 (6.8-103.0)	<.001

OR, Odds ratio.

*A positive skin test response was defined as a mean wheal diameter of 3 mm or greater.

†Five children did not have valid SPT results for all allergens tested.

TABLE III. Prevalence of sensitization to peanut, peanut allergy reported on questionnaire, and peanut allergy confirmed by means of food challenge

	1989 cohort, % (n/total n)	1994-1996 cohort, % (n/total n)	OR (95% CI)	P value
Reported allergy to peanut	0.5 (6/1218)	1.0 (13/1273)	2.08 (0.79-5.49)	.17
Peanut sensitization†	1.1 (11/981)	3.3 (41/1246)	2.95 (1.52-5.70)	.001

OR, Odds ratio.

*Questionnaire information was available, but SPTs were not done in 234 children in the 1989 cohort and 27 children in the 1994 to 1996 cohort.

In the recent cohort 42% of those sensitized to peanut reacted clinically. This figure suggests that the previous estimate (1989 birth cohort) of the number of children likely to clinically react on exposure to peanut was accurate, even though it was derived from questionnaire response alone.¹⁸ This is broadly in agreement with suggestions⁸ that the false-positive rate (allergy to peanut listed on questionnaire but not proved on challenge) is less than 20%, suggesting that the prevalence rates from the questionnaire studies are generally reliable. In young children reported food allergy might underestimate the prevalence because some might be sensitized without knowingly being exposed to peanut. In this study a third of such children (8/24) had positive oral challenge results.

A weakness of this study was that only 43% (1246/2878) of the target population of 3- to 4-year-old children agreed to participate and had SPTs. This can overestimate the prevalence in the population because those with a history of allergic disease in the child or the family are likely to be overrepresented, especially because our data and those of others^{2,8} suggest that the population with peanut allergy is highly atopic. In the 1989 cohort 67% (981/1456) of the population were skin tested, and 84% (1218/1456) responded to the questionnaire.¹⁸ If there was a bias in the recent cohort toward participation of atopic families, we should see an increase in overall atopy compared with that seen in the 1989 birth cohort. However, 19% of 4-year-old children

in the 1989 cohort had a positive SPT response and were classified as atopic compared with only 15% who met the same criteria 6 years later. The lower prevalence in the recent cohort probably reflects the natural history of sensitization in that these children were 10 to 12 months younger when skin prick tested. These children might be in a transitional phase in which food sensitization might have improved but sensitization to aeroallergens has not yet taken hold. However, it also appears to suggest that we were studying an unbiased population because there was not a higher than expected rate of atopy.

We performed open, rather than double-blind, challenges to confirm peanut allergy. Although double-blind food challenges are considered a gold standard, these are cumbersome and not always practical in diagnosing food allergy. There is no evidence to suggest that double-blind challenge is more accurate than open challenge for peanut allergy, especially if objective signs, such as lip swelling or rash, are criteria for positivity. The only study available at present comparing open challenges with double-blind challenges was done by Kaila et al²⁰ in children with suspected cow's milk allergy. No data are available at present comparing double-blind food challenge with open challenge outcomes in peanut allergy. Because we were mainly interested in making a clinical diagnosis in these children, and in view of the lack of evidence in favor of a specific approach, we opted for the less invasive procedure, namely open challenge.

This increase in the prevalence of peanut allergy can not be explained by a general increase in atopy. A possible explanation is increased exposure to peanut in early life and possibly in utero.¹³ Frank et al²¹ suggested that consumption of peanut by the mother during pregnancy and its early introduction to the infant's diet increases the likelihood of peanut sensitization. Hourihane et al⁸ also found a definite decrease in age of onset of peanut allergy over the last 10 years. This might be related to the increased number of foods with small amounts of hidden nuts suitable for young children or the availability of nuts in the form that can be given to young children, such as peanut butter. Increasing numbers of families have become vegetarian or supplement their diet with vegetarian foods, which often contain nuts, particularly peanuts, which are relatively cheap.

Infants can also be exposed to peanut through breast milk. Vadas et al²² have recently analyzed the breast milk of 23 mothers and detected peanut protein in 11 subjects. Both of the major peanut allergens, Ara h 1 and Ara h 2, were detected, providing the potential for sensitization in at-risk infants being breast-fed. Our data tend to support this hypothesis because 88% of children who were sensitized to peanut had been breast-fed for at least a month. All but one child proven to be allergic had been breast-fed for more than a month. Although numbers of symptomatic children are relatively small, our data suggest that it might be necessary for mothers of high-risk infants to avoid eating nuts while breast-feeding.

We have clearly shown a relationship between SPT wheal size and the probability of a positive reaction on

challenge, confirming previous reports.^{8,15} Pucar et al²³ have previously shown that children with a negative SPT response to peanut do not react on open challenge. This is in agreement with our experience in allergy clinics, where we have never seen a positive oral challenge result to peanut in a child with a negative SPT response. However, Sporik et al¹⁷ did report 2 positive reactions in children with negative SPT responses among 95 oral challenges to peanut. They also suggested that a wheal diameter of equal to or greater than 8 mm was invariably associated with an adverse reaction on peanut challenge. By using this measurement as a cut-off point, it might be possible to reduce the requirement for peanut challenges. In our study there were 2 children with an SPT response to peanut of greater than 8 mm who did not have a positive reaction on challenge. Pucar et al²³ also reported 9 patients with a wheal size equal to or greater than 10 mm who had a negative peanut challenge result. Although SPT size provides an indication of the patient's clinical reactivity, it does not obviate the need for oral challenge in those who have not previously been exposed to peanut or in whom the historical evidence is not convincing.

Peanut allergy is becoming an increasing health problem. This might be due to increased exposure to peanut during early life, and lactating mothers should perhaps avoid eating peanut if there is a history of atopy in the immediate family. SPTs cannot be relied on for the definitive diagnosis of peanut allergy, and oral challenges are required if the history is not convincing.

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