

Original article

The impact of government advice to pregnant mothers regarding peanut avoidance on the prevalence of peanut allergy in United Kingdom children at school entry

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Background: In June 1998, the United Kingdom government suggested that atopic pregnant and breast-feeding mothers and their infants should avoid peanuts.

Objective: We report the prevalence of peanut sensitization in the first school cohort (2003-2005) to have been conceived after the advice was issued.

Method: A total of 1072 mother-child pairs were studied in school. Children with positive peanut skin prick test results to peanut had peanut challenges.

Results: Overall, 61% of 957 mothers recalled hearing the advice about peanuts in 1998. This figure was unaffected by maternal atopic status. Only 36 mothers (3.8%) followed the Government's advice by stopping the consumption of peanuts while pregnant. Maternal atopy had no effect on peanut consumption while breast-feeding. Mothers were less likely to change their diet if having a second or subsequent child compared with mothers having their first child (odds ratio 0.635, 95% CIs, 0.543-0.743; $P < .01$). Thirty children (2.8%; 95% CIs, 1.8% to 3.8%) had a positive peanut skin prick test result. Twenty children (1.8%; 95% CIs, 1.1% to 2.7%) were shown to have peanut allergy. This is the highest prevalence for peanut allergy recorded to date.

Conclusions: The prevalence of peanut sensitization in this cohort is 2.8%, and peanut allergy now affects 1.8% of British children at school entry. It is difficult to ascertain any impact (either positive or negative) of the United Kingdom government advice on the prevalence of peanut allergy in British children aged 4-5 years from 2003 to 2005.

Clinical implications: It remains uncertain if peanut avoidance during pregnancy and breast-feeding has any effect on the prevalence of peanut allergy in children. (J Allergy Clin Immunol ■■■■;■■■:■■■-■■■.)

Key words: Anaphylaxis, children, double-blind placebo-controlled food challenge, peanut allergy, prevalence

Peanut allergy starts early in life and persists in most cases. Management depends on awareness of the peanut allergy and on the appropriate provision of rescue medication.¹ In addition to the medical consequences of the peanut allergy, the consequent dietary and social restrictions can significantly impair the quality of life of those persons affected.²

In June 1998, the United Kingdom (UK) government's Chief Medical Officer's Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) published a report on peanut allergy. The key recommendation of this report was that "pregnant women who are atopic or for whom the father or any sibling of the unborn child has an atopic disease, may wish to avoid eating peanuts and peanut products during pregnancy and breast feeding." Furthermore, it was recommended that the infants should not be exposed to these products until 3 years of age. This precautionary advice was issued because of the uncertainty about the link between maternal peanut consumption and peanut allergy, and it was considered unwise to discount possible sensitization of offspring resulting from maternal exposure to allergen.³ No other government has issued such advice to families at high risk of having children that develop allergies. It has been a concern that the advice could possibly have adversely affected (increased) the prevalence of peanut allergy in the UK rather than decreasing the prevalence, as was the intention. It has also been suggested the COT advice may have been acted upon by non-high-risk families, to whom the advice was not targeted.

Avoidance diets in pregnancy are no longer advocated as a means of primary prophylaxis of allergic disease. The European Academy of Allergology, Asthma and Clinical Immunology has recently concluded that allergen avoidance

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Abbreviations used

COT: Committee on Toxicity of Chemicals in Food,
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DBPCFC: Double-blind, placebo-controlled food challenge

OR: Odds ratio

SPT: Skin prick test

UK: United Kingdom

diets while breast-feeding are now recommended only if a breastfed child is showing symptoms of food-related diseases such as eczema.⁴

The prevalence of sensitization to peanuts in the UK was found to have more than doubled from 1.3% to 3.3% in 2 single-center birth cohorts born in 1989-1990 and 1994-1996, that is, children born before the COT advice on peanut avoidance. The ages of the cohorts at testing and the study protocols were slightly different, with the tests on 4-5-year-old children being reported by Tariq et al⁵ and 3-to-4-year-old children by Grundy et al.⁶

We have assessed whether the COT advice had been acted upon by its intended audience and whether it had any measurable impact on the prevalence of peanut allergy. We measured the prevalence of sensitization and allergy to peanut in the first school-entry cohort of children that were conceived after the date of publication of the COT report in June 1998, using the current gold standard diagnostic method, the double-blind, placebo-controlled food challenge (DBPCFC).⁷

METHODS

This study was approved by the appropriate Local Research Ethics Committees (study reference numbers 062/03/t, Southampton, and 03/SM/183, Manchester). Between September 2003 and August 2005, we studied children born between March 1999 (9 months after the COT report) and March 2000. Families were recruited through primary schools in Southampton and Manchester, UK. These cities were chosen because of the local availability of integrated, complete pediatric allergy services.

Information sheets about the study were sent home from school with the children, and research staff attended the schools to recruit interested families directly. At an arranged appointment in the school, a questionnaire was administered to the mother (mothers exclusively were recruited) face to face, by the same research staff member, 1 only in each city. Answers were entered directly onto a laptop computer using SPSS data entry software (SPSS Inc, Chicago, Ill). Data were collected about family structure, maternal and paternal allergic conditions, smoking habits, and maternal recall of the COT advice. Mothers were asked to recall their consumption, while pregnant and breast-feeding the index child, of explicit foods known to them or to the research team to contain peanuts or peanut products. Children were evaluated for maternal recall of the child's peanut consumption in infancy, current or resolved allergic conditions, and for sensitization to common food and aeroallergens, using skin prick tests (SPTs). SPTs were performed with single-tine lancets, pricking the skin at an angle of 90 degrees. The wheal diameter, recorded at 15 minutes, was the mean of 2 perpendicular diameters. SPT results for peanut were considered positive if the wheal was greater than or equal to 3 mm, in the presence of a negative control (saline) and at least a

3-mm wheal to histamine (1:10w/v). Skin test reagents were from ALK-Abelló, Hungerford, UK. All children with positive screening SPT results to peanut were offered a blood sample for peanut-specific IgE, which was performed in each center using the Immucap system (Phadia, Uppsala, Sweden), according to manufacturer's instructions. Formal DBPCFC with peanut was used to confirm the diagnosis, with written parental consent, although it was not performed if a reaction had occurred recently (within 1 year) and skin and specific IGE measurements suggested the presence of the peanut allergy.⁸ Peanut challenges were performed using identical protocols in each center, using peanut flour-based biscuits, prepared in Southampton by an experienced dietician (K.E.C.G.), for use in both units. Children were admitted as day cases to the Children's Day Ward in Manchester or to the Wellcome Trust Clinical Research Facility in Southampton. The doses of peanut protein administered at 30-minute intervals were, 1 mg, 10 mg, 100 mg, 1 g, and 5 g. The end point of the challenge was the identification of an objective allergic reaction with clinical signs or completion of the full challenge with no such signs up to 2 hours after the last dose.^{7,8}

STATISTICS

Data were analysed using SPSS software (version 11.0). The sample size of 1000 was calculated using a 2-sided 95% CI, based on the large sample approximation for the difference between a previous study proportion of 0.616% (6/981 cases)⁵ and a new study proportion of 1.6% (16 cases/1000) extending 0.919% from the observed difference in proportions when the sample sizes are 981 and 1000, respectively. Descriptive analyses were performed with a *P* value $\leq .05$ considered significant. Categorical data were analysed using a χ^2 or Fisher exact test as appropriate. Univariate and multivariate logistic regression were used to explore associations between independent variables and outcome variables. Separate univariate and multivariate models were built using: (1) maternal diet change (yes/no); and (2) peanut allergy status (yes/no) as the 2 outcome variables.

Univariate and multivariate logistic regression analyses were used to explore associations between independent and outcome variables and the significance and weight of each predictor. All variables found significant at the *P* < .05 level were explored further in multivariate models. Multiple logistic regression analysis was used to simultaneously adjust for the independent variables. Independent variables included in the final models were selected based on selected χ^2 analysis. Variables were assessed by using a hierarchical block entry protocol. Nonsignificant predictors were included in both univariate and multivariate models as covariates to investigate possible moderating or mediating influences on outcome variables. All variables related to: (1) risk of confirmed food allergy in children; (2) risk of confirmed food sensitization in children; and (3) likelihood of remembering hearing government (COT) advice. The small sample size or events of interest (in this study, change of maternal diet and the prevalence of peanut sensitization and allergy) did not allow for the inclusion of a large number of independent variables in the logistic regression because of risk of "overfitting."

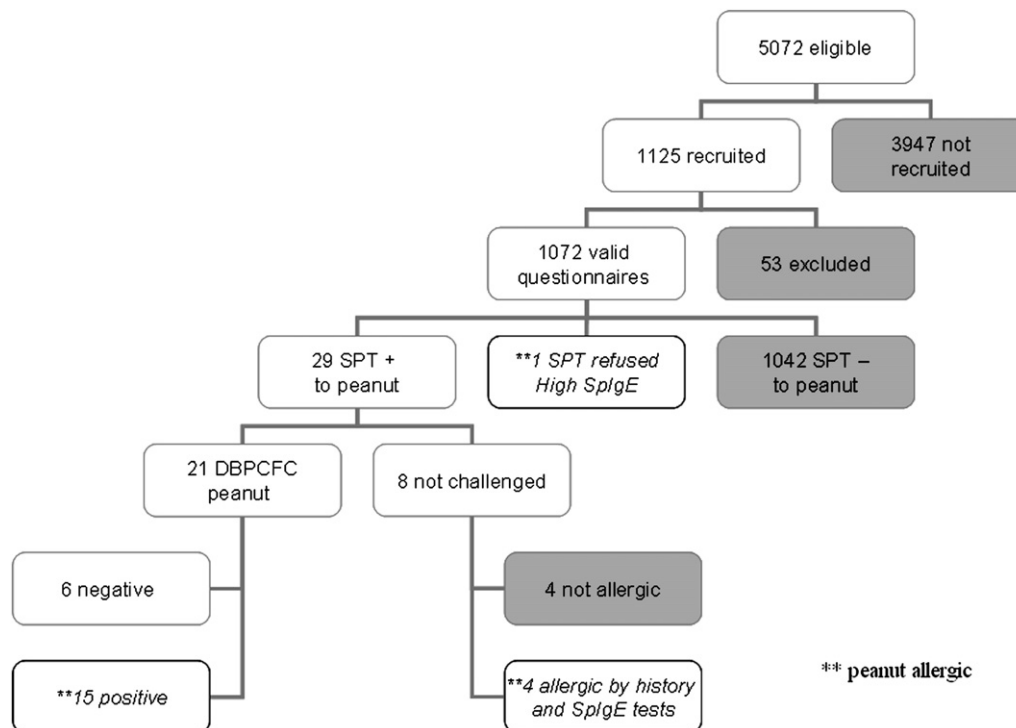


FIG 1. Flow chart for the study.

RESULTS

Recruitment

Families were recruited in 41 schools in Southampton and 73 schools in Manchester. In Southampton, 477 of 1785 eligible families were recruited (26%). In Manchester, 648 of 3287 eligible families were recruited (19%; $P = .001$). The overall recruitment was 1125 families out of 5072 eligible families (22%). Thirty-one families were excluded as SPT was refused or declined by the family; in nearly all cases (30/31), this refusal was because of the child refusing SPT after questionnaire data had been collected. Twenty-one families were excluded because the families had not been resident in the UK at the time of the COT report or the child had been born outside the UK. The final total of eligible families studied was 1072 (Fig 1).

Maternal recall of peanut consumption while pregnant. Data regarding maternal and maternally reported paternal atopic conditions are shown in Table I. Maternal recall of the COT advice was equal in each city, and change of maternal diet was not significantly different in each city (data not shown). The effect of the COT advice on maternal peanut consumption is shown in Fig 2. Maternal atopy had no effect on recall of the COT advice or on dietary changes made on its recommendations (data not shown). Only 36 mothers (10% of those who changed their diet, 6% of those who recalled the advice, and only 3.8% of the whole group) followed the COT advice by stopping consumption of peanuts while pregnant. Mothers who exclusively breastfed their babies reported

TABLE I. Family data (n = 1072)

Mother atopic	476 (45%)
Father atopic (by maternal report)	400 (38%)
Median number of children	2 (1-11)
Birth order of screened child (aged 4-5 y)	1 (median), 1-8
Consumed peanuts while pregnant	611 (57%)
Consumed peanuts while breast-feeding	294 (27%)
Screened child	1072
Current asthma	88 (8%)
Ever had asthma	206 (19%)
Screened child	1072
Current rhinitis	47 (4.4%)
Ever had rhinitis	104 (10%)
Screened child	1072
Current eczema	204 (19%)
Ever had eczema	474 (44%)

a lower consumption of any peanut while breast-feeding (267/670, 40%) than while they had been pregnant (370/670, 55%; $P < .001$). A total of 20/427 (4.6%) atopic and 19/525 (3.6%) nonatopic mothers stopped eating peanut ($P = 0.92$). Overall, 328 (42%) mothers reduced their peanut consumption but did not eliminate peanut from their diet.

Logistic regression analysis

The estimated odds ratios (ORs) with 95% CIs for associations between independent risk factors and maternal diet change are presented in Table II.

Birth order and paternal atopy were associated with maternal diet change. Maternal atopy did not show a

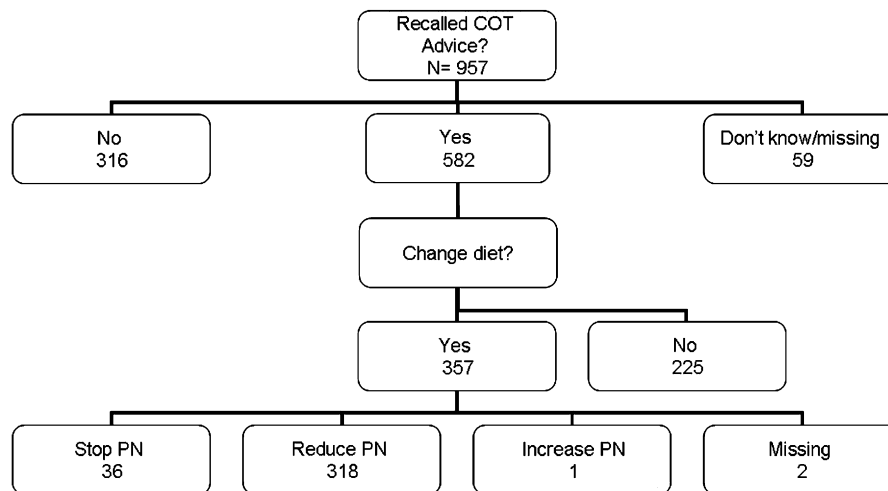


FIG 2. Maternal recall of the COT advice, excluding those who never ate peanuts (n = 111).

significant association. Paternal atopy was significantly associated with maternal diet change even after adjusting for birth order. Mothers with more than 1 child were a third less likely to eliminate or reduce peanuts/peanut-containing products from their diets during pregnancy and breast-feeding. In cases where father was found to be atopic, the odds of mothers changing their diets were a third greater than when the father was not atopic. The significant association of paternal atopy was no longer evident when adjusted for the effect of siblings with a history of allergic disease and a mother who had never consumed peanuts. No other significant associations were found.

Maternal recall of peanut consumption while breast-feeding. A total of 688 mothers who had consumed peanuts regularly before becoming pregnant ultimately breastfed their infant, either exclusively (602) or with formula feeds (86). Overall, 318/688 (46%) changed their diet while pregnant, but only 35 (5%) completely stopped eating peanuts. The remainder merely reduced peanut consumption while pregnant. A total of 282/688 mothers (41%) who breastfed thought they had eaten peanuts while breast-feeding.

Peanut sensitization of children

Overall, 197 children (18%) had 1 or more positive SPT results to the panel of allergens tested. A total of 695 children (65%) were reported by their mothers to have consumed peanuts. The mean age of introduction of peanut was 36 months, which is much later than the 12.6 months reported for the first Isle of Wight cohort.⁵ The prevalence of known peanut allergy was 9/1072 (0.8%). Twenty-nine children were found to have a positive SPT response to peanuts. One child was considered to be peanut allergic, but his parent refused an SPT; he had a known peanut allergy and high peanut antibody levels (>100 KUa/L). Thirty children with positive SPT results or high peanut-specific IgEs provided a prevalence of peanut sensitization of 30/1072 (2.8%) (95% CIs, 1.8% to 3.8%) (Fig 2 and Table III).

TABLE II. ORs for risk of confirmed peanut allergy, for risk of confirmed peanut sensitization in children, and for the increased likelihood of diet change in response to COT advice*

	OR (95% CI)	P value
Likelihood of diet change		
Jointly entered in the same model		
Birth order	.635 (.543-.743)	.00
Paternal atopy	1.33 (1.03-1.72)	.02
Confirmed peanut allergy†		
Separate effects		
Breast-feeding‡	3.50 (1.00-11.70)	.05
History of eczema	4.73 (1.80-12.61)	.002
Jointly entered in the same model		
Breast-feeding‡	(1.00-10.80)	.06
History of eczema	7.05 (2.05-24.25)	.000
Confirmed peanut sensitization†		
Jointly entered in the same model		
History of allergic rhinitis	8.21 (1.38-9.72)	.02
History of eczema	3.45 (1.42-8.33)	.006

*Adjusted for child sex, birth order, sibling atopy, current parental atopy, sibling atopy, marital status, parent country of birth, permanent residence in UK in 1998, parental smoking, level of peanut consumption before pregnancy, level of peanut consumption before first antenatal visit, and level of peanut consumption during pregnancy.

†Two extra variables included just for peanut allergy and peanut sensitization were diet change following COT advice and mixed rather than exclusive breast-feeding.

‡Exclusive breast-feeding.

Overall, 9/30 subjects declined the offer of a food challenge. Four of these subjects were considered likely to have a peanut allergy according to the agreed criteria outlined above and are considered allergic. Four children who refused challenge were considered uncertain to be peanut allergic and have not been included in the estimate of prevalence (Table III). Six challenges were negative, and 15 were positive. A total of 20/1072 subjects were considered to have the peanut allergy (15 by challenge and 5 by strong positive recent history and supportive

TABLE III. Prevalence of peanut allergy in 3 UK studies 1996-2006

Study	No. of children studied	Year of birth	Age of child when studied (y)	Method of testing	Prevalence of peanut sensitization (95% CIs)	Prevalence of peanut allergy (95% CIs)
Tariq et al ⁵	981	1989-1990	4-5	SPT	1.1% (0.5-1.6)	0.5% (0.1-0.8)
Grundy et al ⁶	1246	1994-1995	3-4	SPT OFC	3.3% (2.3-4.3)	1% (0.8-2.1)
Hourihane et al, 2007	1072	1999-2000	4-5	SPT, SpIgE DBPCFC	2.8% (1.8-3.8)	1.8% (1.1-2.7)

OFC, Open food challenge; *spIgE*, specific IgE.

skin and blood test results), which provides a prevalence of peanut allergy of 1.8% (95% CIs, 1.1% to 2.7%) in this cohort of school-entry children born from 1999 to 2000 (Table III). These data represent a real increase in prevalence compared with the Isle of Wight cohort of children born in 1989, before the COT report.⁵ Children shown to have peanut allergy were more likely than non-peanut-allergic children to report either “ever” or “current” asthma, eczema, and rhinitis (data not shown).

No difference was found in the rate of change of peanut consumption between mothers whose children became peanut sensitized and those whose children were not sensitized to peanut (data not shown). Of the 20 children with peanut allergy, 9 had mothers who were atopic and 10 had mothers who were not atopic, whereas 1 mother's atopy status is not recorded. Mothers of 8 (40%) of the 20 children with peanut allergies recalled changing their peanut consumption while pregnant, although only 1 completely stopped eating peanuts. So it seems that the avoidance (or consumption) of peanuts during pregnancy had no effect on the prevalence of peanut allergy in either atopic or nonatopic mothers. Five of these 8 (62.5%) were atopic mothers, and only 2 of the 10 (20%) nonatopic mothers changed their diet; the remaining “changer” was of unknown atopic status.

Peanut was introduced into the diet of children shown to be peanut sensitized at a mean age of 32 months and to the diet of nonsensitized children at 29 months ($P = .42$).

A history of eczema was found to be a significant predictor of peanut allergy (Table II). Children with peanut allergies were 7.4 times more likely to have symptoms of eczema. Type of feeding was also an important risk factor for peanut allergy. Feeding type was significantly associated ($P < .05$) with peanut allergy; children who were breastfed were 3.8 times more likely to be found to have peanut allergies than those who were bottlefed. When this association was adjusted for the presence of eczema, the effect was attenuated (Table II). No other significant associations were found.

DISCUSSION

We have demonstrated here that a significant increase has occurred in the prevalence of peanut allergy from 0.6% to 1.8% in the UK during the last 10 years. This figure is also higher than that reported from a similar study in Canada.⁹ However, we have not yet ascertained any positive or negative effect on the prevalence of peanut

sensitization or peanut allergy of the COT advice to atopic mothers about their own and their child's consumption of peanuts.

It seems that most mothers recalled hearing the COT advice when they were pregnant, but that only 3% to 4% adhered to the advice while pregnant and 5% while breast-feeding, for reasons that remain unclear. Maternal allergy status does not seem to have been an important factor in any decision taken about peanut consumption while pregnant or breast-feeding. Interestingly birth order and paternal atopy had moderate effects. It is not possible to determine whether this effect of paternal atopy is meaningful. Government advice seems not to have had a significant impact on mothers' diets and seems to have been assimilated by the general population, rather than acted upon by the target group identified as at highest risk of having children who would develop allergies. This result needs to be taken into account when advice is formulated and published in the future.

It seems that peanuts have been introduced to the diet of this group of patients at a much later age (36 months) than the 12.6 months reported for the 1989 Isle of Wight birth cohort,⁵ but this has not affected the prevalence of peanut allergy.

Our study has limitations that must be acknowledged. Obviously there is potential for recall bias as mothers were asked to remember their dietary intake of peanuts while pregnant between 5 and 6 years ago. The opportunity to prospectively follow-up a cohort from birth was not available at the time of the implementation of COT advice. However, it is also possible that prospective follow-up may have influenced dietary habits. Only 25% of eligible children were recruited in the 2 sites, so our estimates of prevalence could conceivably be overestimates or underestimates. Checking our clinic records and prospectively seeking eligible children coming to clinic did not identify existing cases that were not being captured, so our figures are unlikely to be an underestimate, especially considering local referral practices in each area, with identified pathways to the relevant clinic being well established. Families may have been reluctant to subject their children who might have allergies to testing, particularly in a school setting. Our clinic experience suggests this reluctance is extremely unlikely, with many such families being characteristically very highly motivated to seek expert assistance for their children with allergies. Overall, 18% of children had 1 or more positive SPT results, which is consistent with recent data from slightly older children in the UK,¹⁰ which suggests our

cohort is representative of the UK population of 4-to-5-year-old children.

In conclusion, it seems that the COT advice on peanut allergen avoidance by pregnant women and breast-feeding mothers has not affected the prevalence on peanut allergy in children at school entry. It is possible that it has affected (increased) the age of introduction of peanut to the diet of children, but this has not had any discernible effect on the prevalence of peanut allergy either, as the children who became sensitized to peanuts had not had it introduced at a different age than those who became tolerant of peanuts. This study's primary finding of a prevalence of peanut allergy of 1.8% is the highest recorded prevalence to date.

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