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Papers

Clinical study of peanut and nut allergy in 62 consecutive patients: new features and associations

BMJ 1996; 312 doi: <https://doi-org.liverpool.idm.oclc.org/10.1136/bmj.312.7038.1074> (Published 27 April 1996)

Cite this as: BMJ 1996;312:1074

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- Accepted 9 January 1996

Abstract

Objective: To investigate clinical features of acute allergic reactions to peanuts and other nuts.

Design: Analysis of data from consecutive patients seen by one doctor over one year in an allergy clinic at a regional referral centre.

Subjects: 62 patients aged 11 months to 53 years seen between October 1993 and September 1994.

Main outcome measures: Type and severity of allergic reactions, age at onset of symptoms, type of nut causing allergy, results of skin prick tests, and incidence of other allergic diseases and associated allergies.

Results: Peanuts were the commonest cause of allergy (47) followed by Brazil nut (18), almond (14), and hazelnut (13). Onset of allergic symptoms occurred by the age of 2 years in 33/60 and by the age of 7 in 55/60. Peanuts accounted for all allergies in children sensitised in the first year of life and for 82% (27/33) of allergies in children sensitised by the third year of life. Multiple allergies appeared progressively with age. The commonest symptom was facial angioedema, and the major feature accounting for life threatening reactions was laryngeal oedema. Hypotension was uncommon. Of 55 patients, 53 were atopic—that is, had positive skin results of tests to common inhaled allergens—and all 53 had other allergic disorders (asthma, rhinitis, eczema) due to several inhaled allergens and other foods.

Conclusions: Sensitisation, mainly to peanuts, is occurring in very young children, and multiple peanut/nut allergies appear progressively. Peanut and nut allergy is becoming common and can cause life threatening reactions. The main danger is laryngeal oedema. Young atopic children should avoid peanuts and nuts to prevent the development of this allergy.

Key messages

The main danger is laryngeal oedema and asphyxia

Avoidance is the key to management but can be difficult to achieve as peanuts and nuts are hidden in foods

Children with peanut allergy are at increased risk of developing allergy to tree nuts

Most patients have other common allergies, and avoidance of peanuts and nuts in this at risk group should be considered

Introduction

There has been a considerable increase in the rate of referrals for food allergy, but the most obvious rise has been in cases of peanut and nut allergy. Many of these patients have had serious reactions, some of them life threatening. Reports of deaths due to peanut or nut allergy in healthy young people in the United Kingdom appear in the press; six patients died of peanut allergy in 1993, and there are case reports of fatal anaphylaxis.^{1 2 3} There have been few reviews of peanut and nut allergy^{4 5} and hardly any studies giving a detailed clinical analysis of reactions.^{6 7 8} Most clinical papers are case reports^{3 9} or are reports on small numbers of patients.¹⁰ Comparatively little is known of the natural history of the disorder.^{11 12} The appropriate management is not always clear cut.

I report on 62 consecutive cases that I saw over one year in the allergy clinic at Addenbrooke's Hospital. I present data on the incidence of allergy to peanuts and different nuts (peanuts are a legume and therefore distinct from nuts), the age of onset of symptoms, and risk factors for the development of this allergy.

Patients and methods

I saw 62 consecutive patients between October 1993 and September 1994. Most presented in childhood: 23 between the ages of 11 months and 5 years and 52 under the age of 18 years. Of the 10 adults, eight were aged between 19 and 32.

HISTORY

A detailed history was taken. This included precise clinical details and timing of the reaction(s); the nature of the food ingested before the reaction(s); an assessment of the amount of putative allergen (peanut or nut) ingested; treatment given; and outcome. The age at onset of reactions, as well as the effect of all types of nuts, was noted. A full allergy history was taken to identify other possibly atopic disorders, particularly asthma, rhinitis, and eczema, and the probable allergens causing them. This included inquiry about the effects of exposure to house dust mite, pollens, seasonal moulds, animal danders, other foods, and drugs. Specific inquiry was made about reaction to pulses (peas, beans, lentils, etc). All drug treatment was noted and whether patients already used inhaled drugs for asthma and had a good technique for using the inhaler. In the case of babies or children those responsible for their care were identified and whether the child had food away from home (including school meals) was determined. Nasal, conjunctival, chest, and skin examinations were performed, and except in toddlers, respiratory function was assessed by measurement of peak expiratory flow, forced expiratory volume in one second, and vital capacity.

SKIN PRICK TESTS

Skin prick tests were performed to detect specific IgE antibodies. Adults were tested with peanut, Brazil nut, hazelnut, almond, and walnut extracts (Soluprick, ALK) and with our routine screen of 13 allergens (including house dust mite and grass, tree, shrub, and weed pollen, alternaria, cladosporium, cat dander, egg, milk, wheat, and mixed nuts (containing Brazil nut, hazelnut, almond, walnut, and chestnut; Bencard) as well as positive (histamine) and negative (saline) controls). Additional allergens, particularly other foods, were added depending on the history. Fresh 10% weight/volume aqueous extracts were prepared for certain foods and cashew nuts, and for some fruits the skin was pricked directly through fresh fruit.

In young children a reduced range of skin tests was performed, the number and type being determined by the history and the child's age and cooperation. Peanut and mixed nut extract were always tested, but individual nuts and common inhalant allergens (house dust mite, grass pollen, and cat dander) were often added. It was usually possible to carry out five skin tests in children aged 1-2 years (three allergens). The weal diameter was recorded at 10-15 minutes.

Results

TYPE OF NUT CAUSING ALLERGY

Table 1 gives details of the individual "nuts" to which patients were sensitive. Several patients were allergic to several nuts so that there were 103 nut or peanut allergies in 62 patients. Peanuts were the commonest cause of allergy (47 patients), followed by Brazil nut (18), almond (14), hazelnut (13), and walnut (8). Allergy to cashew nuts was rare (three patients). A single allergy, to one nut or to peanut alone, was seen in 37/62 patients and multiple allergy in 25 patients (the sensitivities included peanut in 19 of them).

Main cause of allergy	No of patients
Peanut alone	28
Peanut plus other nuts	12
Brazil nut alone	4
Brazil nut plus other nuts	8
Almond	2
Almond plus other nuts	3
Hazelnut	1
Hazelnut plus other nuts	1
Walnut	2
Cashew nut	1

- *When patients were allergic to several nuts, the one causing the most severe allergic reaction is given.

Table 1

Incidence of allergy to different nuts or to pea- nutin 62 patients*

AGE AT ONSET OF SYMPTOMS

Sensitisation to peanut or nut occurred at an early age and considerably earlier than the age at presentation.

Table 2 shows the cumulative figures for sensitisation in relation to age: 33/60 (55%) patients were sensitised by the third year of life, 11 of them in the first year—that is, before the age of 12 months. A total of 55/60 (92%) were

sensitised by the age of 7 years. Peanut was the dominant allergen to cause sensitisation in young children, accounting for all of those sensitised in the first year and 82% in the third year (table 2). In very young children single allergy to peanut was almost exclusively seen, but as children became older multiple allergies developed progressively (table 2): during the first year of life all 11 children were allergic to peanut alone, whereas by the age of 7, 15 of the 41 children allergic to peanuts were also allergic to other nuts.

Age at onset of allergy	No of patients (cumulative)	No (%) allergic to peanut (with or without other nuts)	No % allergic to peanut alone
Onset as young children During 1st year of life	11	11 (100)	11 (100)
By 2nd year of life	24	23 (96)	21 (88)
By 3rd year of life	33	27 (82)	24 (73)
Up to age 5	52	39 (75)	25 (48)
Up to age 7	55	41 (75)	26 (47)
Onset in teens or older Teens onward	5	1 (20)	0 (0)

- *Data unknown in two of the 62 patients in this series.

Table 2

Age at onset of allergic reactions to peanut or nuts and incidence of reactivity to peanut in relation to age in 60 patients*

When the age of onset of symptoms was analysed in relation to whether patients presented as a child (up to 17 years) or as an adult (18 years and over), more of those presenting earlier had been sensitised earlier: 30/48 (63%) v 3/12 (25%) becoming allergic by the age of 2 years, the figures being 43/48 (90%) v 8/12 (66%) for allergy by the age of 5 years. This suggests that sensitisation is occurring earlier, in keeping with my impression that the increased incidence of peanut or nut allergy is real and not attributable only to increased awareness and referral.

CLINICAL FEATURES

Table 3 shows the clinical features of the most severe reaction each patient had suffered. Reactions have been grouped into different categories: cutaneous (angioedema and urticaria); with respiratory involvement (subdivided clinically into laryngeal oedema and asthma); and with hypotension or loss of consciousness. Patients often had multiple symptoms, but the most common problem was facial angioedema. This occurred in 52 patients (16 of the cutaneous group; 33 of the group with respiratory involvement; and three of those with hypotension or loss of consciousness). Respiratory involvement varied from extremely mild laryngeal oedema (an abnormal sensation or a feeling of fullness in the throat) to distinct respiratory difficulty. The two patients who lost consciousness both had severe laryngeal oedema and asphyxia. It is not possible to determine the relative contributions of anoxia and hypotension to the loss of consciousness, but anoxia seemed to be more important from the history.

Reaction	No of patients	No with vomiting
Cutaneous only:		
Contact urticaria or oral pruritus	3	1
Facial angioedema and/or facial urticaria [*]	13	2
Facial angioedema and generalised urticaria	4	0
Respiratory tract involvement (facial angioedema and respiratory symptoms ⁺):		
Laryngeal oedema	27	5
Asthma	6	0
Hypotension or loss of consciousness: Fall in blood pressure ⁺⁺	7	2
Loss in consciousness ^{&}	2	0

- *Most had angioedema. Facial urticaria alone was rare.
- +Ranged in severity from minor to severe.
- ++Three children became floppy; four subjects were faint with documented hypotension.
- &Dominant problem was severe laryngeal oedema with asphyxia.

Table 3

Clinical features of most severe reaction to peanut or nut in each patient. Reactions are categorised using most severe reaction (patients may have had more than one reaction, and minor symptoms are not listed)

PATIENTS WITH LIFE THREATENING REACTIONS

Table 4 shows the clinical features of the reactions in the four patients with the most severe reactions. All were adults who were aware of their allergy and had inadvertently ingested nuts. Facial oedema was generally not a feature, occurring only in one patient who had mild oedema of the lips. In all of these patients reactions began quickly, within a few minutes of ingestion of the allergen, with angioedema or pruritus, or both, inside the mouth. This progressed rapidly to severe choking with a feeling of obstruction in the larynx (laryngeal oedema) and severe respiratory difficulty. Two probably also had asthma. Two patients (cases 1 and 2) had a respiratory arrest and lost consciousness and had to be intubated and ventilated. All were given adrenaline intramuscularly or subcutaneously.

Case No	1	2	3	4
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Case No	1	2	3	4
Age (years)	30	31	31	30
Sex	F	M	F	F
Clinical features Sequence of reactions	Angioedema inside mouth; laryngeal oedema (severe); asthma; vomiting; loss of consciousness	Angioedema of palate and lips; general erythema; laryngeal oedema (severe); choking; respiratory arrest; loss of consciousness	Angioedema of tongue; laryngeal oedema; urticaria	Itching mouth; laryngeal oedema (severe); dyspnoea; vomiting; light headedness
Intubated/ventilated	Yes	Yes	No	No
Adrenaline injection	Yes	Yes	Yes	Yes
Cause Allergen	Almond	Peanut	Brazil nut	Hazelnut
Amount ingested	Trace	Trace	Trace	Trace
Source	Essence in curry	Armenian food	Toffee with Brazil nut extract	Fragment in teaspoon of muesli
Test results Skin prick test weal diameter (mm)	0	10	11	10
Serum IgE (CAP)	6	6	2	3
Age (years) at onset of peanut/nut allergy	4	5	5	2
Asthma Severity	Severe	Mild	Severe	Moderate

Case No	1	2	3	4
Treatment	Inhaled steroids; intermittent oral steroids	Inhaled salbutamol; inhaled steroids ⁺	Inhaled steroids; intermittent oral steroids	Inhaled steroids
Cause	House dust mite	House dust mite	House dust mite; dog; cat	House dust mite; tree pollen; alternaria; cat; dog; guinea pig
Other allergies	Fish; grass pollen; peanut	Brazil nut; cashew nut; cat	Green pepper (anaphylaxis with respiratory arrest and loss of consciousness); aniseed; walnut; (egg and fish as child)	Grass pollen; peanut; Brazil nut
Rhinitis	Yes	Yes	Yes	Yes
Eczema	Yes	No	Yes	Yes

- *ImmunoCAP assay for specific IgE expressed as grade 0 to 6, where 6 is strongly positive.
- +Not taken by patient.

Table 4

Clinical features in four patients with most severe reactions

All of these patients had multiple allergies, including allergy to common inhalant allergens. There was a long history of allergic asthma due to house dust mite and other allergens. Two patients were, or had been, allergic to other foods. In one case (case 3) green pepper had caused a more severe reaction than nuts, with anaphylaxis that included respiratory arrest and loss of consciousness. She was given artificial ventilation for 24 hours. This reaction was shown to be mediated by IgE on skin testing. All four patients were allergic to more than one nut or peanut, and the nut allergy had been present since early childhood—that is, for about 25 years.

DIAGNOSIS

Allergy was diagnosed on the basis of the history combined with the results of skin prick tests to detect specific IgE antibodies. The history was of an acute reaction of varying severity, usually immediately after a food. Often the cause was obvious—for example, a reaction within a few minutes of starting to eat peanut butter; touching a nut; or eating a food subsequently found to contain nuts. Considerable amounts of time were spent in identifying all ingredients and writing to manufacturers. Sometimes nut content is not stated clearly—for example, nut essence or extracts (case 3, table 4). Indian and Chinese restaurants were telephoned to establish ingredients of particular dishes—for example, almond essence in case 1 (table 4). Skin prick tests confirmed or made the diagnosis in 61 of the 62 patients. Weals were often large, commonly in the range 8-15 mm diameter. In only one patient (case 1, table 4) was the result of the skin test repeatedly negative, and the diagnosis was confirmed by detection of serum IgE to almond by ImmunoCAP assay.

Results of skin tests were sometimes positive when the patient was not clinically allergic to that allergen—that is, they could eat that nut without reaction. This is well recognised for common allergens, when the results of skin tests are positive in about 40% of the population, but only about one third of these develop allergic symptoms.

ATOPIC STATUS AND OTHER ALLERGIES

Skin prick tests to common allergens were performed in 55 patients (seven babies and toddlers were not tested): 53 (96%) were atopic—that is, had positive results to one or more of house dust mite, grass pollen, or cat dander. Of the 55, 42 (76%) had asthma, 40 (73%) rhinitis, and 33 (60%) eczema. The causative allergen(s) could be identified from the history and skin tests in most of them. Many of these patients developed symptoms on exposure to multiple allergens (table 5). As might be expected, house dust mite, grass pollen, and cat dander were the commonest causes of allergic disease. Some of the allergens caused serious reactions—for example, anaphylaxis with loss of consciousness and respiratory arrest due to allergy to green pepper; severe angioedema due to egg; laryngeal oedema caused by parsnips in a patient in whom exposure to parsnips cooking caused rhinoconjunctivitis. Of the seven who did not have skin tests, six had eczema (one of these also had asthma) and one had no rhinitis, asthma, or eczema. In this subgroup it was not possible to determine whether these disorders were allergic.

Allergen	No of patients
House dust mite	38
Grass pollen	20
Tree pollen	2
Cat	19
Dog	8
Other animals	5
Alternaria	2
Latex	1
Other foods:	15
Egg	10
Milk	4
Pulses	4
Avocado	1

Allergen	No of patients
Banana	1
Fish	1
Other fruits/vegetables	3
Sesame	4

Table 5

Other allergies in 55 patients with peanut or nut allergy

Peanuts are a pulse, yet only four patients were allergic to other pulses (peas, lentils, beans, soya) and three of these were allergic to peanuts (and other nuts). In these three patients the reaction to pulses was less severe than that to peanuts. The other patient, who was not allergic to peanuts, was more allergic to the pulses than to nuts (almond and hazelnut). Even sitting at table with people who were eating peas or exposure to peas cooking induced periorbital oedema. Ingestion of peas, beans, mangetout, or lentils induced pruritus and angioedema of the oral, pharyngeal, and laryngeal mucosa. Skin prick tests yielded positive results to freshly prepared 10% weight per volume aqueous extracts of peas and lentils (beans not tested). Allergy to many fruits and vegetables (facial, oral, and laryngeal oedema) and to sesame occurred in some of these patients, confirmed by positive skin tests.

Discussion

PATTERNS OF SENSITISATION AND AGE AT ONSET

This study shows that different patterns of sensitisation occur: allergy to peanuts alone or to tree nuts alone, or to both. Patients allergic to peanuts should therefore be considered at risk of developing allergy to tree nuts as about one third of our series were allergic to both. While many patients had multiple peanut or nut allergies, peanut was the commonest cause: 47 of 62 (76%) patients reacted to peanuts, and peanut was the major allergy in 40 of these. Brazil nut was the next commonest cause. The incidence of allergy to each type of nut seemed broadly related to the relative amounts of each ingested in the population. Peanut was the commonest allergy, and consumption of peanuts has increased greatly. The average American is said to ingest 3.5 kg of peanuts annually. In contrast, cashew nut allergy was rare.

Early sensitisation (23 patients before the age of 2 years) was common and seen particularly with peanuts. This probably relates to early introduction of peanuts into the diet. Most of the small children reacted to peanut butter on bread, which had been given before the age of 1 year. Some children reacted to the first known exposure to peanuts, suggesting previous sensitisation—for example, from breast feeding or from peanut allergen hidden in foods—which raises the question of whether peanut oils in baby milks or infant foods are allergenic. This remains to be established. One study of only 10 adults allergic to peanut failed to show any reactivity to peanut oils,¹³ but there are case reports suggesting infants were allergic to infant formula that contained peanut oil.¹⁴ The diet of children one to two generations ago was much simpler, and peanuts or nuts were used less and introduced much later.

CLINICAL OBSERVATIONS

The commonest clinical feature was angioedema of the airways, usually associated with facial oedema and oedema of the oral mucosa. Hypotension was uncommon. In life threatening reactions, laryngeal oedema of rapid onset was important and probably the major problem, leading to asphyxia. Treatment should therefore be directed at this.

Skin prick tests made or confirmed the diagnosis in all but one patient. It is difficult to explain the failure in this patient, who had severe respiratory difficulty that required intubation and ventilation, had inadvertently ingested almond, and had a very high concentration of serum IgE antibody to almond. Skin tests with the same almond extract were reliable when used extensively in other patients. Skin prick tests were completely safe and did not cause any systemic reactions, in keeping with our experience of skin tests in anaphylaxis from other causes. They should, however, be performed in a setting such as an allergy clinic, where adrenaline is immediately available and there is skill in treating allergic reactions.

ATOPY AND ASSOCIATED ALLERGIES

Atopy (in 96%) and other clinical allergy (in 53 of the 55 atopic subjects) was a major feature. While common inhalant allergies were most common, it was striking that clear cut IgE mediated reactions, sometimes severe, to other foods occurred. Of other food allergies, egg allergy was commonest and usually presented with facial and laryngeal oedema and vomiting but sometimes with collapse. In the general population, about 40% are atopic (have positive results of skin prick tests to common inhaled allergens) and only about one third of these develop clinical allergy.¹⁵ In this study, the strong association with atopy and the fact that most atopic subjects were clinically allergic to common inhalant allergens suggests that peanut and nut allergy is occurring in a subpopulation with a strong propensity to develop allergies. There is probably a highly atopic at risk group, which could be identified in early childhood. Avoidance of the allergens during the period when sensitisation seems common, possibly to the age of 7 years, would be justified. There is a case for considering avoidance of peanuts—which are consumed mainly as peanut butter—in these children. The role of peanut oils as a source of allergen requires further investigation.

Peanuts are a legume or pulse and are therefore botanically distinct from nuts. Other legumes include peas, beans, and lentils. It was of interest that only four of our patients were also allergic to other pulses and that one of these patients was not even allergic to peanuts. Allergy to many fruits and vegetables and to sesame was also a feature of this group.

Avoidance is essential, and this requires education. No matter how careful patients are, however, absolute avoidance can be difficult to achieve. Deaths occur after inadvertent ingestion,^{1 2 3} and our patients with life threatening reactions were avoiding nuts. Problems faced by patients include inadequate labelling, no labelling (as in delicatessen foods, loose sweets), or ignorance in the general public—for example, waiters, caterers, or restaurateurs who fail to check for nut essence, powder, or oils in foods or who remove nuts from a food, not understanding that even contact can result in trace contamination sufficient to induce an allergic reaction.

Footnotes

- Funding No additional funding.
- Conflict of interest None.

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