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Randomised, double blind, crossover challenge study of allergenicity of peanut oils in subjects allergic to peanuts

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Objective: To determine the in vivo allergenicity of two grades of peanut oil for a large group of subjects with proved allergy to peanuts.
Design: Double blind, crossover food challenge with crude peanut oil and refined peanut oil.
Setting: Dedicated clinical investigation unit in a university hospital.
Subjects: 60 subjects allergic to peanuts; allergy was confirmed by challenge tests.
Outcome measures: Allergic reaction to the tested peanut oils
Results: None of the 60 subjects reacted to the refined oil; six (10%) reacted to the crude oil. Supervised peanut challenge caused considerably less severe reactions than subjects had reported previously.
Conclusions: Crude peanut oil caused allergic reactions in 10% of allergic subjects studied and should continue to be avoided. Refined peanut oil did not pose a risk to any of the subjects. It would be reasonable to recommend a change in labelling to distinguish refined from crude peanut oil.

Key messages

- Peanut (groundnut) allergy is the most common cause of deaths related to food allergy. Peanut oil is often suspected of causing reactions to meals in which a more obvious source of peanut cannot be found
- Refined peanut oil is odourless and flavourless and is commonly used in catering. Crude peanut oil, which is known to contain considerable amounts of protein is used only rarely, when a peanut flavour is deliberately required
- In vivo challenges of 60 subjects with proved peanut allergy showed no reaction to refined peanut oil, but six (10%) reacted to the crude peanut oil
- If refined peanut oil is used properly and is not reused after cooking peanuts, it seems to be safe for most people with peanut allergy; crude oil represents a risk
- The confusing use of the term groundnut oil should be stopped, and food labelling should distinguish between refined and crude oils

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People allergic to peanuts characteristically take great care in avoiding products containing peanut, but many are accidentally exposed to peanut.[1] Most fatal reactions to peanut occur outside the sufferer's home, often during restaurant meals, despite the person's best efforts to ensure the absence of peanuts from the meal.[2 3 4] Peanut allergy and the potential for fatal reaction to unseen peanut constitute a "sword of Damocles" over people who are allergic to peanut. One great concern has been the widely held belief that reactions can be caused by peanut oil–also known as groundnut or arachis oil–particularly when it is presented as "vegetable oil."

Highly processed oils, including peanut oil, form the vast majority of oils used in the food processing and catering industries and on sale to the general public. The oil is subjected to physical and chemical methods of purification, including degumming, refining, bleaching, and deodorisation. It is then generally referred to as refined peanut oil. Protein has not been detected in unused refined peanut oil.[5 6]

The absence of detectable protein in refined peanut oil means it should have no potential to cause allergic reactions when ingested by people allergic to peanut. If such an oil is used to cook peanuts, however, peanut protein can subsequently be detected in the previously pure oil.[6] Such contamination of an oil is potentially a great hazard to people with peanut allergy when they eat outside their home environment. The reuse of vegetable oils is widespread in British homes, particularly for deep fat frying, and in fast food outlets (for instance, in fish and chip shops). The reuse of a vegetable oil to cook potato chips after it had

been used to cook fish is considered to have caused the death of a person allergic to fish.[2]

Clearly, there is potential for reaction to less processed oils, known as cold pressed or crude peanut oils, though the degree to which this occurs has never been established. Crude peanut oils are strongly flavoured and have been shown to contain protein. Hoffman and Collins-Williams showed that one brand of crude peanut oil contained 3.3 µg of allergenic protein per millilitre of oil.[5]

The minimum amount of protein considered necessary to cause a reaction in a double blind, placebo controlled food challenge is between 50 mg and 100 mg.[7] [8] To consume 50 mg of peanut protein in crude peanut oil a person would need to drink more than 15 litres of crude peanut oil. It is clearly more practically relevant to evaluate the safety of peanut oil at the volumes that may be used in cooking. The label on an average 25 g packet of potato crisps (for example, Ready Salted, KP Foods, Leicester) states that the crisps contain 9.2 g of fat, which would be derived mostly from the vegetable oil used to fry the crisps.

The issue of the safety of peanut oils for people allergic to peanuts has been studied before but only in small series. Bock and Atkins safely administered up to 30 ml of purified oil to four subjects with confirmed peanut allergy.[1] Taylor *et al* reported that 10 subjects allergic to peanut did not react to peanut oil in glycerin capsules to a maximum dose of 5 ml of oil.[9] On the basis of population statistics and by assuming a true prevalence of reaction to the oil in 5% of sensitive subjects, the study of Taylor *et al* proved to a probability of only 40% that no reaction would be observed.[10] Furthermore, in their study the capsules of oil were swallowed whole, and the oil therefore bypassed the oral mucosa–the most common site of exposure and first symptoms.[11] Therefore there has been uncertainty surrounding the safety of peanut oils for people with peanut allergy.

A food challenge study with a sample size of more than 58 subjects who do not react to the test substance has a 95% probability of showing that a reaction is likely in less than 5% of affected people.[10] We compared the in vivo allergenicity of two peanut oils–crude peanut oil and refined peanut oil–in a double blind, crossover trial with 60 subjects with proved peanut allergy.

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Subject selection

From a group of 215 adult subjects who participated in a questionnaire study of peanut allergy conducted by the University of Southampton,[12] 69 subjects volunteered to participate in this study. All were skin prick tested with peanut (1:10 wt/vol peanut mix, (Runner, Virginia, Spanish) Miles, Indiana) and with each peanut oil. The result was considered positive if the test elicited a weal equal to or greater than the response to 1% histamine (positive control) in the absence of any reaction to saline (negative control). Subjects who had a negative skin prick test result with peanut were offered an open peanut

challenge to prove or disprove peanut allergy.[13] Subjects who had positive skin prick results with peanut undertook the oil challenges on the same day in a clinical investigation unit equipped for resuscitation.[14]

Historical reactions and reactions observed during the challenges were defined as mild, moderate, or severe. Mild reactions were pruritus, rhinoconjunctivitis, local urticaria, swollen lips swelling, and erythema. Moderate reactions were facial swelling and pharyngolaryngeal oedema. Reactions that were characterised by dyspnoea, wheeze, cyanosis, or hypotension were considered severe.

All subjects gave personal and informed written consent. This study was approved by the local hospital ethics subcommittee.

Double blind challenge protocol

The oils (crude or refined) were tested in random order determined by a member of staff not involved in the evaluation of the subjects. Forty subjects (63%) received the refined oil first. Each oil was administered in increasing doses of 1, 5, and 10 ml disguised with 0.1% peppermint oil or 1% cocoa malt flavouring. Six subjects were offered the oil with bread and one with soya milk. The remaining subjects were given the oil mixed with rice pudding. An interval of 10 to 15 minutes between the doses was allowed for observation of the onset of any symptoms. If a reaction occurred to the first oil at least an hour was allowed to elapse before the second oil was administered.

Peanut challenge

Protein comprises 24.3% of the average weight of a peanut kernel.[15] We found that 100 peanut kernels (roasted and salted, KP Foods, Leicester, bought in the hospital newsagent's shop) weighed 66.35 g. The average protein content of one peanut kernel was therefore 0.6635 gx24.3%=161 mg; 32 peanuts contain 5.16 g of protein.

If the subject reacted to neither oil up to the maximum dose of 10 ml (total dose 16 ml of each oil) a controlled open challenge with peanuts was undertaken. The peanut challenge was performed with increasing doses starting with peanut rubbed on the lip (labial challenge). The dose was increased in steps until a reaction was observed or until the subject had eaten up to an arbitrary total of 32 peanuts without reaction. Subjects were observed for one hour after the completion of the challenge or until one hour after any symptoms had subsided.

Results

Sixty nine subjects were enrolled (54 women). The mean (range) age was 26 years (14-48) years. Figure 1) summarises the study results.

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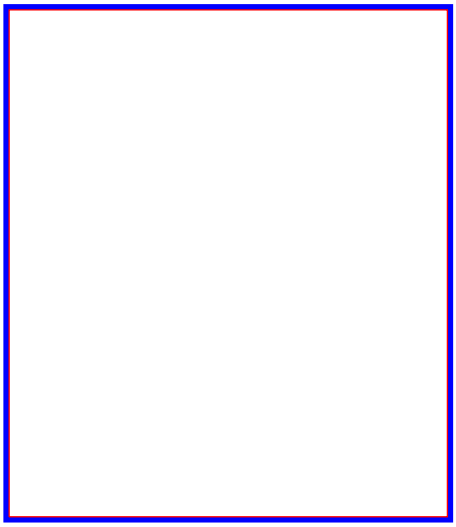

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Fig 1 Summary of study results

Skin prick tests

Seven subjects (10%) had negative results on skin prick tests with peanut, of whom six also had negative responses to challenge with peanuts. The remaining subject developed symptoms four days after exposure to peanuts and was therefore considered unsuitable for this study (table 1). The 62 remaining subjects (90%) underwent oil challenges.

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Table 1 Characteristics of nine subjects who proved not to be allergic to peanuts

Challenges

Oil challenges–No subject reacted to refined peanut oil. Six subjects (10%) reacted to crude oil (table 2).

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Table 2 Reactions to crude oil in six subjects

Peanut challenge–Fifty eight peanut challenges were undertaken by subjects who had positive results on skin prick testing with peanut. Four subjects who reacted positively to skin prick testing with peanut did

not have peanut challenges because they reacted to challenge with crude oil. Two subjects who had positive results on skin prick testing with peanut had negative results on peanut challenges. Both ate a cumulative dose of 32 peanuts without any reaction (table 1). Fifty six patients with positive results on peanut skin prick test had positive results on challenges to peanut. If we included the four subjects who reacted to crude oil but were not challenged with peanut a positive response to peanut was seen in 60 of 62 subjects positive for skin prick tests (96%) (tables 3 and 4). Twenty nine (48%) had reacted to peanut in the preceding year; only six (10%) had avoided peanuts successfully for more than five years.[1] Table 5) summarises other atopic disorders reported by the subjects with proved peanut allergy.

View this table: [in this window] [in a new window]	**Table 3** Results of peanut challenge. Figures are numbers (percentages) of subjects unless stated otherwise

View this table: [in this window] [in a new window]	**Table 4** Comparison of severity of reported previous reactions and observed reactions to peanut challenge. Figures are numbers (percentages) of subjects

View this table: [in this window] [in a new window]	**Table 5** Summary of reported allergies and skin prick test results in 60 adults with proved peanut allergy

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Importance of study's findings

Peanut allergy is the commonest cause of fatal and near fatal allergic reactions to foods in the United States.[3] It is being recognised increasingly in the United Kingdom[12 16] and may affect as many as 1-2% of 4 year old children.[17] The increasing incidence probably reflects increasing consumption of peanuts in a wide range of food products. Heightened public awareness has driven increased medical involvement in the care of

affected people who previously have had little access to scientific and medical information. Affected people have rarely had adequate provision and training in the use of rescue treatments such as adrenaline inhalers and injections.

In addition to reporting that they felt ill equipped to treat reactions to peanut themselves, many allergic people have commented that they have greater fear of exposure to the more widespread peanut oil than to peanut itself. Peanut oil is often implicated by those allergic to peanut as a cause of an allergic reaction, particularly in restaurant meals. The absence of antigenic protein in refined peanut oil[5 6] and its presence in such oil after cooking peanuts in the oil[6] suggest that oils may become adulterated with allergenic peanut proteins rather than being intrinsically allergenic themselves.

We believe our results confirm that refined peanut oil is safe for most people who are allergic to peanuts. This finding supports those of previous small studies[1 9] and provides statistically sound data on which to base more confident recommendations to patients, regulatory authorities, and the food and catering industries.

Reactions to crude peanut oil

Six subjects (10%) reacted to crude peanut oil. All these patients had had moderate or severe reactions previously, but only one suffered a comparable reaction to the crude oil. Four of these six had subjective reactions to the crude oil–there were no visible or measurable signs of reaction. These reactions may have been psychologically mediated and the real rate of measurable reaction to crude oil may be 3.3% (2/60) rather than 10% (6/60) of those with peanut allergy. The double blind nature of the challenge minimises the role of psychological reactions, and we have therefore considered the subjective, mild reactions to be real.

The low rate of reaction to crude peanut oil and the generally mild nature of the observed reactions to crude oil provide reassurance to sufferers that the reactions to crude oil are generally considerably less severe than reactions to peanut itself, even in those who normally have severe reactions. This may be a dose effect. Sufferers must continue to avoid the so called "gourmet oils" that are deliberately blended with crude peanut oil to give them a characteristic peanut flavour. Different crude peanut oils may contain different concentrations of peanut protein,[5] so the relative risk of other crude oils may differ from that of the oil we tested in this study.

Peanut challenges

There was a striking disparity between the severity of previous reactions and reactions observed during supervised peanut challenge. This is probably due to a combination of two factors. Firstly, the subjects were evaluated when they were otherwise well and were being supervised in a calm, clinical setting with all appropriate precautions taken. Clearly, anxiety that is generated by reactions away from medical help may exacerbate reactions. Also, the controlled dose of peanut that elicited reactions in the challenges was probably much lower than the dose to which subjects are exposed in meals and prepared foods that caused reactions in the community.

Use of refined peanut oil

Our results do not suggest that it is completely safe for all people with peanut allergy to eat in restaurants

where refined oils are used. Such oils may come into contact with peanuts and thereby become contaminated.[6] This risk, of course, applies to any oil used in cooking,[2] not just to peanut oil. To minimise the risk to people allergic to peanuts and other foods, it is vital to increase awareness of food allergy among catering and restaurant staff. They must be aware of the risk to people with life threatening reactions to foods of reuse of oils, especially after cooking foods that are known to be allergenic, such as peanuts, tree nuts, fish,[2] and shellfish.

Labelling

Discontinuation of the use of the term groundnut and clear labelling distinctions between refined and crude oils would simplify many of these issues. Such steps are now justified as a consequence of this study. Refined peanut oil does not seem to pose a risk to most people with peanut allergy.

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Conflict of interest: The research was funded by SCOPA, the trade association for companies who manufacture refined and crude peanut oils.

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