Nut allergy in children: investigation and management

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Peanut allergy, whose incidence is thought to have doubled in the past 10 years¹, now affects about 1% of British preschool children². Consequently, referrals to allergy clinics of children with allergy to nuts—in particular peanuts but also tree nuts (almonds, brazil nuts, hazelnuts and walnuts)—have increased considerably³. Nut allergy is an important condition not only because of its high and apparently increasing incidence but also because it starts at an early age, is lifelong and can be fatal^{3–6}. The potential severity of the symptoms of allergic reactions to nuts dictates that patients have to carefully avoid any nut contact and to carry adrenaline at all times throughout their lives. Therefore, all doctors dealing with children should be familiar with the presenting symptoms, investigations necessary to confirm or refute the diagnosis and emergency and long-term management. We have developed a protocol from our own experience⁷ and that of others^{3,8,9} for the diagnosis and management of nut allergy (Figure 1). We believe this is usable in settings that do not have specialist allergy services, allowing health professionals to evaluate and manage this condition without tertiary referral.

CLINICAL FEATURES

Allergic reactions to nuts present with symptoms which are characteristic of allergic reactions to foods in general¹⁰. They differ between individuals in extent (which organ systems are involved) and severity but tend to be milder in children than in adults⁶. Symptoms can occur with minimal contact, even through intact skin, since the lowest oral dose causing symptoms is 100-fold less than that of other foods⁶. Symptoms develop in most individuals within 30 minutes of contact⁶ and may manifest without previous exposure, although some authors suggest occult sensitization to very small amounts of nut protein^{11–13}. The first symptom is frequently a sensation of burning, irritation or itching of the mouth, throat or tongue. Very young children cannot report this sensation but may immediately spit the food out because of it. Subsequent symptoms affect the skin (itch, urticaria and angio-oedema), respiratory system (sneezing and itchy eyes, cough, wheeze, breathlessness and stridor),

gastrointestinal tract (abdominal pain, diarrhoea and vomiting), central nervous system (dizziness and fainting) and circulatory system (shock)^{3,6,14}.

If the clinical presentation is at all atypical, the diagnosis should be queried and be subject to fuller evaluation including dietary challenge. We would consider a reaction to be unusual or atypical if:

- Symptoms were very mild—for example, a very slight evanescent rash
- Symptoms involved one organ system, excluding the skin, since most patients experience multiple symptoms involving more than one organ system^{3,9}
- Onset was more than 90 minutes after contact with the nut (most patients react within 30 minutes)⁶
- Presenting symptoms are not characteristic of food allergy (as described above).

In other food allergies in which severe reactions are not common (e.g. milk or egg allergy) suspected associations between exposure and symptoms can be confirmed with dietary diaries. In nut allergy, however, there is greater risk of severe or even fatal reactions and furthermore the child presenting for evaluation has had a reaction that may have been severe enough to warrant emergency treatment and possibly hospital admission. Repeated exposure outside the controlled environment of, for example, a hospital day ward, for the purposes of recording in a dietary diary, is therefore potentially dangerous. In addition, in our experience many parents will be anxious about further contact with nuts either because of the nature of their child's initial reaction or because they will have learnt about unfortunate, even fatal, reactions through the lay media.

ALLERGY TESTS

A careful history is extremely important but judgment may be hampered by parents' claims that the cause of symptoms is clearly a specific nut. Doctors need to make sure that the reaction is not caused by another coinciding food allergen or concomitant factor such as a virus infection with rash. We recently had a patient who reacted to peanut butter on a sesame seed roll, tested negative to peanuts on skin-prick testing and peanut dietary challenge but tested positive to sesame seed dietary challenge. Therefore, the diagnosis of

Figure 1 Diagnosis and treatment of nut allergy

nut allergy cannot be based solely on the history of a reaction; diagnosis must be confirmed by demonstration¹⁵ of IgE-mediated allergy through either skin-prick testing with commercially manufactured nut extracts (Soluprick, ALK) or measurement of serum allergen-specific IgE.

A negative skin-prick test (SPT) is highly predictive of the absence of nut allergy, but the false-positive rate is high. Sampson *et al.* found that 30% of patients with positive SPTs to peanuts tolerated peanuts on dietary challenge¹⁷. Furthermore, in our experience, patients often react to more than one nut allergen on skin-prick testing. Although this skin test 'cross-reactivity' amongst nuts occurs commonly, too few patients have been challenged to determine whether this represents symptomatic or asymptomatic sensitivity¹⁶. If one is skin-prick testing an individual presenting with, for example, a clear-cut history of an allergic reaction to peanuts and he or she reacts to peanuts *as well as* other nuts, current practice is to avoid all 'offending' nuts. However, we challenge the patient, once school age is reached, to a

mixture of these nuts *if* further clarity is required—particularly, for example, in older children who object to the restriction of total nut avoidance.

The serum specific IgE (serum IgE) assay is less sensitive than skin-prick testing, more expensive¹⁷, and in our experience more distressing to small children. We use it in situations that preclude skin-prick testing—that is, patients with widespread eczema or taking oral antihistamines¹⁷. We do not feel that there is any justification for use of blood tests rather than skin-prick tests *on safety grounds*. Anaphylactic reactions have never been reported from skin-prick tests with commercially produced allergen extracts.

FOOD CHALLENGE

Although the allergy tests have the limitations described, not every patient needs a food or dietary challenge. Most will have a clear-cut history of a recent reaction with a confirmatory positive SPT or serum IgE. Food challenges

are reserved for those with unusual or atypical histories (as listed above), those with results that contradict the history; and those who may have had exposure to the offending nut subsequent to the initial diagnosis without reacting (possible development of tolerance, or initial misdiagnosis). A contradictory result is a negative result in the face of a history of a reaction, a positive result without any previous reaction or reactions to nuts other than that to which the reaction being investigated occurred (cross-reactivity or 'wrong nut' diagnosis).

The double-blind placebo-controlled challenge is regarded as the reference standard for food challenges but this is a time-consuming and expensive procedure that can be offered only in specialist centres¹⁵. This test is designed to overcome bias that is likely in older children or where objective signs are absent. Since most children undergoing nut challenges are young and present with clinically detectable signs (most commonly skin and respiratory)^{3,6}, open challenges have been used successfully to make a definitive diagnosis where required^{7,8}.

We have developed an open nut challenge which we believe is easy to perform, economical, safe and effective⁷. The challenge follows a standard protocol but the doses and the time delays between doses are specific to the individual. The initial dose is always smaller than that which provoked the initial reaction. The challenge also considers the child's age: children over 7 years old are given whole nuts to eat whilst younger children receive peanut butter, ground tree nuts or home-made biscuits containing specific quantities of nuts (prepared under the supervision of a paediatric dietitian).

We conduct the challenges in our paediatric day ward. There are written guidelines, available on the ward, that describe the signs of and rescue treatment for anaphylaxis in children¹⁰ and that include an emergency drug chart. On admission to the ward the child is weighed, vital signs (blood pressure, pulse, respiratory rate) are recorded and he or she is carefully examined for any evidence of allergy. Abnormal respiratory signs such as wheeze or breathlessness will necessitate delay of the test until the child is well. Any evidence of eczema and, if present, its distribution is carefully marked out since it commonly coexists with food allergy but may also be confused with an urticarial reaction. Once we are satisfied that the challenge can go ahead, the emergency drug chart is completed and an intravenous cannula is inserted.

In the challenge, the child ingests visually measured amounts or 'doses' of nuts at 15–30 minute intervals, starting with a nut touching the oral mucosa. We do not start by rubbing a nut on the skin since a reaction may reflect contact urticaria only. Typically, the challenge (for peanut for example) would progress by the child eating a portion of nut the size of a pinhead, then two pinheads,

then a sixteenth of one peanut half, then an eighth of one peanut half and so on. These are eaten at 20-minute intervals until a dose of 5 peanuts (approximately 5 g total peanut) has been ingested. Day care staff are trained in visually doubling 'doses'. We find this to be a safe practice and to be more practical than weighing these very small quantities.

The entire procedure takes 2–3 hours, depending on the willingness of the child to cooperate. Throughout the challenge the child is observed for any allergic reaction. Between 'doses', vital signs are recorded. Non-visual signs such as abdominal pain and chest tightness warrant a longer observation period before progressing. If these are thought to be true early symptoms and these occur without any overt signs, the child will need a blind challenge at a later date. Children are observed for a minimum of 60 minutes before they are discharged home, even if there has been no reaction. If there have been minor symptoms⁶ the observation period is extended to 4 hours after the last ingestion, whilst moderate and severe reactions warrant overnight observation to monitor any delayed reaction to nuts already ingested. If a reaction occurs it is promptly assessed by a doctor: mild reactions (skin only) are to be treated with an antihistamine, moderate and severe reactions with an antihistamine plus adrenaline. Since we stop our challenges at the first sign of any reaction, all have been successfully treated with antihistamines alone.

Our standard challenge involves a single nut type. Occasionally patients are challenged to more than one nut—the mixed nut challenge. This approach is used where one is faced with the following dilemmas:

- A reaction is suspected to be caused by a nut but the identity of nut in the food ingested was not known and allergy testing has been inconclusive
- A patient requires clarity of his or her allergy status after skin-prick testing shows cross reactivity
- Where a patient with a history of an allergic reaction to a specific nut has not reacted on challenge, to give the 'all clear' on total absence of nut allergy.

Nuts used in this challenge are usually those to which the patient reacted on skin-prick testing and we find these easiest to give in the form of increasing amounts of home-made biscuits containing specified quantities of pulverized mixed nuts. If there is no reaction, all are simultaneously excluded as culprits. If, however, the patient does react, one then needs to repeat the challenge for each individual nut on separate occasions.

Occasionally a patient shows a positive SPT test to a nut without previous known exposure to that nut. About half such children will react when exposed to nuts, confirming the SPT result¹⁷. The child may have been tested to

determine the influence of diet on an allergic condition (e.g. eczema) and a positive result to nuts is found as a consequence, or he or she may be the sibling of a nut-allergic child and tested at the behest of the parents. Here our current practice is to advise nut avoidance in preschool children since we are concerned about a risk of actual sensitization to nuts with exposure at that age¹⁸. In older children we challenge with the suspected nut or nuts to aid future management.

MANAGEMENT

The management of nut allergy encompasses the triad of patient education, dietary avoidance and provision of treatment for emergency use. The child, parent and other care providers need education on the allergy—how to recognize anaphylaxis and how to administer antihistamines and adrenaline (inhaler and injection)—and should furthermore have a detailed plan of action on getting medical assistance in an emergency.

Clearly the cornerstone of long-term management is avoidance of the offending nut or nuts, but accidental exposures do occur commonly and these have sometimes been fatal^{19,20}. In the event of such an exposure patients need to be able to administer adrenaline themselves, either to abort the reaction or to 'buy time' until further treatment can be obtained from paramedics or in a hospital emergency department. Adrenaline is the most important drug in an anaphylactic reaction and therefore the treatment of choice. It can be administered by patients themselves by inhaler or injection. The injections or 'injectable pens' currently available in the UK are the EpiPen (ALK) and the Anapen (Allerayde). These are single-dose pressure-activated syringes that deliver either 0.3 mg or 0.15 mg per syringe, the latter labelled the 'Junior' form and recommended for children < 30 kg. Injections should be given into the outer aspect of the thigh. A second injection can be given after 5–10 minutes since adrenaline is rapidly metabolized.

Adrenaline aerosol is a suitable alternative to injection. The only aerosol currently available in the UK is the Asthmahaler Mist (Menley and James Laboratories). It is not licensed for this use and therefore can be prescribed only on a named-patient basis. Approximate dosages are 10 puffs in young children and 20 puffs in children > 30 kg every 5–10 minutes. Some workers recommend that the injection be given in the first instance¹⁴. Inhalers are a useful adjunct to injected therapy for two reasons. First, repeated doses can be given from the inhaler ('injectable pens' are single-dose); second, since inhaler therapy for asthma is very common amongst atopic children, we feel that there would be less anxiety about inhaler use than about self-injection (parents might be inclined to delay injecting their child until '200%

certain of a reaction whereas inhaled adrenaline might be given more promptly).

Both parents and patients must understand that adrenaline should be given early. It is better to give an 'unnecessary' dose than to delay until too late. The most important single factor contributing to fatal outcomes in anaphylactic reactions to peanuts is failure to administer adrenaline immediately after the onset of symptoms²¹. We routinely prescribe two adrenaline inhalers and 'injectable pens' for our patients—one set to be left at school, the other to be kept at home.

Although we have emphasized the use of adrenaline, antihistamines too are effective in treatment of allergic symptoms. We do offer the parents 'permission' to treat a very slight reaction—a mild localized rash, usually on the face, or local or generalized pruritus—with an oral antihistamine. However, the child needs careful observation and any progression of the allergic reaction will necessitate administration of adrenaline.

All the team members in the allergy clinic can take part in education of the family. The physician and nurse will concentrate on the clinic presentation and use of emergency treatment. After the doctor's consultation the nurse can reinforce the clinical facts and how to use the inhaled and injectable adrenaline. The dietitian can discuss dietary problems and ensure that the child's diet remains nutritionally adequate. Further information, booklets and pamphlets are available to the public from the Anaphylaxis Campaign and the British Allergy Foundation.

FOLLOW-UP

Long-term follow-up studies suggest that peanut allergy, unlike other food allergies in children, is seldom outgrown^{4,22}. Presumably the same is true of tree-nut allergy. Hence patients are discharged, following one or two clinic visits, back to their general practitioner with lifelong advice. They have to continue a strict dietary avoidance regimen and ensure that they have adrenaline with them at all times. This is an enormous burden which could be removed if we showed a patient no longer to be allergic. Since skin-prick testing has a high negative predictive value, a change from a positive to a negative test may well indicate the development of tolerance. We propose therefore that patients should undergo annual SPTs and those who become negative should undergo a dietary challenge to confirm or refute the continued presence of nut allergy. We appreciate that this may have huge implications for health services, given that 1 in 100 children may be nut-allergic. Healthcare providers therefore need to be innovative and provide the facility where all nut-allergic patients can have annual skin-prick tests, with reinforcement of dietary advice and checking of their emergency treatment techniques.

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