Improved prospects for food allergy prevention

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ABSTRACT

Three recent publications from Professor Gideon Lack have fundamentally changed our understanding of how to prevent food allergy. His team has shown that early introduction of allergenic foods may prevent food allergy in most but not all high-risk children. Various allergy and paediatric societies around the world are changing their recommendations based on these three studies. It appears there is a window of opportunity to safely introduce allergenic foods to high-risk children. This has resource implications, as some of these children will need testing and food challenges.

KEY POINT: Allergenic foods must be introduced as soon as safely possible to at-risk children.

Introduction

Food allergy, defined as an adverse immunological reaction to food proteins, has become increasingly common.[1] The carefully conducted HealthNuts study from Melbourne (Victoria, Australia) indicated that up to 10% of 1-year-old children had a definable food allergy.[2] Our own pilot study in 2009 also suggested food allergy was a significant burden for children attending Plunket clinics.[3] The reasons for the apparent increase in incidence are not known.[1]

Currently, there is no specific treatment for food allergy apart from strict avoidance in New Zealand. Food desensitisation and tolerisation is promising, but still viewed as experimental by leading world experts. Desensitisation occurs with the gradual introduction of an allergen and patients do not react even if the allergen is withdrawn. Tolerisation occurs only if there is continued exposure to the allergen. If the allergen is withdrawn, patients may revert to their allergic state. These terms describe overlapping immunological phenomena of non-responsiveness to antigens and allergens. These procedures are not universally effective and carry significant risks. The ability to prevent food allergy would obviously be of great benefit to infants at risk of food allergy. Until 2015, there was intense debate about whether allergenic foods should be introduced early or later in allergy prone children to mitigate the risk of food allergy.

Three recent studies from Professor Gideon Lack and his team have suggested prevention of food allergy may be possible in most but not all infants.[4–6] It is timely to review these studies, as they are likely to fundamentally change clinical practice. These studies suggest there may be a window of opportunity to introduce allergenic foods to high-risk infants. There will be potential resource issues, as there will be greater need to undertake specialist clinical assessments and testing in high-risk infants and, if required, food challenges, to prevent progressive sensitisation and allergy. Food challenges are undertaken in specialist or hospital settings where food is slowly introduced under careful medical supervision. Food challenges can either be open challenges or single- or double-blind depending on the clinical circumstances.

I have arbitrarily divided food allergy prevention into three categories:

- Primary prevention - where both sensitisation and food allergy are prevented. In

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this situation, food allergy testing is negative and patients can tolerate the food.
- Secondary prevention - where patients have IgE antibodies to a food they have not consumed, but can consume the food following a food challenge. Sensitisation may have occurred through the gut or, more likely, through the skin. Secondary prevention has also been defined as interrupting the development of IgE in sensitised children.[7]
- Tertiary prevention - where patients already have one food allergy but new food allergies are prevented. Alternatively, this has also been defined as preventing end-organ disease in food allergic children.[7]

These arbitrary divisions may apply to the same individual for different foods at different times. Food allergy is a dynamic process, hence the need for ongoing evaluation.

Secondary and tertiary prevention

The Learning Early About Peanut Allergy (LEAP) study published in 2015[4] sought to determine if high-risk children with eczema or egg allergy could be given peanuts early to prevent the onset of peanut allergy. This study hypothesis originated from Professor Lack's observation that Jewish children in Israel had a much lower prevalence of peanut allergy than their Jewish counterparts living in the UK.[8] Professor Lack observed that Jewish children in Israel began consuming peanuts at a much younger age than children in the UK. These infants were given a traditional preparation (bamba), which was rich in peanut protein. He hypothesised early introduction protected Israeli Jewish children from peanut allergy.

The LEAP study enrolled 640 high-risk children aged 4–11 months. Some children had both eczema and egg allergy while others had either.[4] They were randomised to either avoid peanuts or to introduce peanuts after testing. Children testing negative for peanuts were given peanuts and patients testing positive underwent a food challenge. Children passing the peanut challenge continued to eat peanuts.

After 5 years of follow up, 13.7% of children avoiding peanuts had developed peanut allergy, while only 1.3% children who had early introduction of peanuts had developed peanut allergy. This was a highly significant result, indicating secondary and tertiary prevention of peanut allergy is possible in many children. At the start of the study, there were 98/640 children who already had positive allergy tests (sensitisation) to peanuts, who needed a food challenge. Some of these children reacted to peanut challenge and were advised to avoid peanuts as they had already developed peanut allergy. Others who had large skin prick test reactions to peanut were assumed to be allergic and were excluded from the study.

The second study, the LEAP-ON study[5] determined the durability of the peanut allergy remission and prevention. Patients who had early peanut introduction and were not allergic to peanuts were asked to stop consumption of peanuts for a year and then were retested and underwent food challenges as appropriate. This study showed the majority of children who had early introduction of peanuts continued to safely eat peanuts, confirming long-term prevention of peanut allergy.

Early introduction of peanuts to low-risk children

The third and perhaps the most important study was the Enquiring About Tolerance (EAT) study, also from the same group.[6] One-thousand and three breast-fed, mostly low-risk infants from the UK were randomised to either continue with their usual diet or to begin consuming six allergenic foods at age 3 months. The children randomised to early introduction were given eggs, milk, sesame, peanuts, fish and wheat. They were also followed over 3 years to determine how many developed food allergy compared with children on their usual diets.

The results showed no difference between the two groups. That is, early introduction made no difference to the risk of food allergy. However, when the results were more closely examined, it appeared only 31% of mothers complied with the early introduction protocol. In children whose parents did comply, there was a significant reduction in the incidence of food allergy, but only for

eggs and peanuts. This study for the first time demonstrated that early introduction of eggs and peanuts may reduce the risk of food allergies in low-risk children. Early introduction of other foods (milk, sesame, fish and wheat) did not alter the risk of developing allergy in this study. Further studies will be needed to determine if prevention strategies should differ for each food allergen.

Primary prevention in high-risk children

There are no studies that definitively address primary prevention of food allergy in high-risk children. It is currently unknown if a maternal diet devoid of nuts, seafood, eggs and milk reduces the risk of food allergy.[7] There are two small studies indicating regular application of an emollient may reduce the risk of food sensitisation. These observations are consistent with the Lack hypothesis, which states that sensitisation probably occurs through the skin. Improved skin barrier function might therefore reduce the risk of food sensitisation. A full discussion of this topic can be found in a recent review published by Professor Lack et al.[7]

Comment

Professor Lack's three recent publications have major implications for clinical practice.[4–6] They suggest early introduction of food allergens in non-allergic, low-risk infants may reduce the risk of egg and peanut allergy. They also suggest secondary and tertiary prevention of food allergy is possible in most but not all high-risk children. These three studies offer the first robust evidence that prolonged avoidance can lead to sensitisation and allergy, at least for peanuts and eggs. There are resource implications also as food testing and challenges will become increasingly important in paediatric allergy practice.

The 2010 National Institutes of Allergy and Infectious Diseases (NIAID) food allergy prevention recommendations have been updated based on these observations.[9] The NIAID suggests specialist assessment and testing of infants for peanut allergy if they have severe eczema or definite egg allergy.[9] If safe to do so, peanuts should be introduced at age 4–6 months. Families of low-risk infants are advised to introduce peanut at ~6 months without prior testing. Food challenges can be offered in cases of parental anxiety.[9] Many paediatric and allergy societies around the world are similarly changing their recommendations based on these studies. It is, however, unlikely the World Health Organization will change its advice on exclusive breast feeding for 6 months given the serious threat of diarrheal illness in developing countries.

In my practice, the goal is normalisation of the diet as soon as safely possible, given the new evidence that this may prevent food allergy. Depending on their history and testing, I make a decision whether children should continue to avoid each food or undergo a food challenge if safe to do so. Given Professor Lack's observations, it seems prudent to test children with moderate-severe, early-onset (<6 months) eczema or children with egg allergy as per the revised NIAID guidelines.

It is essential for children to continue eating foods that they tolerate, regardless of any test results, as there is a risk of breaking tolerance and potentially creating a life-long food allergy. There are some situations where infants with severe eczema have strongly positive allergy tests but continue to eat these foods. A careful discussion needs to take place where the benefits of a short-term improvement in the skin are balanced against the risk of long-term morbidity from breaking tolerance to the food leading to food allergy. This is analogous to pet allergy where children born to families with pets, particularly cats, have a lower risk of pet allergy. Similarly, if children do not react clinically to a pet, a positive test is irrelevant. Removal of a pet may result in severe pet allergy as a result of breaking tolerance.

Eczema treatment must be optimized. In most cases, eczema can be managed and frequently improves over time. The food-specific IgE tests often improve over time in children who continue to consume these foods. There is also an argument these foods should not be tested if they are being consumed regularly, without any clinical evidence of other adverse reactions.

Expert advice should be sought in these complex situations.

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COMPETING INTERESTS
The author has no competing interests to declare.