

PEANUT ALLERGY: CHANGING EPIDEMIOLOGY AND MANAGEMENT

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ABSTRACT

Allergy to peanut is a severe and life altering health problem faced by increasing numbers of children and adults. It affects 1 to 2% of children in Westernised countries.^{1,2} Peanut allergy is the leading cause of anaphylaxis and death due to food allergy. Over the last 10-15 years the prevalence of peanut allergy has doubled in the United Kingdom (UK) and United States of America (USA). Precise figures for prevalence in Africa are unknown, but clinical experience of local allergists indicates a rising prevalence in local populations.³ Peanut allergy develops early in life and most often persists lifelong. The strongest predictors known to be associated with an increased risk of peanut allergy are severe eczema and egg allergy.⁴ This article aims to review recent research and new findings in the field of peanut allergy as well as new directions in management.

LOCAL AND GLOBAL DIFFERENCES IN FOOD ALLERGY

Food allergy is an evolving public health issue. The 'first wave' of increase in atopic conditions involved asthma and allergic rhinitis. This increase was seen more than 50 years ago and reached a peak in Westernised countries (Australia, UK, and USA) in the 2000's.⁵ Food allergy during this time was uncommon. It is only in the last 15 years that a 'second wave' of allergy has emerged in the same countries that has led the respiratory allergy rise.⁶

In the 1970's, asthma and allergic sensitisation had a very low prevalence rate in black South Africans, especially in rural settings. Over the last 4 decades the prevalence of asthma as well as other atopic disorders, allergic rhinitis and atopic dermatitis, has increased in South African children in rural and urban communities.⁷ No specific data regarding a possible similar rise in prevalence of food allergy is yet available for the South African population. Current research is underway to determine the prevalence in unselected 1 to 3 year old children.

PREVIOUS MANAGEMENT GUIDELINES FOR FOOD ALLERGY

During the previous decade international food allergy guidelines promoted avoidance of the consumption of allergenic foods (milk, eggs, peanuts, etc.) during pregnancy, lactation and infancy. However, elimination of these food allergens during the foetal and early childhood periods consistently failed to prevent the onset of IgE-mediated food allergy in children. Two possible explanations for this failure are that firstly, sensitisation does not only occur via the oral route, but rather by other routes such as epicutaneously especially if the skin barrier is broken, and secondly,

early oral exposure might be advantageous to induce tolerance.⁸ These avoidance guidelines were withdrawn in 2008 after research from the UK showed a lower prevalence of peanut allergy in a population consuming peanut during infancy compared to those who were avoiding early peanut consumption.⁸

ENVIRONMENTAL AND SKIN BARRIER INFLUENCES ON PEANUT ALLERGY

Early onset (<6 months of age) and increasing severity of eczema increases the risk of peanut allergy in children. Food sensitisation can occur through the skin.⁸ Recent research in a South African cohort of children with atopic dermatitis found 44% were sensitised to peanut, while 24% had proven peanut allergy.⁹

Research has shown differential proliferation of peanut-specific skin-homing versus gut-homing memory T-cells in the presence of peanut in peanut allergic children versus peanut tolerant children. Those with established peanut allergy showed skin-homing T-cells proliferate and produce a predominantly Th2 cytokine profile, while those who were peanut tolerant had gut-homing T-cell proliferation and produced predominantly Th1 cytokine profiles. This research suggests that allergic sensitisation occurs via the skin in those who develop peanut allergy, while tolerant subject become tolerant via exposure through the gut and that allergic sensitisation only occurs through the epicutaneous route in the absence of the protective effect of oral exposure. This concept is referred to as the dual-allergen exposure hypothesis.¹⁰

Environmental peanut exposure can occur through household dust containing peanut protein. In homes where

peanut is consumed dust and surfaces will contain peanut protein. These proteins are stable in the environment and are difficult to remove from porous surfaces and textiles. Machine washing of pillows and sofa covers were shown to decrease, but not remove peanut proteins. Peanut proteins were not found to be airborne in the environment, apart from the immediate area where fresh peanuts were being deshelled, however, these proteins rapidly settled onto the surface area.^{10,11}

Environmental peanut proteins are able to activate mast cells and basophils, be captured by dendritic cells and presented to T-cells in the context of a Th2 driven immune response, leading to allergic sensitisation.^{10,11} In the context of infantile eczema, household peanut consumption is a risk factor for the development of peanut allergy. The levels of peanut protein present in dust have not been found to be sufficient to cause clinical allergic reactions.^{10,11}

Since sensitisation can occur via the skin, it would be logical if there were some intervention into improving the skin barrier, this could lead to a decrease in the rates of sensitisation. A recent randomised controlled trial in 124 infants at risk of developing eczema (parental eczema, caesarean section births) showed that applying emollients at least once a day, starting within the first 3 weeks of life, led to a 50% relative risk reduction for the development of eczema by the age of 6 months.¹² Early emollient use is a safe and effective management strategy to decrease the prevalence of infantile eczema and possibly allergic sensitisation.

LEGUMES AND PEANUT PROTEINS

Legumes including peanuts, soybeans, lentils, beans, peas, etc., are consumed worldwide due to their high protein content and variable lipid and vitamin content. For these reasons legumes are also recommended as staple foods by health organisations.¹³ However, due to the rising prevalence of peanut allergy, increasing numbers of individuals will not be able to follow these general nutritional guidelines. This may have significant effects on socioeconomic and nutritional status, especially since the addition of peanut butter, to the diet of children with poor growth, is a frequently used nutritional intervention tool.

Peanut allergy is the most common of the legume allergies. Most peanut allergens are seed storage proteins, e.g. the 7S globulin named Ara h1 and the 2S albumin named Ara h2.¹³ Peanut components of highest clinical significance include Ara h1, 2 and 3 as well as Ara h6 and 9. In clinical practice, it is sufficient to do specific IgE to peanut and Ara h2 only.

Component resolved diagnostics improve our ability to determine the significance of peanut specific serum IgE results. Raised specific IgE to Ara h2 is linked with true peanut allergy. Children who were tolerant to peanut had

significantly lower rates of sensitisation to Ara h2 versus those who were clinically reactive, therefore IgE to Ara h2 can be used as a predictor of true peanut allergy and increased persistence of peanut allergy over time.¹⁴

Like many other food products, the allergenicity of peanuts is affected by heat treatments. Roasting peanuts enhances their IgE-binding capacity and the allergenicity, while boiling decreases the allergenicity.¹³ Cross reactivity between different legumes occur in 5% of those allergic to one legume. Peanut allergic individuals can also experience cross reactivity with tree nuts and rates of between 20 and 40% have been reported. Sesame allergy was also found in 25% of children with peanut allergy.^{8,15} Rates of cross reactivity differ between individuals and different populations. When evaluating individuals with a history of peanut allergy it is important to review consumption history and tolerance to other legumes, tree nuts and sesame.

CONSUMPTION HAS A ROLE IN PEANUT ALLERGY

Research by Du Toit et al. compared peanut allergy between children of similar ethnic backgrounds in industrialised countries; the UK and Israel, with known high rates of atopy. The prevalence of peanut allergy was found to be 1.85% in the UK and 0.17% in Israel. Peanut allergy rates were increasing in the UK, while remaining stable in Israel. The difference in prevalence could not be explained by age, sex, ancestry, atopy or socioeconomic differences. Significant differences were found in rates and ages of peanut consumption and introduction. Peanut consumption at the age of 9 months was found in 69% of children in Israel, who often consume a peanut snack regularly and at an early age, versus only 10% in the UK. This research proved a strong inverse relationship between peanut consumption in infancy and prevalence of peanut allergy in childhood.⁸

Peters et al., of the Australian Healthnuts group, examined the natural history of peanut allergy in children. This research is unique in that oral food challenges were done in all willing participants at baseline as well as follow up, irrespective of skin prick test or serum IgE results, thus minimising the potential effect of bias. At baseline there were 156 one year old infants with confirmed peanut allergy, they were followed up until the age of 4, at which point they were reviewed and again underwent peanut oral food challenges. At the age of 4, 21% of previously peanut allergic children had outgrown their peanut allergy. There were no significant demographic differences between children with resolved versus persistent peanut allergy. Those children whose peanut allergy resolved had lower initial IgE levels and SPT wheal sizes and these values decreased over time, while the converse was true for those with persistent peanut allergy. Tolerance to peanut developed in 47% of children whose SPT wheal size decreased over time and 26% whose IgE levels decreased over time. Ninety per cent of those whose SPT's increased over time and all

children whose IgE's increased over time remained allergic to peanut at the age of 4 years. Therefore, an increase in peanut specific serum IgE and SPT wheal size is much more predictive of persistence of peanut allergy, than a decreasing level is of resolution.¹⁶

Du Toit et al. published the much awaited results of their peanut research project, the LEAP trial, early this year. Theirs was a randomised controlled trial that recruited infants between the ages of 4 and 11 months who were at high risk of peanut allergy (a diagnosis of severe eczema and/or the presence of egg allergy). Sensitisation and presence of peanut allergy was assessed at baseline with skin prick tests and oral food challenges. Six hundred and forty children were included in the study cohort, 98 were sensitised to peanut at baseline (SPT 1-4 mm) and 542 were not sensitised (SPT 0 mm). These children were randomised to consumption and avoidance groups, the consumption group had to eat at least 6g of peanut protein per week. At the age of 60 months they were re-evaluated with oral food challenges. Rates of peanut allergy were consistently higher in the avoidance groups than the consumption groups. For those not sensitised at baseline, 13.7% in the avoidance group versus 1.9% in the consumption group, were found allergic to peanut at endpoint. This reflects an 86.1% relative reduction in peanut allergy prevalence in the consumption group. For those who were sensitised at baseline, 35.3% of the avoidance group versus 10.6% in the consumption group, were peanut allergic at endpoint. This was a relative reduction in peanut allergy prevalence of 70% in the consumption group. The rate of serious adverse events during the study period was no higher in the consumption group versus the avoidance group. Peanut consumption was confirmed with household dust collection and analysis. Limitations of this research included the baseline exclusion of children with skin prick tests above 4 mm, as they were assumed to be allergic already. Also, this work does not provide us with answers for those children with mild to moderate eczema.¹⁷

IMPLEMENTATION OF RECENT RESEARCH

The results of the LEAP trial have provided us with answers as well as ongoing questions regarding peanut introduction and consumption. The results have provided good quality evidence that the early introduction of peanut is safe and effective in a selected population of high-risk infants. Unanswered questions remain for those who had higher SPT wheal sizes (>4 mm) at study recruitment and infants at lower risk (those who did not have severe eczema) for peanut allergy. Questions also remain whether the amounts and duration of peanut consumption could be changed with similar preventative effects in the long term. The World Allergy Organization (WAO) published a Consensus Communication on Early Peanut Introduction online on the 2nd of June. They suggest that infants with early onset atopic disease (severe eczema or egg allergy) in the first 4-6 months of life may benefit from evaluation by

an allergist. This evaluation may include peanut skin prick testing, peanut oral food challenges and recommendations on the ingestion of peanut by such infants.¹⁸

The WAO also comments that the LEAP trial results do not address the use of alternative doses and duration of peanut exposure in the tolerogenic effect of peanut consumption.¹⁸ The LEAP trial has, however, demonstrated that high risk infants can successfully be introduced to peanut. This will need to be done in a team approach with parent, physician and dietician involvement.

TAKE HOME MESSAGES

- Food allergy is an important public health issue and improving health care provider knowledge and accessibility to and increased availability of allergology services will significantly improve the quality of life of patients who suffer from this disease.
- Prevalence studies, mainly in Westernised countries, have shown a significant increase in peanut allergy over the past few decades.
- Peanut allergy is of particular concern as it can be severe, unpredictable and is usually not outgrown.
- Skin barrier defects, such as atopic dermatitis, are a significant risk factor for peanut sensitisation via the epicutaneous route.
- Physicians should look out for children at risk of peanut allergy and commence the discussion and possible work-up for peanut allergy early in the life of the infant, rather than delaying it until after the child is 6 months old, in order for peanut consumption to start soon after the child starts consuming solid foods. This evaluation may include peanut skin prick testing between the ages of 4 and 6 months.
- Infants with severe eczema who are not consuming peanut yet should be evaluated with good history, clinical examination and skin prick testing to peanut protein. Those with negative SPT's should be advised to introduce peanut to the diet immediately, while those with reactive SPT's may need in-hospital peanut oral challenges.
- Recommendations of peanut avoidance during pregnancy and in high risk infants have been withdrawn.

REFERENCES

1. Al-Ahmed N, Alsowaidi S, Vadas P. Peanut allergy: An overview. *Allergy Asthma Clin Immunol* 2008;4(4):139-143.
2. Skripak JM, Wood RA. Peanut and tree nut allergy in childhood. *Pediatr Allergy Immunol* 2008 19(4):368-373.
3. Gray CL, Kung S. Food allergy in South Africa: Joining the food allergy epidemic? *Curr Allergy Clin Immunol* 2012;25(1):24-29.
4. Du Toit G, Roberts G, Sayre PH, Plaut M, et al. Identifying infants at high risk of peanut allergy: The learning early about peanut allergy (LEAP) screening study. *J All Clin Immunol* 2012;131(1):135-143.
5. Asher MI, Montefort S, Bjorksten B, Lai CKW, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC phase one and three repeat multicountry cross-sectional surveys. *Lancet* 2006;368(9537):733-743.
6. Prescott S, Allen KJ. Food allergy: Riding the second wave of the allergy epidemic. *Pediatr Allergy Immunol* 2011;22(2):155-160.