

The role of environmental exposure to peanut and the development of peanut allergy



Peanut affects around 2% of children in developed countries and is the leading cause of food-related anaphylactic deaths in the United States and United Kingdom. Peanut allergy is rarely outgrown and, although peanut desensitization has been shown to increase the threshold of reactivity to peanut, the evidence for oral tolerance induction remains elusive. The Learning Early About Peanut (LEAP) study showed that high-dose regular peanut consumption from 4 to 11 months of age up until 5 years of age was highly effective in preventing peanut allergy in high-risk children.¹ However, 76 of 834 (9.1%) children screened for the LEAP study were excluded as they already had a peanut skin-prick test of ≥ 5 mm, and therefore they were presumed to be peanut allergic. Thus, although effective, this intervention was not appropriate for these patients. To prevent and treat peanut allergy, understanding the mechanism of peanut sensitization and allergy is imperative.

Children usually react on first oral exposure to peanut, which implies previous sensitization through an alternative route. Several studies have assessed the role of peanut exposure in utero and via breastmilk; the results have been conflicting and previous recommendations to avoid peanut during pregnancy and breastfeeding were reversed in 2009.² The strongest risk factors for peanut allergy are egg allergy and severe eczema.^{3–5} The relationship between eczema and peanut allergy is dose dependent, and children with increasing severity and duration of eczema are at increased risk of developing peanut allergy. Furthermore, children with filaggrin loss-of-function mutations, leading to a more disrupted skin barrier and often eczema, are also at increased risk of peanut allergy,⁶ making the skin barrier a major focus.

There is an increasing body of evidence supporting the role of cutaneous sensitization in the development of peanut allergy.^{4,5} Epicutaneous sensitization to peanut has been demonstrated in various mouse models (with tape stripping before topical application of peanut protein and without tape stripping), in-vitro models (where skin-homing T-cell proliferation was predominant in peanut-allergic individuals), and human observational studies (where application of arachis oil onto the skin of children with eczema increased the risk of peanut allergy 6.8-fold). However, now that very few eczema creams contain arachis oil, epicutaneous exposure to peanut could be occurring through other routes.

The role of peanut in the environment, leading to epicutaneous sensitization, has been explored in a number of studies.^{5,8,10,11} Household peanut consumption during an infant's first year of life increased the risk developing peanut allergy as compared with children whose households did not consume peanut in their first year of life.⁷ The risk of peanut allergy increased further if household peanut consumption was in the form of peanut butter (rather than peanuts covered in chocolate), which the authors hypothesized may be due to peanut butter being more sticky and therefore amenable to transferring onto surfaces and the infant's skin. Household peanut consumption was subsequently shown to be highly correlated

with peanut levels in dust and surfaces of the infant's cot and play area, even if the infant was not consuming peanut.⁸ Of note, if the infant did consume peanut, household peanut consumption did not increase their risk of peanut allergy, in keeping with the dual allergen exposure hypothesis.^{4,7}

Peanut protein found in the dust of the infant's home environment is biologically active in that it stimulates activation of basophils from peanut-allergic children in a dose-dependent manner.⁸ Thus, the peanut in dust has the capability of binding high-affinity immunoglobulin E (IgE) receptors on the basophils of peanut-allergic individuals, triggering downstream intracellular signaling that leads to degranulation; therefore, peanut protein in dust could also interact with peanut-specific receptors on other immune cells in the skin such as mast cells or antigen-presenting cells, with the capability of inducing sensitization, although this is yet to be proven. Of note, the levels of peanut protein in dust (micrograms per gram of dust) are generally below the threshold levels (milligrams) found for clinical reactivity, and therefore would be unlikely to cause immediate hypersensitivity reactions.⁹

Subsequently, 2 studies described a dose-response relationship between peanut levels in dust in early life and the development of peanut allergy, especially if the infant had a disrupted skin barrier (as defined by filaggrin loss-of-function mutations or a history of eczema).^{4,10} In a population-based study from the United Kingdom, children with wild-type filaggrin did not have an increased risk from early environmental peanut exposure⁴; however, children with a filaggrin loss-of-function mutation had 3-fold increase in risk of challenge proven peanut allergy per natural log increase in environmental peanut exposure. In a study from the United States, in a high-risk group of children, the risk of peanut allergy increased with higher levels of peanut in dust and this was amplified if the infant had a history of eczema, and even further if the history of eczema was severe.¹⁰ These studies support the concept that children become allergic to peanut through the environment, either directly through peanut protein found in dust or the dust could just be a marker of hand-to-hand transfer of peanut.

The studies just described meet only some of the Bradford Hill criteria for epidemiologic risk factors for disease, including: strength of association; consistency of results in population-based and high-risk cohorts in different locations; biological gradient in terms of a dose-response relationship between peanut in dust and peanut allergy; temporality; coherence in that it fits with previous household peanut consumption data; and that peanut in dust has been shown to be bioactive. To prove causation, a randomized, controlled trial to reduce environmental exposure to peanut during the first 4 months of life would be required; thereafter, in children with moderate to severe eczema, early peanut consumption would be recommended from 4 to 6 months of age.¹ One study showed that peanut levels in the dust of household soft furnishings and bedding could be reduced by 1,000-fold and 40-fold, respectively, using thorough cleaning measures.¹¹

Other food allergens have previously been quantified in dust, including egg, milk, and fish allergens.¹² However, the assays used in those studies have not undergone validation for quantifying food allergens in dust as was done for the Veratox polyclonal peanut enzyme-linked immunoassay.¹¹ The role of other foods allergens in dust on the development of respective food allergens has not been evaluated; however, a study from Spain showed that household consumption of almond was associated with almond sensitization.¹³

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