



PEANUT ALLERGY PREVENTION

Research shows introducing peanut products in early infancy is efficacious in reducing risk of peanut allergy in children.

By **Marsha McCulloch, MS, RD, LD, LN**



inding a way to reduce the risk of developing peanut allergy is of great interest in the medical community. Peanut allergy affects 1.4% to 3% of children in Western countries, requires vigilant dietary management, and is the leading cause of death due to food allergy.¹⁻⁵

What's encouraging is that because children aren't born with peanut allergy, there may be ways to prevent it. "We've known for a long time that children are not born allergic to things," says John Kelso, MD, allergist in the division of allergy, asthma, and immunology at Scripps Clinic in San Diego. "Children don't inherit a specific allergy, but rather, a genetic tendency to develop allergic disease."

Recent landmark research has identified a key strategy to reduce peanut allergy in at-risk infants: introducing age-appropriate peanut products early in life rather than delaying their introduction. Based on this research, at press time, new peanut allergy prevention guidelines from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, are expected to soon be released. Here's a closer look at peanut allergy and this paradigm-changing evidence.

Understanding Peanut Allergy

Peanut allergy is particularly common in young children, and it's outgrown in only about 20% of cases, says Michael Young, MD, allergist in the division of allergy and immunology at Boston Children's Hospital, and author of *The Peanut Allergy Answer Book*.

"The high allergenicity of peanut has to do with its protein structure," Young says. "It's a very stable molecule compared to cow's milk and egg protein. Children more commonly outgrow milk and egg allergies compared to peanut allergy."

Sensitization to peanut in utero or during lactation is unlikely.^{6,7} It appears that the way most children become allergic to peanut, especially if they aren't eating it directly, is through sensitization through their skin, Kelso says. "If minute amounts of peanut are in the house, such as on the counter or in the air, the body can become exposed to the allergen through damaged skin. In fact, one way to help reduce food allergy risk may be aggressive use of moisturizers in infants who have dry or damaged skin or eczema."

According to Young, early oral exposure to peanut may prevent children from developing the allergy via their skin.

"If you have broken skin as in eczema, and exposure to the food is through the skin, you're more likely to develop allergy than if you have oral exposure, which seems more likely to promote tolerance," Young says. "So, early oral introduction of a food is more likely to reduce the risk of becoming allergic to that food."

"The odds of unintentionally getting exposed to peanut through the skin are high," says Laura Noonan, MSN, FNP-C, at O&O Alpan, LLC, a medical center in Fairfax, Virginia, that specializes in diagnosing and treating rare and complicated medical conditions. "Researchers can measure peanut dust in homes where people eat peanut or peanut butter. Although it may not be enough to cause anaphylaxis (severe allergic reaction), it could sensitize an infant to peanut—that is, cause them to develop IgE antibodies against peanut."

Former Thinking on Prevention

"In 2000, guidelines from the American Academy of Pediatrics (AAP) recommended withholding allergenic foods from young children's diets due to concern that such exposure would sensitize them, and in a subset of the children, would lead to clinical food allergy," says Daniel Rotrosen, MD, director of the division of allergy, immunology, and transplantation at the NIAID in Bethesda, Maryland.⁸

"However, the early research that led people to think that withholding the introduction of allergenic foods was a good idea was kind of murky and didn't come from large, randomized, well-controlled studies," Rotrosen says. "In those studies, if there was any

benefit of withholding potential allergens, it was very marginal."

In addition, during the time when pediatricians were recommending delaying introduction of particularly allergenic foods, there was an epidemic of food allergy, especially peanut allergy, Kelso says.

As a result, in 2008 the AAP changed its guidelines to recommend that the introduction of allergenic foods not be withheld from young children's diets.⁹ This change also is reflected in the NIAID's 2010 Guidelines for the Diagnosis and Management of Food Allergy in the United States.¹⁰

Trail to Prevention

Insight into peanut allergy prevention came from infant feeding practices abroad. "While parents in the US were being told to delay the introduction of peanut until age 3, in Israel virtually all infants are fed treats called Bamba, which are like soft Cheetos but instead of having cheese in them, they have peanut protein in them. Peanut allergy was virtually unheard of in Israel," Kelso says.

Based on this, a 2008 study in *The Journal of Allergy and Clinical Immunology* compared peanut allergy rates in Israeli Jewish children, where peanut products are widely consumed starting around 6 or 7 months of age, with rates in London among Jewish children of similar genetic background where peanut products were largely avoided in young children.¹¹ The rate of peanut allergy in London was about 10-fold higher than that in Israel.

That sparked the idea that instead of delaying the introduction of highly allergenic foods, perhaps it's better to introduce

TIPS FOR EARLY PEANUT INTRODUCTION

- **Refer to an expert.** "Dietitians who get questions about peanut allergy and early introduction should refer clients to someone experienced in this area, ideally an RD who works full time in food allergy," says Deb Indorato, RDN, LDN, CLT, nutrition advisor for Kids with Food Allergies. Some dietitians work in an allergist's office or have private practices focused on food allergy.

- **Recommend medical evaluation in high-risk patients.** "If the infant has a history of eczema or egg allergy, or if there's a family history of food allergies or asthma, parents should discuss early peanut introduction with their pediatrician and allergist first," says Vandana Sheth, RDN, CDE, founder of vandanasheth.com and a spokesperson for the Academy of Nutrition and Dietetics. In such cases, patients may be given skin tests and a blood test (serum IgE) for peanut allergy before considering a supervised oral challenge in the allergist's office.

- **Realize allergy testing isn't 100% accurate.** "Usually the skin prick tests for peanut allergy are pretty reliable," says Laura Noonan, MSN, FNP-C, at O&O Alpan, LLC, a medical center in Fairfax, Virginia. "However, occasionally a person may have a negative skin test for peanut allergy but still react to peanut when they eat it."¹¹

- **Explain that anyone can react.** "There will be some lower-risk patients, and even patients not really at risk, who are going to have reactions to peanut at home, even though they don't have a history of eczema or other food allergy. So parents need to be aware that can happen," says David Fleischer, MD, director of the food challenge unit at Children's Hospital Colorado in Aurora.

- **Introduce peanut in a graded fashion.** The new recommendations from the NIAID will include guidelines on how to introduce peanut in a graded manner at home. "That means gradually giving it to the infant in

several divided doses rather than giving a full serving all in one bite," Fleischer says. "That's basically how we do food challenges for patients in the clinic. We start with a very small amount and gradually increase it over four to six doses every 15 to 30 minutes until a normal serving is eaten. By doing it that way, the chance of having a severe reaction is lessened."

- **Watch for signs of allergy.** "The most common sign of an allergic reaction in infants is a skin reaction, including hives (welts) or swelling, which can be anywhere on the body, but most commonly it would occur on the face first," Fleischer says. "Vomiting is also common." If there's a severe reaction at home, such as wheezing or severe facial swelling, quickly seek emergency care, including calling 911 and administering medication, such as an epinephrine injection.

- **Check developmental readiness to try solid foods.** "That's something parents

the food during infancy. This was tested in the landmark study known as LEAP (Learning Early About Peanut Allergy), which was published in the February 2015 issue of *The New England Journal of Medicine*.

LEAP: Paradigm-Shifting Research

In the LEAP study, which was a prospective, randomized controlled trial conducted in the United Kingdom and funded by the NIAID, researchers studied 640 infants between 4 and 11 months old and of varying ethnicities (white, black, Asian, or mixed) who were allergy prone. They either already had developed severe eczema or egg allergy, or both.^{12,13}

The scientists first gave the infants a skin-prick test for peanut allergy. Those with a skin-testing wheal above 4 mm were excluded from the intervention, since it was assumed they would likely react in an oral peanut challenge.

The infants with a nonreactive skin test or with a wheal of 1 to 4 mm in diameter, which was considered minimally positive, were instructed to either consume age-appropriate peanut products at least three times per week (specifically 6 g of peanut protein weekly, which is equivalent to about 1½ tablespoons or three heaping teaspoons of peanut butter, 50 g Bamba, or 24 g peanuts, which is 0.85 oz) after first passing an oral peanut challenge, or to completely avoid peanut products until age 5.^{12,13}

“What they found was that the percentage of children with peanut allergy at age 5 was much, much lower in the children who had been introduced to peanut early, compared to children

who had a delayed introduction to peanut,” Kelso says. Specifically, those who originally had a negative peanut skin-prick test and consumed peanuts to age 5 had an 86% relative reduction in peanut allergy risk, and those with a minimally positive skin prick test at study entry had a 70% reduction in peanut allergy rate, compared with peanut avoiders.

LEAP-On: Does the Effect Last?

Although these results were extremely encouraging, some scientists wondered if they could be simply delaying the development of peanut allergy with this early introduction strategy. In a follow-up study called LEAP-On, the children who were eating peanut until age 5 in the LEAP study and had not become allergic were instructed to stop eating peanut for one year. At age 6, after one year of peanut abstinence, there was no significant increase in peanut allergy (compared with the children who had avoided peanut since infancy), showing that the benefits of early and continued consumption persisted.¹⁴

“We don’t think we’re just delaying the development of peanut allergy,” Rotrosen says. “We think we’re intervening during the window of susceptibility, and if the child gets through that window, the child is unlikely to become peanut allergic.”

Researchers aren’t stopping there though. “We’re working on a continuation of the LEAP study,” Rotrosen says. “We’re hoping that new peanut allergy will not emerge and will formally explore this issue through continued follow-up of the LEAP participants who are consuming peanut as desired until about age 10.”

should discuss with their child’s pediatrician, who will have seen their child at regular intervals,” Fleischer says. “Developmental signs they should look for would include being able to hold their head upright on their own and loss of the tongue-thrust reflex that pushes food out of the mouth. Usually by 6 months of age that tongue thrust is gone.”

- **Be aware of choking hazards.** Any discussion with parents about introducing peanut should include a warning not to give children under age 4 whole peanuts since they’re a choking hazard.² That includes avoiding chunky peanut butter. “Even smooth peanut butter can be difficult for a young child to eat since it can stick to the roof of the mouth,” Indorato says.

- **Make it developmentally appropriate.** “Make sure the peanut product, whether peanut butter, Bamba, or roasted peanut powder, is presented to the child in an age-appropriate and developmentally appropriate form,” says Drew Bird, MD, director of the Food Allergy Center at Children’s Medical Center in Dallas and an assistant

professor of pediatrics at the University of Texas Southwestern Medical School in Dallas. “For example, if the child is tolerating stage 1 purées, then dilute peanut butter with water to give it a soupy consistency.” In the LEAP study, Bamba was softened with water or milk and mixed with milk or with puréed fruit or vegetables for infants younger than 7 months.² Bamba is available in the United States, including at Amazon.com.

- **Be consistent.** “Just because a child passes a food challenge doesn’t mean they’re always going to be protected,” Bird says. “If peanut is tolerated, we encourage the family to put the food into their diet at least three times a week, as was done in the LEAP study.”

- **Get creative.** It may get tricky trying to get infants to eat peanut products several times per week. Lisa Musician, RD, LDN, of foodallergydietitian.com, likes to use powdered peanut butter with young children. One tablespoon of peanut butter powder provides about 2 g peanut protein.^{3,4} “You can mix it into applesauce, pudding, yogurt,

or infant formula,” she says. “When I did food challenges in the allergist’s office, I found young kids didn’t always like the taste of peanut butter, but mixing it with chocolate syrup and milk helped.”

- **Consider caloric content.** “If we start introducing high-fat foods like peanut early, there could potentially be an increase in obesity rates, so dietitians are going to be an important part of this process and will need to step in if pediatricians are seeing a rapid rise in their patients’ weights,” Fleischer says.⁵ Research published online in June in *The Journal of Allergy and Clinical Immunology* showed that peanut consumption in the LEAP study didn’t interfere with the duration of breastfeeding and didn’t impact height, weight, or BMI compared with peanut avoiders at any point during the study.⁶

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Why Early Introduction Doesn't Work for All

As noted in the LEAP study, a small percentage of children randomized to the peanut consumption group based on skin-prick testing developed peanut allergy. So why doesn't early introduction work for everyone? "Most of the children in the consumption group who had peanut allergy at age 5 were allergic to peanut at the start of the trial (based on an oral challenge) and were advised to avoid peanuts. Nonetheless, these children were included in the formal analysis of results under the stringent criteria used in this study," Rotrosen says. "In contrast, only one child who initially consumed peanut as directed in the study protocol developed peanut allergy by age 5. So, it is possible that at the time they start peanut, some children will have progressed through the first immunologic steps that may eventually lead to peanut allergy. We are also exploring genetic associations that may explain why some children in the LEAP avoidance arm progressed to peanut allergy and others did not."

Young adds, "The development of food allergy is a very complex interaction between the child's genes, immune system, and environment (both diet and food exposures); the timing of food introduction is important, but it's not the only determining signal. In some cases, early exposure may be enough to overcome a genetic predisposition. However, in other cases, the genetic signal may be so strong that it overpowers the environmental dietary signal. It's a classic interaction between your genes and your environment. It's really complex and one of the most active areas of research in allergy."

Future Research

"The LEAP study is unlikely to be replicated because many people would say it's unethical to withhold peanut-containing foods from high-risk young children," Rotrosen says. "However, the NIAID is funding a study to determine how the guidelines being developed based on the LEAP study results can be implemented in a population-based manner without all of the infrastructure and support that came with the LEAP study. There are going to be some things that emerge in widespread implementation that wouldn't have been anticipated from the LEAP clinical trial."

If dietitians are wondering whether the early peanut introduction strategy could apply to other highly allergenic foods, they're not alone. "The induction of oral tolerance is unlikely to be specific

to peanut," Rotrosen says. "However, the other two major pediatric food allergens, milk and egg, may require earlier intervention because those usually appear early within the first year of life, whereas peanut allergy may take a little longer to develop. We're designing a study right now that will be a milk and egg allergy prevention study with a similar hypothesis—that early introduction of milk and egg will reduce the occurrence of milk and egg allergy. There was an egg allergy prevention study done in Germany that showed that introducing eggs at 3 to 4 months of age is probably too late,¹⁵ so we're thinking about starting much earlier."

Researchers in the United Kingdom published the EAT, or Enquiring About Tolerance, study in May of this year, which was designed to determine whether introducing infants to allergenic foods starting at 3 months of age, including cow's milk, peanut, egg, sesame, whitefish, and wheat, decreases food allergy risk.¹⁶ In those who could stick with the protocol (which was demanding, given the number of foods), there was a significant reduction in peanut and egg allergies.

Rewriting the Guidelines

The weight of the evidence for early peanut introduction in allergy prevention is now strong enough that experts convened by the NIAID are writing specific guidance based on the LEAP study. "The new guidelines will be restricted to the early introduction of peanuts. They won't cover any of the other pediatric food allergies because we don't have the evidence base to make strong recommendations about anything but peanuts," Rotrosen says.

Twenty-six different organizations are overseeing the development of the new guidelines by the expert panel, and public comments were invited and considered. "We anticipate the final guidelines will be published this fall or winter," Rotrosen says. They will be available on the NIAID website (www.niaid.nih.gov) and likely will be published in one or more professional journals.

In the meantime, interim guidelines from other organizations can be helpful. In 2015, David Fleischer, MD, director of the food challenge unit at Children's Hospital Colorado in Aurora, and other allergy experts representing a global collaboration of 11 medical organizations developed interim guidance on early peanut introduction based on the group's consensus, which was published in several journals, including the August 2015 issue of *The Journal of Allergy and Clinical Immunology*.¹⁷

Based on the LEAP study findings, some parents already are asking what can they do to avoid peanut allergy in their children. It's important to convey that the guidelines don't apply to older children or those with existing peanut allergy. They only apply to infants who have never eaten peanut products. For guidance on how to address questions from clients, read the sidebar, "Tips for Early Peanut Introduction" on page 52. Stay tuned for the release of formal guidelines from the NIAID.

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