The Peanut Allergic Patient: Diagnosis, Treatment, and Prevention

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The Peanut Allergic Patient: Diagnosis, Treatment, and Prevention

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**ABSTRACT**

The prevalence of peanut allergies (PAs) continues to rise through recent decades, despite the best attempts to reverse that trend. PAs are unpredictable and can be life-threatening. Therefore, it is imperative that nurse practitioners (NPs) are fully aware of the most recent guidelines and evidence regarding diagnosis, treatment, and prevention of PAs. This article presents information on the current research in the diagnosis and treatment of PAs as well as the latest guidelines established to prevent PA development. NPs should understand this information, allowing them to provide the best care possible for their patients.

**Keywords:** diagnosis, immunotherapy, peanut allergy, prevention guidelines, treatment

A PA diagnosis can be frightening and life-threatening. Consequently, a PA alters what one eats and creates anxiety for people with PAs, their families, and friends. Some countries require precautionary advisory labels to indicate any possibility of the product containing peanuts, yet these labels may be inconsistent and inadequately represent the possibility of peanut contamination. Other methods to promote public safety include increasing the awareness of PAs and implementing policies and practices that improve safety at schools and early care/education programs. Despite strategies to cope with PAs and minimize exposure, a risk of accidental exposure remains.

Avoidance has been the only recommendation over the past several decades. However, recent studies show promise in the effectiveness and safety of oral immunotherapy (OIT), sublingual immunotherapy (SLIT), and epicutaneous immunotherapy (EPIT). Additionally, improved diagnostic testing provides more accurate results while minimizing risk. Because of the increasing PA prevalence, nurse practitioners (NPs) should understand PA development, the available tests and treatments, and the associated risks. With this knowledge, NPs can educate patients about appropriate management and help them cope with their allergy.
The purpose of this clinical feature is to present what NPs need to know about their role in the care of PA patients. Specifically, it includes an overview of PA development, typical history and physical examination (PE) findings, the latest research on effective diagnostic and treatment techniques, the latest guidelines on preventing PAs, and tips for teaching patients and families.

DEVELOPMENT OF PA
Understanding allergy development may reveal a pathway to prevention. Several theories attempt to explain PA development, yet the exact cause remains unknown. Theories include the hygiene hypothesis,13 maternal-fetal pathway,14 external exposure,15 and the dietary hypothesis.13

According to the hygiene hypothesis, improved sanitation minimizes exposure to bacteria and viruses, which previously strengthened immune systems. Without these exposures, some people react against nonharmful agents13 like peanuts.

The maternal-fetal pathway hypothesizes initial exposure to peanuts occurs in utero and/or through breastfeeding, causing infants as young as 4 months old to test positive to peanuts.14 In contrast, maternal ingestion of allergenic foods during pregnancy provides protection against midchildhood allergies.3

According to the external exposure theory, exposure occurs through inhalation or compromised skin.15 If peanut exposure occurs at the compromised site, the immune system might recognize peanuts as an offending agent and react in subsequent exposures.

The dietary hypothesis is based on differences between Western and Mediterranean diets. The Mediterranean diet provides exposure to various foods, including peanuts, which theoretically helps the immune system recognize harmful agents.13 For example, children in the United Kingdom have a PA rate 10 times higher than their Israeli counterparts, who began consuming peanuts earlier in life.16

CLINICAL PRESENTATION
History of Present Illness
The integumentary, cardiopulmonary, and gastrointestinal systems are most commonly affected with food allergies.8 Therefore, patients with a PA typically present with a history consistent with allergic reactions including complaints of itching; rashes; hives; swelling; wheezing; coughing; voice changes; or gastrointestinal issues including nausea, vomiting, and diarrhea. The timing of symptoms after ingestion is also important. A PA is a type 1 immunoglobulin E (IgE)-mediated response, and symptoms occur rapidly after exposure, usually only minutes later.14,15 The amount of peanuts consumed contributes to the severity of the reaction.15 Other cofactors that can influence the reaction threshold and severity include recent exercise, current medications, and comorbid conditions.8,12

Past Medical and Family History
Patients with a family history of PAs and/or concurrent diagnosis of eczema or asthma are at increased risk for developing a PA. Eczema, asthma, and food allergies are often concurrently diagnosed because of an atopic gene.8 PAs develop in 25% to 30% of patients with a strong atopic history.12 Similarly, 90% of people with PAs have a history of eczema, asthma, rhinitis, or other food allergies.15 Thus, NPs should ask about these conditions or symptoms in patients and family members. A concurrent diagnosis of a PA and asthma, particularly if undertreated, increases the risk of an anaphylactic reaction.15 Additionally, patients with asthma have an increased likelihood of a severe reaction during oral peanut challenges.17

Physical Examination
Patient history should be the primary cause to suspect a PA because PE findings may be unremarkable at the time of evaluation. NPs should evaluate all systems affected by an allergic reaction, including integumentary, cardiopulmonary, and gastrointestinal, because some symptoms may be overlooked by the patient/family. Information gathered from the history of present illness, past medical and family history, PE, and timing of reaction help an NP decide whether to order diagnostic testing or refer to a specialist who is a provider trained and experienced in diagnostic testing, the associated risks, and how to manage them.18

DIAGNOSIS
Early, accurate diagnosis is imperative because anaphylaxis is more common in PAs than other foodborne allergies.6 Diagnostic tools include oral food challenges (OFCs), skin prick testing (SPT),
peanut-specific serum (sIgE), and component IgE testing (cIgE). No one diagnostic test is perfect. Using them in combination will provide more accurate information than any one test alone. Additionally, PA testing should be limited to patients with a history of symptoms because positive results can occur in both SPT and slgE in people without a history of symptoms. Positive SPT and/or slgE results without a history of symptoms or peanut sensitization do not always indicate a PA. In fact, the majority of the population who are peanut sensitized are not allergic.

**OFCs**

An OFC is typically supervised by a specialist and is the "gold standard" for PA testing because it is the most definitive test available, but it has flaws. An OFC is simple but can be time-consuming and potentially dangerous. An allergic reaction of unpredictable severity may develop, with anaphylaxis being the greatest risk. Any patient with a recent history of anaphylaxis should not be tested using an OFC. In an OFC, patients eat a peanut product and are monitored for signs of an allergic reaction. Emergency supplies and medications are available in case a severe reaction develops. NPs should be familiar with OFCs and the risks involved and educate their patients accordingly.

**SPT**

SPT is less risky but not as accurate as an OFC and is typically performed by specialists. A skin prick introduces a small amount of antigen into the tissue. After 15 minutes, the allergen prick site is compared with a control prick site and assessed for the development of hives, indicating a reaction. Typically, a wheal ≥ 3 mm indicates a PA but only if paired with a positive history suggesting a PA. However, some studies used wheals of > 4 mm and ≥ 8 mm to diagnose a PA, even without a positive history. Limitations of SPT for PAs include low specificity (30%), variability in concentration of test reagents, pressure applied when prickling the skin, location placed, and timing of reading results.

**sIgE Testing**

sIgE testing measures the amount of peanut-specific IgE in the patient’s serum. Elevated levels correlate with an increased likelihood of allergy. Sicherer and Wood found slgE concentrations above 15 kUA/L had more than a 95% chance of clinical reactivity. However, Dang et al found slgE had a high specificity (98%) but low sensitivity (26%) when using the cutoff of 15 kUA/L to diagnose PAs with a positive predictive value of 95%. Sensitivity refers to the likelihood of a positive result if actually positive, and specificity refers to the likelihood of a negative result if negative. Therefore, a low specificity means there is an increased risk of false-negative results. slgE testing can be completed in a primary care clinic but requires access to a laboratory capable of running this test. Correct test ordering and interpretation can be complex. NPs unfamiliar with these tests should refer patients to a specialist.

**cIgE Testing**

cIgE is another blood test that can be completed in a primary care clinic. This test measures IgE levels for each of the identified peanut protein components, which are Ara h1-h17. Each component has properties that may correlate to an allergic response. Ara h1, 2, and 3 were more often positive in subjects who failed OFC, and Ara h8 was more frequently positive in people who passed OFC. Ara h2 was more sensitive and specific for PAs than Ara h1, 3, 8, or slgE testing. Despite these results, increased Ara h2 has not been directly correlated to severe reactions. Nevertheless, Dang et al found cIgE more accurate than either SPTs or slgE in determining PAs. Their participants first underwent SPTs and OFCs to determine allergy status and then completed slgE and cIgE for Ara h2. Results were then compared with OFCs to determine testing accuracy. cIgE accurately diagnosed more patients than either SPT or slgE. Using cIgE as a follow-up test to slgE could minimize the need for OFCs by as much as two thirds. Additional study is needed to further evaluate peanut components among various populations.

Each testing modality has benefits and limitations. OFCs remain the "gold standard" but have risks of anaphylaxis. SPTs deliver quick results when history suggests a PA. OFCs and SPTs are typically performed by specialists. Conversely, Ara h2 and slgE testing can be performed in primary care clinics. Current recommendations suggest that if patient
history is positive for allergic reaction, then SPT or sIgE may be sufficient. If these test results are not definitive, then an OFC is recommended.\textsuperscript{20} Patients without a history of an allergic reaction should not be tested because it is costly and can cause undue burden on patients.\textsuperscript{12}

**TREATMENT**

In addition to knowing about available tests, NPs should be aware of current treatment options to better educate patients. The initial treatment recommendation should be avoidance,\textsuperscript{8} which can be very difficult.\textsuperscript{23} Beyond that, any patient diagnosed with a PA should be prescribed EpiPens (Mylan, Canonsburg, PA), or a similar product, because of the risk of anaphylaxis.\textsuperscript{8,17} Antihistamines are beneficial for the treatment of acute mild reactions.\textsuperscript{24} Recent advancements can help patients develop tolerance to varying amounts of peanuts. This progress in treatment will, hopefully, lead to complete desensitization, allowing worry-free peanut ingestion.

**Investigational Treatment Modalities**

Subcutaneous immunotherapy for PAs was associated with a high rate of systematic adverse events (AEs), some of which were severe, which necessitated research on other modalities.\textsuperscript{25} Two investigational treatment options are SLIT and OIT. SLIT is administered by placing drops of peanut extract under the tongue, and OIT is administered through ingesting the allergen, typically peanut powder. Both methods are relatively safe and effective in creating a level of tolerance to peanuts.\textsuperscript{9,10}

The administration of SLIT and OIT follows a similar protocol, beginning with an escalation phase followed by a maintenance phase. Therapy begins at low doses, and the dose is increased every 1 to 2 weeks under clinic supervision. Patients take the safely consumed dose at home until the next increase. If an allergic reaction occurs, families treat as instructed and notify the clinic, dosing adjustments are made, and patients are again advanced as tolerated. Once the maintenance dose is reached, patients continue on that same dose. The time frame for each phase varies from several weeks or months (escalation) to years (maintenance).\textsuperscript{10,25}

SLIT doses are much lower than OIT doses because sublingual administration is systemically absorbed faster than oral administration. SLIT’s lower doses result in fewer adverse events (AEs) than OIT. In a pilot study, AEs occurred in 9% of SLIT doses and 43% of OIT doses ($P < .001$).\textsuperscript{9} Reactions in both groups were typically mild; however, moderate reactions and reactions requiring antihistamines, beta2-agonists, and epinephrine were more common in the OIT group. Additionally, more participants withdrew because of intolerable symptoms in the OIT group than the SLIT group.\textsuperscript{9} Although this evidence suggests using SLIT, effectiveness should be considered. In both groups, participants experienced at least partial desensitization, but differences between the groups were significant. The OIT group developed better desensitization, tolerating an average of 24 peanuts compared with an average of 1 or 2 peanuts in the SLIT group.\textsuperscript{9} Similarly, Fleischer et al\textsuperscript{10} found that desensitization from SLIT was not clinically significant.

Unlike SLIT and OIT, EPIT is administered through a patch placed on the skin. A recent study compared 2 different strengths, 100 and 250 $\mu$g, against placebo.\textsuperscript{11} Participants ($N = 74$) went through an escalation phase, which focused on tolerance to the patch for longer time periods each day, thereby increasing the amount absorbed. Although the ongoing study is designed for 130 weeks, evaluation based on OFC results after 52 weeks indicated EPIT created greater tolerance to peanuts with both the 100 and 250 $\mu$g doses than placebo ($P = .005$ and $P = .003$, respectively).\textsuperscript{11} The difference between the treatment groups was insignificant ($P = .48$). Children younger than 11 years responded best to treatment. Although there were no severe reactions, mild AEs, usually limited to the patch site, occurred in 79.8% of doses.\textsuperscript{11}

SLIT, OIT, and EPIT show promise in treating PAs, but studies are limited by small sample sizes,\textsuperscript{9,10,23} high dropout rates,\textsuperscript{9,10} and exclusion of subjects with history of anaphylaxis or other severe reactions.\textsuperscript{9-11} Further study is needed.

**MANAGEMENT**

**Prevention**

The devastating nature of PAs has encouraged research on PA prevention. Du Toit et al’s study,\textsuperscript{21}
Learning Early about Peanut Allergy (LEAP), found introducing peanut into the diet of high-risk infants in their first 11 months can reduce the risk of developing PAs.18 Infants (4-11 months old) who had severe eczema, egg allergy, or both were classified as high risk. Children were excluded if they were low risk (no history of egg allergy or severe eczema) or they had an SPT result for peanuts larger than 4 mm because this increased their likelihood of being allergic.21 Participants were randomly assigned into either the peanut consumption or peanut avoidance group. Among participants with a negative SPT (0 mm) at baseline, regular peanut consumption resulted in an 86.1% relative reduction in PAs at 60 months of age with a PA prevalence of 13.7% in the avoidance group and 1.9% in the consumption group (95% confidence interval, 3.4–20.3; P < 0.001).21 Among participants with a positive SPT (< 4 mm) at baseline, regular peanut consumption resulted in a 70% relative reduction in PAs at 60 months of age with a PA prevalence of 35.3% in the avoidance group and 10.6% in the consumption group (95% confidence interval, 4.9–43.3; P = 0.004).21

LEAP-ON, the follow-up study, involved the same participants and researched whether early peanut consumption provided long-lasting tolerance. After the LEAP study, the consumption group was asked to abstain from peanuts for 12 months, and the avoidance group continued avoiding peanuts.26 After this 12-month period, the early peanut consumption group had a significantly lower PA prevalence (4.8%) than the early peanut avoidance group (18.6%) (P < .001). Although 3 children in the consumption group became peanut allergic over the 12-month period, the prevalence difference at 60 months versus 72 months was not statistically significant (P = .25). Thus, LEAP-ON found a sustained benefit from the early introduction of peanuts.26

Perkin et al27 evaluated which age is best for introducing allergenic foods into infants’ diets. Inclusion criteria were being 3 months old and being strictly breastfed. Participants were randomized into 2 groups: standard (6 months) and early (3 months) introduction. Introduced foods included peanuts, cooked egg, cow’s milk, sesame, whitefish, and wheat. The standard group began introduction of these foods at 6 months of age at the parents’ discretion. The early group had baseline SPTs completed, and, if positive, then OFCs were completed. Those with a negative SPT or OFC were instructed to continue with this introduction protocol (ie, first cow’s milk; then peanut, cooked egg, whitefish, and sesame, in any order; and, finally, wheat).27 If an SPT and OFC were positive for any of these foods, participants avoided those particular foods and continued per protocol with the others. For peanuts, the early introduction group had a lower prevalence (0/310) of PAs compared with the standard introduction group (13/525) (P = .003) in the per-protocol analysis.27 However, in the intention-to-treat analysis, there was no statistical benefit (P = .11) in the early introduction of peanuts at 3 months compared with 6 months.27

Research has impacted practice guidelines. For example, the LEAP study influenced the National Institute of Allergy and Infectious Diseases to develop the 2017 addendum to the 2010 Guidelines for the Diagnosis and Management of Food Allergy in the United States.18 The addendum recommends, when appropriate, the early introduction of peanuts to prevent PAs.18 Furthermore, it specifies that products containing peanuts should be introduced between 4 and 11 months of age for most infants. The timing of introduction coincides well with the introduction of solids into infants’ diets. The guideline recommendations are for specific groups of varying risk levels for developing PAs (Table 1).18 The early introduction of peanuts to an infant’s diet minimizes the risk of developing a PA but does not eliminate the risk completely.21 Current guidelines are essential for primary care providers to understand and implement to help reverse the trend of increasing PAs.

Role of the NP
NPs have important roles in PA prevention, diagnosis, and proper education in developing an allergy plan. Additionally, NPs should help patients understand what to expect from the specialist and current treatment options.

At a minimum, an allergy plan (Table 2) should include the following: remaining safe with PAs and avoiding exposure, identifying allergic reactions and/or anaphylaxis, treating reactions, and referring to a
specialist. As mentioned previously, patients with a suspected PA should be prescribed EpiPens. NPs should emphasize the possibility of a biphasic reaction, a secondary anaphylactic reaction that can occur up to 72 hours after resolution of the initial reaction. EpiPens come in pairs for this reason as well as the need for backup in case an EpiPen is faulty. Whenever an EpiPen is used, the patient should be transported to the nearest hospital for monitoring and further treatment.

**CONCLUSION**

PA prevalence has increased over recent decades, which increases the likelihood that NPs will be

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<th>Table 1. National Institute of Allergy and Infectious Diseases’ Addendum Guidelines for Early Peanut Introduction</th>
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<td><strong>Risk level</strong></td>
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| Low (no eczema and no food allergies) | • Introduce peanuts freely into diet according to age-appropriate guidelines, family preferences, and cultural practices  
• Introduce peanuts at home |
| Moderate (mild to moderate eczema) | • Introduce peanuts around 6 months of age according to age-appropriate guidelines, family preferences, and cultural practices  
• Introduce other solids before peanuts to ensure developmental capability |
| High (severe eczema, egg allergy, or both) | • Introduce age-appropriate peanut-containing foods at 4-6 months of age  
• Introduce other solids before peanuts to ensure developmental capability  
• Evaluate peanut sIgE, SPT, or both before introducing peanut into diet and follow recommendations based on results  
  • sIgE done in PCP office, SPT with specialist  
  • sIgE < 0.35 kUA/L, introduce peanut into diet  
  • sIgE ≥ 0.35 kUA/L, refer to specialist  
  • SPT ≤ 2 mm, introduce peanut into diet  
  • SPT 3-7 mm, refer to specialist for OFC  
  • SPT ≥ 8 mm, avoid peanuts and refer to specialist |
| Children with identified peanut allergy | • Strict avoidance  
• In families with known peanut allergies, discuss risks and benefits of adding peanuts to an infant’s diet |

OFC = oral food challenge; PCP = primary care physician; sIgE = peanut-specific immunoglobulin E; SPT = skin prick test.

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<th>Table 2. Peanut Allergy Plan</th>
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| **Safety** | • Avoid peanuts, including restaurants with environmental exposure  
• Read/trust nutrition fact labels  
• Notify school/friends/family  
• Keep EpiPen available |
| **Identify reactions/anaphylaxis** | • Watch for itching, rashes, hives, or swelling after peanut exposure  
• Anaphylaxis can include coughing, wheezing, fatigue, drop in BP, closing of airway, and loss of consciousness |
| **Treatment** | • For mild reactions treat with antihistamine  
• For severe reactions, use EpiPen as directed and go to the local emergency department  
• Can use short-acting beta-agonist to help with symptoms after EpiPen administration if asthmatic |
| **Refer to specialist** | • If unable to manage symptoms or family would like further consultation  
• See SPT/sIgE results in Table 1 |

BP = blood pressure; sIgE = peanut-specific immunoglobulin E; SPT = skin prick test.
involved in assessing and managing patients with PAs. This article addressed the recent advancements in diagnosis, treatment, and prevention that are important for NPs to understand. Developing desensitization through new immunotherapy options can greatly improve the quality of life for children with PAs. Following the National Institute of Allergy and Infectious Diseases guidelines for the management of food allergies can minimize PA development, and the implementation of an allergy plan will improve safety in day-to-day living. NPs fill an important role in helping patients manage this life-altering condition.

References


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