

Oral Immunotherapy in Infants

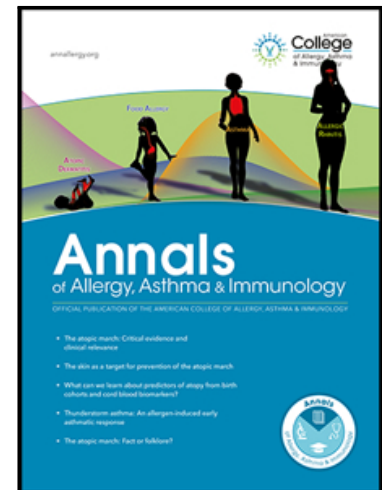
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Oral Immunotherapy in Infants

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Running Head: OIT Infants

IgE-mediated food allergy presents an increasing public health burden in the developed world.¹ An estimated 4 - 10% of children have an IgE-mediated food allergy by 1 year of age.²⁻⁴ The Learning Early About Peanut Allergy (LEAP) trials revolutionized our understanding of food allergy development and shifted recommendations toward early introduction of peanut into the diet as a preventative measure.^{5,6} Early introduction has also shown promising results for the prevention of egg allergy.⁷ Unfortunately, early introduction is insufficient to prevent all food allergy. There is tremendous interest in developing a safe and effective strategy to reverse or cure food allergy in those already afflicted.

In children 4 years and older, peanut oral immunotherapy (OIT) is approved by the Food and Drug Administration (FDA).⁸ In this age cohort, the limitations of peanut OIT include a twofold increase in need for injectable epinephrine versus avoidance alone and low rates of sustained unresponsiveness (cure).⁹ Vickery et al. suggested that outcomes may improve if desensitization is performed earlier in life.¹⁰ There may be greater immunoplasticity in younger children, and as such, infancy may serve as a 'critical window' for a safe and efficacious OIT.¹⁰

While strict avoidance remains the standard of care in food-allergic infants, it is increasingly apparent that physicians and patients are sometimes attempting OIT on their own. Rather than endorsing this approach, we seek to share a few stories brought to our attention to add to the meager data currently available regarding OIT in infants. While these cases of infant OIT were performed separate from a medical institution, we have reviewed each case history and photographs in detail and believe these cases will promote important discussion on OIT in infancy. Here, we present three infants who independently underwent OIT in their home under the guidance of physician parents trained in recognizing and treating allergic reactions. Each had antihistamines and injectable epinephrine readily available and none had access to clinic-based infant OIT in their community.

The first case was a 4-month-old female with eczema who developed diffuse urticaria and irritability with no additional symptoms within minutes following her first ingestion of a small bite of peanut butter (PB). She was given diphenhydramine with prompt resolution of symptoms. During a graded oral food challenge (OFC) with PB at 5 months, she tolerated a “smear” of PB but developed

a diffuse urticarial rash on her face and body with no additional symptoms' minutes after ingesting 300 mg peanut protein (PNP). OIT was started at 7 months with approximately 17 mg PNP. By 13 months, she was ingesting 300 mg of PNP daily with no symptoms.

The second case was a healthy 5-month-old male who initially ingested PB without symptoms, though 15 days later experienced an immediate-onset urticarial rash around his mouth and face with lip edema after ingestion of a small bite of PB. The rash lasted 60 minutes, and self-resolved without treatment. During a blinded OFC he developed an erythematous perioral rash minutes following ingestion of "pea-sized" bite of dilute PB with no contact exposure. He had no symptoms ingesting 1 tsp almond butter. At 6 months of age, OIT was initiated with approximately 24 mg PNP daily. The first several weeks he developed perioral hives following his daily dose that would self-resolve without treatment. The disappearance of rashes was interpreted as a sign to increase the dose. At 9 months, he was tolerating several grams of PNP daily and had no symptoms with

an OFC to 3,600 mg PNP, after which he transitioned to variable amounts of daily PNP maintenance.

The third case was a healthy 9-month old female who developed a diffuse urticarial rash associated with swollen eyelids within minutes of ingesting several bites of cashew butter (Figure 1). She was given diphenhydramine with resolution within hours. OIT in the form of weighed cashew butter was initiated at 10 months with a starting dose of roughly 1 mg of cashew protein (CP). This was gradually increased over time until perioral hives developed, maintained until no hives were noted, then increased again. After gradual build-up over approximately 3 months, she tolerated an OFC with 5,000 mg CP. She then transitioned to daily maintenance of variable amounts of daily CP.

Of note, 5 weeks into cashew OIT infant three developed an immediate-onset urticarial rash after exposure to ~50 mg pistachio protein (PIP). She then abstained from pistachio ingestion until tolerating multiple grams of CP, at which point she consumed a higher dose of PIP without symptoms. At 16 months of age,

she abstained from cashew and pistachio for 32 days after which she had no symptoms with ingestion of each nut protein.

In each case of infant OIT there was no need for antihistamines, injectable epinephrine, ER visits, or hospitalization. These cumulative findings warrant further investigation as to whether infant OIT is a safe therapeutic modality in infants as young as 6 months. The short time to desensitization observed may be a reason to consider OIT in infants. It remains to be seen whether infant OIT may increase the likelihood of achieving sustained unresponsiveness. This case series is limited by the small sample size; and will require validation in a larger cohort. The medical background of these parents significantly limits the generalizability of this case series and the lack of comprehensive testing limits our understanding of the degree of sensitization to food allergens and may call into question the underlying food allergy diagnosis. Additionally, the long-term outcomes of food desensitization remain to be seen.

Given the global burden of IgE-mediated food allergies, strategies to mitigate the overall morbidity and mortality associated with this disease is critical.

This limited case series should not be utilized to change clinical practice. Rather, we hope sharing these stories will encourage clinics with more robust data on infant OIT to come forward, to better define the risks and allow informed decision-making for both physicians and parents. This case series highlights a need for more research exploring the safety and efficacy of infant OIT.

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Figure 1: Several photographs were reviewed for each infant following various adverse food reactions throughout OIT. This figure shows case 3 infant at 9 months of age when she developed a diffuse urticarial rash and bilateral eyelid swelling associated with rhinorrhea without additional symptoms within minutes following ingestion of several bites of cashew butter with no contact exposure. She was given diphenhydramine and symptoms resolved within hours.