



Perspective

Reaching for best practices in food oral immunotherapy

Report on the second annual Food Allergy Support Team meeting

Richard L. Wasserman, MD, PhD ^{*,†}; Douglas H. Jones, MD [‡]; Hugh H. Windom, MD [§]; and the Meeting Faculty

^{*} Allergy Partners of North Texas, Dallas, Texas

[†] Medical City Children's Hospital, Dallas, Texas

[‡] Rocky Mountain Allergy at Tanner Clinic, Layton, Utah

[§] Food Allergy Center of FL, Sarasota, Florida



ARTICLE INFO

Article history:

Received for publication March 9, 2019.

Received in revised form April 15, 2019.

Accepted for publication May 6, 2019.

The Food Allergy Support Team (FAST) is a group of allergists dedicated to enhancing food oral immunotherapy (OIT). The second annual FAST meeting in July 2018 was attended by 109 clinicians who represented 80 allergy practices. This report summarizes the opinions of practitioners who had treated more than 7800 patients and outlines the core principles of safe and effective OIT use in clinical practice.

Selecting the right patient for OIT is critical; clinicians consider food reaction history, supportive testing, age, comorbid conditions, social, psychological, and logistical factors. It is important to ensure that atopic conditions are well controlled before initiating OIT. Patients with severe allergic rhinitis or asthma may need aero-allergen immunotherapy before starting OIT.

Patients with an unequivocal history of an IgE-mediated reaction with supportive testing are solid OIT candidates. The patient with positive diagnostic test results but no history of reacting to a food is more difficult. Oral food challenges are required for patients with low-moderate test results. The role of oral food challenges in confirming food allergy is discussed elsewhere.¹ Participants agreed that clinicians and informed families must balance the risks of a severe reaction with the burden of unnecessary OIT. Contraindications to OIT are listed in Table 1.

Clinicians should be aware that anxiety about OIT and food challenges is common among food allergic children and their parents. These anxieties should be addressed directly with reassuring but accurate information about adverse events associated with OIT.

Because of the demands of OIT, the entire family should agree about OIT, particularly in divorced families. Families, especially those who travel a distance for treatment, should be fully informed about the burdens of OIT: obtaining school cooperation, scheduling athletic activities, and adhering to frequent clinic visits.

FAST's core mission is to standardize safe and effective OIT protocols. Attendees use protocols modeled after clinical trials² or reported clinical experiences.^{3,4} Protocols begin with an escalation day using a subeliciting dose and increasing to a predetermined target 100 to 1000 times the starting dose, followed by home dosing and weekly or biweekly dose increases under observation. The optimal interval between dose increases remains undefined. Longer intervals are used for convenience (eg, vacation or school or work conflict) or safety (eg, an intercurrent illness). The process continues until the target dose is consumed (see eTable 1 for protocol parameters).

An escalation target dose of 1 to 10 g of protein typically represents a full serving of the food, a goal particularly for patients with egg and milk allergy (eTable 1). Most patients tolerate at least 3 to 4 times their maintenance dose and, thus, no longer have to avoid the food in their diet.⁵ OIT target doses may be lower for patients who dislike and intend to avoid the food.

Maintenance dosing is usually daily, but less frequent dosing may be possible at some point during maintenance. Many clinicians assume a relationship between the maintenance duration and the likelihood of developing sustained unresponsiveness, but the issue has not been studied directly and the ideal regimen remains undefined.

The most allergenic form of the food is preferred for OIT (eg, raw egg and roasted peanuts). eTable 2 lists the OIT foods and sources. Most participants use different forms of a food interchangeably; however, some practices insist that changes of dosing forms be

Reprints: Richard L. Wasserman, MD, PhD, Allergy Partners of North Texas, 7777 Forest Lane, Ste B-332, Dallas, TX 75230; E-mail: drichwasserman@gmail.com.

Disclosures: None.

Funding Sources: The meeting was partially funded by a grant from Mylan Specialty LP (protocol 16-004 investigator-initiated trial).

<https://doi.org/10.1016/j.anai.2019.05.002>

1081-1206/© 2019 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

Table 1
Relative (Possibly Absolute) Contraindications to OIT

Contraindication	Comments
Anxiety in the patient	OIT patients have been taught that the treatment food could make them sick or kill them and they need to avoid it. Most patients are able to overcome the anxiety with a full explanation of OIT and the ability to adjust (customize) the treatment to them.
Anxiety in the parent	Parental anxiety is often the prime motivation for OIT. Most of the time parents can control their anxiety. If they can't, the other parent or a surrogate should attend the visits.
Psychiatric diagnosis	Anxiety disorders and related problems from obsessive-compulsive disorder to psychosis may be exacerbated by the stress of OIT. Such disorders may also interfere with the development of a therapeutic relationship with the allergy team.
Dietary inflexibility	Patients with a history of food refusal or a very limited diet may have difficulty eating the OIT food regularly and may be unreceptive to masking efforts.
Eosinophilic esophagitis	By definition, the OIT food did not cause EoE because it has been avoided. At this time, it is unclear whether having EoE triggered by a food increases the risk of EoE caused by another food. Some OIT practitioners consider EoE to be an absolute contraindication and others do not.
Uncontrolled irritable or inflammatory bowel disease	Because gastrointestinal symptoms are common during OIT, it is important that other causes of symptoms be fully controlled. If that is not possible, OIT will be difficult.
Atopy	Poorly controlled concurrent allergic conditions may exacerbate when OIT food builds up. Severe asthma may be an absolute contraindication.
Reaction history	Some practitioners exclude patients with a history of a severe, life-threatening anaphylactic reaction and others treat patients regardless of the severity of their reaction history.

Abbreviations: EoE, eosinophilic esophagitis; OIT, oral immunotherapy.

done in the office. Wheat appears to pose special problems. Wheat OIT desensitizes to wheat grain but not reliably to rye, oat, or barley. The ideal source of wheat for OIT has yet to be established.

Very low doses of OIT food are prepared by serial dilution of food suspensions. Patients must be cautioned to shake the suspension thoroughly just before removing the dose. Potential dosing inconsistencies have not been a problem. Although thousands of patients have been treated without apparent problems, suspension stability is unknown.

Many patients have multiple food allergies. Among experienced OIT practitioners, half or more of their patients are doing multifoed OIT. Many different food combinations have been used. Some practices exploit cross-reactivity (cashew/pistachio or walnut/pecan) to minimize the number of treatment foods. Multiple foods are typically administered together and follow the same protocol used for single-food OIT; however, many attendees reduce the day 1 target dose by 1 or more steps. Because it is seldom possible to identify the food that accounts for an adverse event, when a reaction occurs the doses of all the foods are adjusted. Allergists should be aware of the increased preparation time and space that is required at each visit to accommodate multifoed OIT.

A few participants reported successful OIT for garlic, shrimp, chickpeas, lentil, and other less common causes of food allergy using protocols derived from those used for more common foods,

demonstrating the generalizability of the strategy. Repeated reactions, gastrointestinal symptoms, and taste aversion are major causes of OIT discontinuation. Although many reactions are attributable to intercurrent infection or postdose physical activity, sometimes reactions occur for no identifiable reason. Most clinicians reduce the dose after a reaction and continue escalation. Patients who react repeatedly may benefit from longer intervals between dose increases and smaller incremental increases (slow-and-low dosing) or sublingual immunotherapy (eTable 3).

Gastrointestinal symptoms may indicate a systemic reaction, a local IgE-mediated reaction, or eosinophilic esophagitis—like OIT-related syndrome. The slow-and-low escalation controls most gastrointestinal symptoms and allows many patients to reach their target. To assist allergists considering adding OIT to their practice, eTable 4 lists considerations for self-assessment to determine office OIT readiness. Principles of OIT risk management are given in eTable 5. A sample electronic medical record page is shown in eFigure 1.

FAST has developed a national OIT registry with more than 2000 patients entered to date to help answer important OIT management questions. The experienced allergists who participated in this meeting addressed the major elements of shared decision making, standard operating procedure, protocol development, and various nuances of this much needed and highly successful form of patient care designed to normalize the lives of patients with food allergy and their families. Important questions remain, however, including the optimal age for initiating OIT, the risk of eosinophilic esophagitis during maintenance, and the effect of the long-term tolerability of OIT on adherence.

Acknowledgments

The meeting faculty include Sakina S. Bajowala, MD, Kaneland Allergy and Asthma Center, North Aurora, Illinois, Warner W. Carr, MD, Allergy and Asthma Associates of Southern California, Thomas Chacko, MD, Chacko Allergy and Asthma, Atlanta, Georgia, Paul F. Detjen, MD, Kenilworth Medical, Chicago, Illinois, Jennifer Fergeson DO, Food Allergy Center of Florida, Sarasota, Florida, David J. Fitzhugh, MD, Allergy Partners of Chapel Hill, Chapel Hill, North Carolina, Angela R. Hague, PA-C, Allergy Partners of North Texas, Dallas, Texas, Jean Ly, MD, Food Allergy Center of Florida, Sarasota, Florida, Chad W. Mayer, DO, Allergy & Asthma Institute of SE Michigan, Novi, Michigan, Deanna M. Pence, RRT, Allergy Partners of North Texas, Dallas, Texas, and Atul N. Shah, MD, New York Food Allergy & Wellness Center, Centereach, New York.

Supplementary Data

Supplementary data related to this article can be found online at <https://doi.org/10.1016/j.anai.2019.05.002>.

References

1. Frischmeyer-Guerrero PA, Rasooly M, Gu W, et al. IgE testing can predict food allergy status in patients with moderate-severe atopic dermatitis. *Ann Allergy Asthma Immunol*. 2019;122(4):393–400.e2.
2. Varshney P, Jones SM, Scurlock AM, et al. A randomized controlled study of peanut oral immunotherapy: clinical desensitization and modulation of the allergic response. *J Allergy Clin Immunol*. 2011;127(3):654–660.
3. Wasserman RL, Factor JM, Baker JW, et al. Oral immunotherapy for peanut allergy: multipractice experience with epinephrine-treated patients. *J Allergy Clin Immunol Pract*. 2014;2:91–96.
4. Wasserman RL, Hague AR, Pence DM, et al. Real-world experience with peanut oral immunotherapy: lessons learned from 270 patients. *J Allergy Clin Immunol Pract*. 2019;7:418–428.
5. Vickery BP, Vereda A, Casale TB, et al. AR101 oral immunotherapy for peanut allergy. *N Engl J Med*. 2018;379:1991–2001.

Supplementary Data

eTable 1

Standard OIT Protocol Design

Variable	Among
Day 1	
Starting dose	0.02-0.2 mg of protein ^a
Target dose	1-5 mg of protein
Buildup	
Dose increment	50%-100%
Frequency of visits	1-2 weeks
Maintenance	
Target dose ^a	1-10 g of food protein depending on the food treated ^b
Frequency of dosing	2-7 days a week

^aLower initial doses can be used to reassure overly anxious patients and families.^bSome practitioners escalate to a dose 50% greater than the maintenance dose before beginning maintenance; examples of common targets are as follows: half to 1 egg, 60 to 240 mL of milk, 4 to 8 peanuts, 1 to 30 tree nuts, one-third of a bagel to 1 slice of whole wheat bread, and 30 to 120 g of sesame seeds.**eTable 2**

OIT Food Sources

Food	Sources
Almond	Almond milk (Silk Pure Almond, Almond Breeze [Blue Diamond], Elmhurst Almond Milk) and almonds
Barley	Bob's Red Mill flour
Brazil nut	Nut flour (www.sincerelynuts.com), brazil nut butter (Dastony), and brazil nuts
Cashew	Nut flour (www.nuts.com), Elmhurst milk, cashews
Chickpea (garbanzo bean)	Flour (Bob's Red Mill Garbanzo Bean Flour), chickpeas
Coconut	Flour (Bob's Red Mill Organic Coconut Flour), shredded coconut
Egg	Liquid egg white (All Whites 100% Liquid Egg Whites or Eggland's Best Liquid Egg Whites), powdered egg white (Henninsen Dried Egg Whites [www.judeesglutenfree.com])
Hazelnut	Flour/meal (Bob's Red Mill), butter (Fastachi Roasted Hazelnut Butter), Elmhurst Hazelnut Milk (contains almond), hazelnuts
Macadamia nut	Flour (www.sincerelynuts.com), butter (Wilderness Poets Raw Macadamia Nut Butter), macadamia nuts
Milk	Whole milk during escalation, whole or 2% during maintenance
Peanut	Flour (Byrd Mill [www.byrdmill.com]), peanut butter, flavored peanut butters (Peanut Butter & Company flavored peanut butters), powdered peanut butter (TruNut [no tree nut cross-contamination], PB2 (may have tree nut cross contamination), peanut M&M's, Reese's Pieces, Bamba, peanuts
Pecan	meal (www.nuts.com), butter (Ziegelmeier's Toasted Pecan Butter), pecans
Pistachio	Flour (Santa Barbara Pistachio Company), butter (Fastachi Roasted Pistachio Butter), pistachios
Rye	Flour (www.nuts.com), bread (Mestemacher Organic Whole Rye Bread), cracker (Wasa Light Rey Crispbread)
Sesame	Unhulled sesame tahini (Max Sesame Tahini Spread), unhulled sesame seeds (www.nuts.com); some clinicians use hulled seeds
Soy	Milk (Original Silk Soy Milk), soybeans
Sunflower seed	Flour (Organic Roasted Sunflower Seed Flour [www.eatseed.com]), Sunbutter, seeds
Walnut	Meal (www.nuts.com), butter (Fastachi Raw Walnut Butter), Elmhurst Walnut milk, walnuts
Wheat	Whole wheat flour, bread, Wheat Chex, Wheat Thins, Dave's Awesome Bagel

eTable 3
Alternatives to Standard OIT

Method	Description	Advantages	Disadvantages
Low OIT or slow OIT	Reduced starting dose, may increase intervals between doses to weeks or months, decreased incremental dose changes	Adapts the routine OIT protocols to the individual needs of the patient. By extending the dose increase intervals and reducing the dose increments, the risk of reactions is decreased.	Escalation takes longer and requires more office visits. Desensitization is delayed. Exercise restrictions are more prolonged. Burden of OIT increases.
SLIT	Daily sublingual dosing; 0.25 µg escalating to 1000 µg protein (eg, peanut)	The approach least likely to cause a reaction. May have a lower risk of esophagitis. Few to no activity restrictions.	Delays the start of OIT by 6 months. Extracts are costly.

Abbreviations: OIT, oral immunotherapy; SLIT, sublingual immunotherapy.

eTable 4
Questions to Ask Before Implementing OIT in an Allergy Practice

1. Assess the motivation for offering OIT to your patients.
2. Will there be adequate staff and physical space for food preparation, dosing and postdose observation, and managing anaphylaxis? How will you adjust your office flow and scheduling?
3. Are oral food challenges an established part of your practice? Challenges will be needed to confirm or refute food allergy in many patients. Experience with food challenges is essential preparation for OIT.
4. Because OIT physicians must provide continuous backup, you will need to consider how you cover after-hours calls. All covering physicians in the group need to be versed in OIT management. Some clinicians provide their cell phone number to OIT patients.
5. Should you discuss OIT with your malpractice carrier?
6. How do you plan to learn about OIT? What protocol will you use? What are the available resources to learn about how to conduct day-to-day operations?

Abbreviation: OIT, oral immunotherapy.

eTable 5
OIT Risk Management Procedures

1. Before the visit, review the record and confirm the next planned dose.
2. Prepare the dose before the patient's arrival.
3. Complete an interval history and physical examination and confirm readiness to increase the dose.
4. Staff verifies the dose with the physician and patient or parent. Each sign off on the dose. Each dose is labeled with the patient's name, birthdate, food, concentration, and volume to be given.
5. Administer the dose and monitor the patient for adverse events. When the dose is a liquid, an oral syringe precisely marked at the volume to be delivered is supplied.
6. Review the administered dose, confirm that the supply to be dispensed is correct. Patient is provided a discharge sheet that contains all this information and emergency numbers along with dose adjustment parameters.

Dosing Decision

☒ Advance as scheduled
☐ Repeat current dose
☐ Reduce dose
☐ Dose not increased because of dosing problems
☐ Dose not increased because of active symptoms
☐ other

at patient is here for Peanut oral immunotherapy.

Today's Dose

Scheduled: 750 mg Protein: Peanut M&Ms Concentration: 5 pieces Amount: 5 pieces
 Given: 750 mg Protein: Peanut M&Ms Concentration: 5 pieces Amount: 5 pieces
 Time of today's dose: 4:30 PM

Next Dose Information

Next dose increase in: 1 week
 1 days ☒ weeks ☐ months

Protein: 1000 mg Concentration: Peanut M&Ms Amount: 6 pieces

Protein/dose (mg): ☐ 0.002 mg ☐ 0.004 mg ☐ 0.01 mg ☐ 0.02 mg ☐ 0.04 mg ☐ 0.1 mg ☐ 0.2 mg ☐ 0.4 mg ☐ 1 mg ☐ 2 mg ☐ 4 mg ☐ 6 mg ☐ 8 mg ☐ 10 mg ☐ 15 mg ☐ 20 mg ☐ 26 mg ☐ 53 mg ☐ 79 mg ☐ 105 mg ☐ 158 mg ☐ 250 mg ☐ 500 mg ☒ 750 mg ☐ 1000 mg ☐ 1500 mg ☐ 2000 mg (1-3 y/o final escalation dose) ☐ 2500 mg ☐ 3000 mg (4+ y/o final escalation dose) ☐ [4000 mg (1-3 y/o final challenge dose only)] ☐ 6000 mg (challenge) ☐ other

Food Type: ☐ peanut flour solution ☐ peanut flour ☐ peanuts ☐ Tru-Nut ☐ peanut butter ☒ Peanut M&Ms ☐ Bamba ☐ Reeses Pieces

Dose recheck 1: Denise R Whisenhunt MA October 3, 2017

Dose recheck 2: Angela R Hague PA October 3, 2017

Next Dose Information

Next dose increase in: 1 week
 1 days ☒ weeks ☐ months

Protein: 1000 mg Concentration: Peanut M&Ms Amount: 6 pieces

Protein/dose (mg): ☐ 0.002 mg ☐ 0.004 mg ☐ 0.01 mg ☐ 0.02 mg ☐ 0.04 mg ☐ 0.1 mg ☐ 0.2 mg ☐ 0.4 mg ☐ 1 mg ☐ 2 mg ☐ 4 mg ☐ 6 mg ☐ 8 mg ☐ 10 mg ☐ 15 mg ☐ 20 mg ☐ 26 mg ☐ 53 mg ☐ 79 mg ☐ 105 mg ☐ 158 mg ☐ 250 mg ☐ 500 mg ☐ 750 mg ☒ 1000 mg ☐ 1500 mg ☐ 2000 mg (1-3 y/o final escalation dose) ☐ 2500 mg ☐ 3000 mg (4+ y/o final escalation dose) ☐ [4000 mg (1-3 y/o final challenge dose only)] ☐ 6000 mg (challenge) ☐ other

Food Type: ☐ peanut flour solution ☐ peanut flour ☐ peanuts ☐ Tru-Nut ☐ peanut butter ☒ Peanut M&Ms ☐ Bamba ☐ Reeses Pieces

Dose recheck 1: Angela R Hague PA October 3, 2017

Dose recheck 2: Shalyni N Ware CRT October 3, 2017

eFigure 1. Sample EMR record of an OIT dose increasing visit.