

1

Objectives

- At the conclusion of this program you should be able to
 - Identify appropriate candidates for food allergen immunotherapy
 - Outline the strengths and weaknesses of available treatments for peanut allergy
 - Explain the options available for peanut AIT peanut drug, retail peanut, extract SLIT, and retail SLIT



2

Who?

Indications for Food Allergy Immunotherapy

- History of an IgE-mediated reaction to a food
 - Proximate (less than two years) history of any reaction

 - Any history of a severe reaction
 Demonstration of food-specific IgE
- Patient and family (as appropriate depending on age) motivation
- No history of an IgE-mediated reaction to food
 - Food-specific IgE strongly suggestive of a high risk of reaction
 - Positive basophill activation test
 - · Positive oral food challenge
 - Patient and family (as appropriate depending on age) motivation

4

Contraindications for OIT - Absolute

- · Less than six months of age
- Active or uncontrolled systemic disease
- · Active or poorly managed asthma, eczema or gastrointestinal disease
- · Currently updosing with another immunotherapy
- Inability or unwillingness to treat anaphylaxis with prompt administration of epinephrine
- Poor adherence to treatment and safety recommendations
- Pregnancy (for treatment initiation)
- Uncontrolled psychiatric or eating disorder

5

Contraindications – Conditional

- Conditions which increase the risk of anaphylaxis (e.g., mastocytosis)
- · History of severe life-threatening anaphylaxis
- · Medications that may interfere with anaphylaxis treatment (i.e., beta-blocker or ACE inhibitor)
- Poor understanding of OIT
- Prior eosinophilic esophagitis or eosinophilic gastrointestinal disease
- · Controlled eating disorder

Why?

7

Standard of Care For Patients and Families with Peanut Allergy is the Avoidance Management Strategy (AMS)

- The (AMS) treatment plan
 - Careful avoidance of exposure by label reading and avoidance of risky settings (i.e., social isolation)
 - Reaction recognition and timely treatment with epinephrine
- AMS results in reactions
 - 12% to 35% of patients experience accidental exposures
 - >200,000 ER visits/year est. 90,000 for anaphylaxis
 - Only 25% of severe reactions treated with epinephrine
 - <30 deaths/year
 - Most anaphylactic deaths caused by allergens the victim was avoiding
- Psychosocial consequences are not addressed

Reycs JA, Activid A, Next JAVI, Next SAV, Surgeon NA, Wood BA J, Allerg Clin Immund, 2010 Dec 1565, (9) 51-56.
CHAY E, Epidosa J, Andredos SA, Barrey B, A. Change CA Li. Frequency of US emergency department viols for food related acute allergic reactions. J Allerg Clin Immund, 2011;12(1):5184-683.
Allerg Clin Immund, 2011;12(1):5184-683.
Many Limman Limman

8

AMS Distorts Patient Life

The New York Times

In a Children's Theater Program, Drama Over a Peanut Allergy



- Anxiety about having a reaction
 - Fear of hidden ingredients or contaminants
 - Fear of epinephrine use
 - Relationships with friends and family members
 - Patient limitations
 - Isolation no play dates or sleepovers
 - The peanut table
 - 40% have been bullied

AMS Distorts Family Life

- · Parental anxiety
 - Duration of the disease in the absence of a cure is unpredictable at best, may be life long
- Anxiety about having a reaction
 - Fear of hidden ingredients or contaminants
 - Accidental reactions may occur from trace amounts, reaction severity is poorly predictable
 - Fear of epinephrine use
 - Conflict with schools and other parents
 - Disrupts relationships with friends and family members
- · Family limitations
 - Restaurants many families never eat out
 - Vacation travel is severely limited or avoided completely

Cohen BL, et al. JACI 2004; 114:1159-63. Gupta et al JAMA Pediatr 2013; 167: 1026-31. Greenhaw M. Ann Allergy Asthan Immunol 2014; 113: 506-12. Anagnostou et al Lancet 2014: http://dx.dol.org/10.1016/S0140-6736(13)62301-6.

10

Anorexia in Early Childhood Following an Accidental Ingestion of Nuts

- 5 yo with known peanut/tree nut allergy given food with "may contain" label by her teacher after she asked if it contained nuts
- Immediate reaction of tongue itch that lasted 36 hours without other GI, respiratory or cutaneous symptoms
- For the subsequent six weeks she refused to eat at school, lost 5lbs and became dependent on Pediasure
- With education, reassurance, immediately available epinephrine and support, feeding normalized

Poster Presentation ACAAI, 2018. Hernandez-Trujillo, V. With permission.

11

Food Allergy Avoidance Management Strategy Results in Significant Costs to Families and Society



- Food allergy costs patients and society a lot of money, annually
- These cost estimates include obvious and somewhat latent sources, and heavily weight costs from lost opportunities
- These cost figures are not experienced proportionally!

Gupta, RS et al. JAMA Pediat 2013: 1026-1031. Slide courtesy of Ruchi Gupta, adapted

Options for Food Allergy Patients

• The Avoidance Management Strategy (AMS)

The New Hork Times
In a Children's Theater Program,
Drama Over a Pennut Allergy











- "FDA-Approved" peanut drug treatment
- Peanut food treatment oral immunotherapy or OIT
- Peanut extract sublingual immunotherapy SLIT
- Peanut food sublingual immunotherapy SLIT

13



14

The AIT Process

- Parents of appropriate patients are offered the opportunity to have their child treated
- Parents and patients hear an explanation of the process including a discussion of reaction risks and ELORS (Eosinophilic esophagitis-Like OIT-Related Syndrome)



- A written description and explanation of OIT and SLIT processes is provided
- Parents are given a custom consent form
- Approximately two weeks before Day 1, patients are evaluated for stability of asthma and allergy and perform a pulmonary function test if they are able

The Process at DFAC - Day 1 OIT

- Patients arrive and are examined
 - Vital signs, weight, epinephrine, IV diphenhydramine and oral cetirizine doses are recorded on the flow sheet
- Dosing is initiated with 200µg of peanut protein
- Serially diluted suspensions of peanut flour/peanut butter powder are used
- Before each dose the patient is asked how they feel,
- Up to 5 doses are administered at 20 minute
- Two-hour observation after the last dose



16

Dose Escalation Protocols

- Initial dose
 - Regimen based (DAFC) the same starting dose for all patients
 Challenge based
 - - Challenged as an outpatient until reaction occurs
 - Challenged inpatient to a target dose (Israeli approach)
- - Typically, 50-100% of the previous dose
 - Multi-dose rechallenge to a new target (Israeli approach)
- Dosing interval

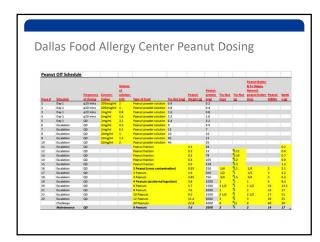
 - 7 or 14 daysFour weeks (Israeli approach)

17

Escalation at the Dallas Food Allergy Center

- · After the first day, dose increases are usually a doubling of the previous dose
 - $-\$ Near the target, the dose increases are as small as 25%
- Doses of powder, nuts, Bamba are weighed
- Patients take the dose tolerated in the office once daily for at least seven days
- Return to the office for a challenge to the next dose
- Interval history is obtained and the patient is examined
- Patients are observed for 45 minutes







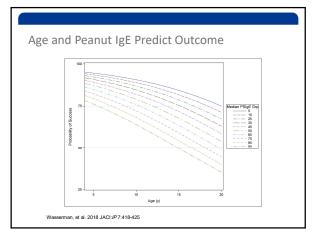


Goals of Peanut AIT

- - The eliciting dose has been raised above the level expected to be in a food labeled "manufactured in a facility..."
 - Impossible to know the correct amount, an estimate
 - 100mg of peanut protein is probably enough
- Label reading still required but manufactured food choices expanded
- 300mg of peanut protein protects against 95% of accidental exposures
 Label reading still required but anxiety reduced and QoL improved
- Free eating

 - The patient is able to routinely incorporate the food into the diet
 A peanut butter sandwich contains ~6000mg of peanut protein Label reading not required
- Sustained unresponsiveness
 - Desensitization endures in the absence of frequent ongoing exposure
 The Holy Grail of OIT realistic for only some patients

22



23

Maintenance at the Dallas Food Allergy Center

- - Peanut free eaters ~2 g protein
 - $-\;$ Patients continuing avoidance and children <4 yo ~1 g protein
- · Dose frequency
 - 7/7 days a week until six months on maintenance
 - 6/7 days a week after six months
 - Frequency reduced may be reduced annually based on decreases in slgE
 - Shared decision-making based on the burden of dosing and the available data

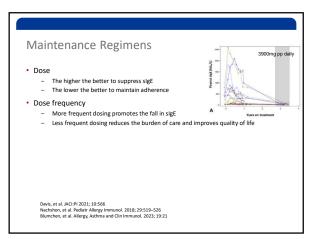
Maintenance Regimens

Maintenance Regimens

• Dose

- The higher the better to suppress sigE

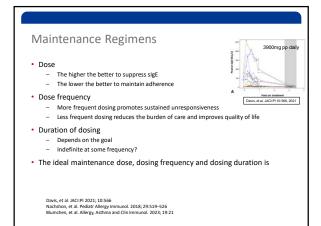
- The lower the better to maintain adherence



Maintenance Regimens • Dose - The higher the better to suppress sigE - The lower the better to maintain adherence • Dose frequency - More frequent dosing promotes the fall in sigE - Less frequent dosing reduces the burden of care and improves quality of life • Duration of dosing - Depends on the goal - Indefinite at some frequency?

Davis, et al. JACI:PI 2021; 10:566 Nachshon, et al. Pediatr Allergy Immunol. 2018; 29:519–526 Blumchen, et al. Allergy, Asthma and Clin Immunol. 2023; 19:21

28



29

Maintenance Regimens • Dose - The higher the better to suppress sigE - The lower the better to maintain adherence • Dose frequency - More frequent dosing promotes sustained unresponsiveness - Less frequent dosing reduces the burden of care and improves quality of life • Duration of dosing - Depends on the goal - Indefinite at some frequency? • The ideal maintenance dose, dosing frequency and dosing duration is UNKNOWN Davis, et al. IACIPI 2021; 10-566 Nacharbon, et al. I-Regist Allergy Immunol. 2018; 29-519-526 Blunchen, et al. I-Regist, Adhma and Chin Immunol. 2013; 19-21

Sustained Unresponsiveness Challenge

- - At least three years of maintenance dosing with no maintenance reactions during the previous 2 years
 - Fall in specific IgE to <1-2 kU/L
- Patients were instructed to completely avoid the allergenic food for one $month\ before\ sustained\ unresponsiveness\ challenge$
- · All challenges were performed in an allergy office setting
- About 2/3's of patients decline the challenge
- Passing the challenge means sustained unresponsiveness, achievement of true tolerance is uncertain
- 37/43 (86%) patients passed the challenge

31

OIT Risks

- Anaphylaxis requiring epinephrine treatment
- Systemic allergic reaction that is self-limited or treatable with antihistamine
- ELORS Eosinophilic esophagitis-Like, ORal immunotherapy Syndrome
- Mild GI symptoms
- · Mild peri-oral hives
- Oral itch
- Food aversion, especially to peanut
- Family disruption around dosing

32

Foods For Peanut Oral Immunotherapy

- Peanut flour has been monopolized by Aimmune and is no longer available
- Tru Nut Powder is tree nut free 50% peanut protein
- PB Powder is not tree nut free 42- 46% protein tsp = 0.8-1 gm protein (3-4 peanuts)
- Peanut butter ~1 tsp = 4-5 peanuts
 - Jif and Santa Cruz Organic are tree nut free Peanut Butter & Co. 1 tsp = 4 peanuts
 - Cinnamon Raisin Swirl
 - White Chocolate Wonderful
 - Dark Chocolate Dream
 The Bee's Knees

 - Mighty Maple



Alternative Peanut Products • Bamba - An average Bamba stick weighs 850 mg - Contains ~100 mg peanut protein - ~3 Bamba sticks = 1 peanut - Alternatives may be different • Peanut M&M's (regular size) - ~1/3" of peanut/M&M • Reese's Pieces Candy (candy shell) - ~50 mg protein/piece • Reese's Peanut Butter cups: - 1.5 oz package = ~7 peanuts - Wrapped gold foil

34

Managing Peanut Aversion

1 piece weighs ~9 gContains ~3 peanuts

- Store peanut products in the freezer
- Homemade single dose chocolate peanut and raisin disks (store in the cold)
- Mix peanut butter powder in a vehicle such as applesauce or pudding

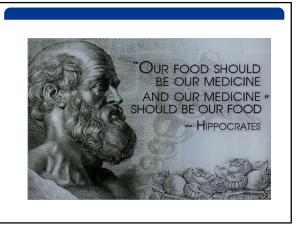
 Minimize the volume
 - Mask with mint, orange, or raspberry extract
- Mix peanut butter powder with salsa and eat with chips
- Mix peanut butter powder with curry
- Make a smoothie and mask with fruit extract

35

Evidence Supporting the Need for a "Standardized", GMP-Produced Product for Peanut Allergy Treatment

Peanut Drug Pros and Cons Pros Cons FDA Approved Risk Evaluation and Mitigation Strategy "Standardized" protein content Standardization is not data supported Pre-made capsules Limited peanut forms for dosing No ad hoc dose preparation Multiple capsules per dose Customization of dosing is difficult No variations caused by different foods 16 dose levels vs 20-25 using retail food protocols Per package insert recommends high initial and day one target doses Large dose increments result in more reactions in the office Peanut avoidance is required; free eating is not an option No option for Sustained unresponsiveness Peanut (Arachis hypogaea) Allergen Powder - \$1133.20/ 30 capsules (300mg) vs peanut butter powder - \$15.99/lb

37



38

SLIT: where does it fit?



- A 'ladder' to OIT
- Salvage treatment after failed OIT
- Stand alone desensitization
- A waste of time, too weak

Adapted by permission, Dr. Hugh H. Windom

Literature Review: The Science Behind SLIT



- 11 pediatric participants peanut SLIT treated + 7 placebo
- 6-month buildup, 6-month maintenance (2 mg pp)
- No epinephrine use
- 1 year OFC: 1700 mg pp median cumulative dose vs 85 mg placebo

Kim EH. J Allergy Clin Immunol 2011;127:640-6 Adapted by permission, Dr. Hugh H. Windom

40

CoFAR Peanut SLIT



CoFAR

- 20 SLIT vs 20 placebo
 - 12-40 year olds (tough crowd)
- 42-week buildup, 2-week Maintenance of 1.4 mg pp
- OFC 2.5 gm (10 nuts), none passed
 - Epinephrine used once
 - However, the median dose went from 3.5 to 496 mg pp

Fleischer DM. J Allergy Clin Immunol 2013;131:119-27 Adapted by permission, Dr. Hugh H. Windom

....,

41

CoFAR 3 Year Follow up Study

- 20 placebo patients crossed over to 3.7 mg pp SLIT
- Annual OFC's, high dropout rate
 - 14/40 remained, no Epinephrine use
- 3rd year OFC 5 g peanut protein after 8 weeks avoidance
 - 2/5 in the cross over group passed
 - 2/9 in the 3 year SLIT group passed



Burks AW. J Allergy Clin Immunol 2015;135:1240-8 Adapted by permission, Dr. Hugh H. Windom

Peanut SLIT vs OIT



- 5 d/c 1st year, 4 in OIT group
- SLIT 3.7 mg pp (n=10), OIT 2 gm/day (n=11)
- Epinephrine in 4 OIT pts (36%), none in SLIT
- OFC after 1 y on maintenance
 - OIT group: 141-fold increase threshold
 - SLIT group: 22-fold SLIT (21 to 496 mg pp)

Narisety SD. J Allergy Clin Immunol 2015;135:1275-82 Adapted by permission, Dr. Hugh H. Windom

43

Long term Peanut SLIT

- 3-5 years of 2 mg peanut protein SLIT
- 47 1-11 yo participants
 - 37/47 completed (79%)
 - 2 dropped because of GI symptoms
- No epinephrine use
- 32% passed 5 gm pp OFC
- 86% tolerated ≥750 mg

Kim EH. J Allergy Clin Immunol 2019;144:1320-6 Adapted by permission, Dr. Hugh H. Windom

44

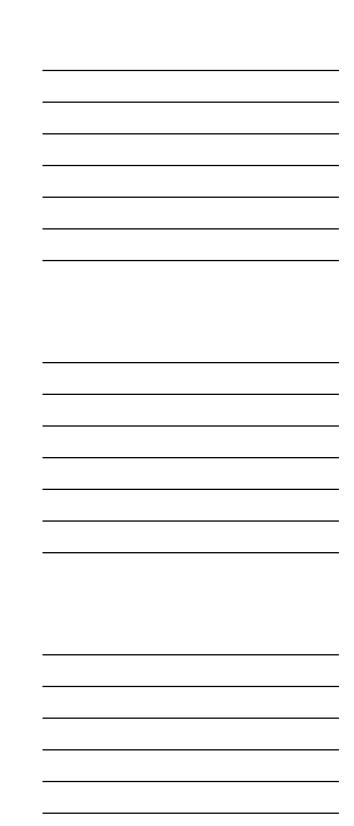
Long Term Peanut SLIT Extended

- 55 participants
 - Ages 1-11 years with challenge proven peanut allergy
 - +positive OFC 0-425 mg, median 0, mean tolerated dose 48mg
- 4 mg peanut protein open label SLIT x 4 years
 47/55 completed 48 months of SLIT and DBPCFC

 - OFC to 5000 mg peanut protein
- Mean tolerated dose 2723 mg
- 70% tolerated >800mg
- 36% tolerated 5000mg
- SLIT discontinued for 1-17 weeks
 - Modeled loss of clinically significant desensitization was 22 weeks

Kim, et al. 2023. JACI; 151:1558-1565





The Right Treatment for the Right Patient: SLIT vs OIT

- SLIT may be better for
 - Scary, highly allergic patient
 Too busy for regular visits

 - Unable to avoid exercise
 - Long distance from centerConcerns about EoE, ELORS
 - Unable to afford OIT
 - Older children and adolescents
- OIT may be better for
 - Staple foods (culturally determined)
- Free eating
- Children under 5



46

Unanswered SLIT Questions



- Does SLIT really need a slow build up?
- What is the appropriate maintenance dose?
- What is the duration of daily dosing? Indefinite?
- Should patients be transitioned to OIT?

47

Does Food SLIT Need Dose Escalation?

SCIT buildup 1:1,000 0.1 / 0.2 / 0.4 1:100 0.1 / 0.2 / 0.4 1:10 0.05 / 0.1 1:10 0.15 / 0.2 1:10 0.3 / 0.4 1:1 : 0.05 1:1 : 0.15 1:1 : 0.3 1:1 : 0.4

SLIT (e.g. Odactra)

House Dust Mite matophagoides farinae and Dermatophagoides pteronyssinus) lergen Extract Tablet for blingual Use 12-SQ-HDM 1 tablet



1:1 : 0.5 Adapted by permission, Dr. Hugh H. Windom

Peanut SLIT Dosing Regimens

	Commercial Extract ¹	Peanut Powder ²
Initial dose	0.25 mcg PP	1 mcg
Maintenance dose	1000 mcg PP	4 mg (5 or 6 mg)
Updoses	21	16
Office visits	21	7
Product cost	>\$10,000 for 36 months of treatment	\$15.99 for hundreds of patients



1. Sakina Bagowala, MD adapted from Kim, et al. JACI. 2011;127:640-6.e1 2. Hugh Windom, MD

49

"Primum non nocere" (First do no harm)

- - Nachson L. JACI:IP 2022;10:1170-6
 1,270 OIT patients
 Escalation epinephrine 15.7%
 - Solar L. JACI:IP 2022;10:1113-6
 - Solar L. JAC1:IP 2022;10:1113-6
 352 preschoolers treated with OIT
 Escalation epi in 1.6% of <13 mo
 Escalation epi in 5.9% of 13-70 mo
 Dallas Food Allergy Center: Jan, 2021-April 2023
 141 patients, multiple foods
 Escalation epi in 0.7%
- SLIT

 - Many SLIT studies
 Epinephrine use 0 to rare

Adapted by permission, Dr. Hugh H. Windom

50

SLIT versus OIT for Food Allergy

	07	
SLIT	OIT	
Stable extract or mixed locally	Needs to be mixed in house – must train staff	
Expensive - high dose SLIT can cost >\$10K for a 36-month course	Material costs are low	
Less taste aversion than OIT	Taste aversion is a problem for many	
New technique to learn – can be difficult for toddlers/young children	Suitable for all age groups	
Can bypass gut with hold/spit method	Theoretical risk of triggering EoE	
Shorter exercise restriction than OIT	5-15% may need epi during escalation	
Favorable safety profile – low rates of systemic reactions	Mild to moderate GI reactions are common	
Local reactions (oropharyngeal itching) are common	Enables free eating	
Can achieve high levels of tolerated doses and very rarely sustained unresponsiveness	Some patients can achieve sustained unresponsiveness	

Mini-Dose OIT

- Who?
- infants and toddlers too young for SLIT
- - Provides cross contamination protection and some degree of accidental ingestion protection

 - Reactions and epinephrine use are rare
 Reduced burden of care fewer office visits
 - Low dose makes home dosing easier
- - Eliciting dose OFC to a limited target dose (133mg of peanut protein)

 - Elicumg uose of Color ...
 Daily dosing
 After 6-12 months measure slgE and consider repeat eliciting dose challenge to a higher target

Adapted from multiple publications of Motohiro Ebisawa

52

Who Would You Rather Be?

Food Allergist Not Doing AIT Food Allergist Providing AIT





53

You Can Change Lives!

(When you and your practice are ready)



55

Ongoing OIT Support

- OITAdvisors A closed Google Group with >550 members that functions as a listserve for questions relating to food allergy diagnosis and treatment.
 Open to all Board Certified allergists and their staffs. Contact Neetu Talreja, neetutalreja.com to join.
- <u>FASTOIT.org</u> The website of the Food Allergy Support Team, a non-profit organization that supports OIT allergists. Slide decks from FAST 2021, FAST 2022, and FAST 2023 are available for download