

FOOD ORAL IMMUNOTHERAPY FOR SEVERE FOOD ALLERGIES

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GOALS

- REVIEW UP TO DATE GUIDANCE ON THE DEVELOPMENT AND COSTS OF FOOD ALLERGY
- KNOW HOW AND WHEN TO TEST FOR FOOD ALLERGY
- DISCUSS FORMS OF THERAPY THAT ARE OR SOON WILL BE MARKETING
- DISCUSS FORMS OF THERAPY THAT ARE NOW AVAILABLE AT UBMD PEDIATRIC ALLERGY & IMMUNOLOGY

1. SEVERE FOOD ALLERGY MAY BE PREVENTABLE

- LEARNING EARLY ABOUT PEANUT (DUTOIT ET AL , NEJM 2015) TAUGHT US THAT OUR 20 YEAR OLD STRATEGY OF DELAYING ALLERGENIC FOOD INTRODUCTION TO INFANTS WAS WRONG
 - THEY SHOWED IN A LARGE RANDOMIZED TRIAL THAT;
 - INFANTS OFTEN HAVE POSITIVE SKIN TESTING FOR ALLERGENIC FOODS BEFORE ORAL EXPOSURE, ESPECIALLY IF THEY HAVE SIGNIFICANT ECZEMA OR ONE CLINICAL FOOD ALLERGY ALREADY- THIS IS TERMED SENSITIZATION AND MAY BE A STAGE OF THE ALLERGIC MARCH WE CAN TURN AROUND
 - EARLY INTRODUCTION OF EGG, MILK AND POSSIBLY CASHEW ARE SHOWN TO LESSEN LATER ALLERGY
 - INFANTS WITH POSITIVE SKIN TESTS TO PEANUT ARE NOT ALL DANGEROUSLY ALLERGIC
 - INFANTS WITH PEANUT WHEEL < 8MM OFTEN TOLERATE CHALLENGE AND IF THEY CONTINUE TO EAT IT ROUTINELY THEY HAVE >85% RISK REDUCTION FOR PEANUT ALLERGY AT SCHOOL AGE

2. FOOD ALLERGY ONCE CONFIRMED CAN BE LIFE CHANGING

- ALL CHILDREN DIAGNOSED BY CLINICAL REACTION WITH CONFIRMATORY TESTING, OR BY ORAL FOOD CHALLENGE NEED TO BE TAUGHT;
 - HOW TO READ A FOOD LABEL AND THAT FOODS 'PROCESSED IN A FACTORY THAT ALSO PROCESSES 'THEIR ALLERGEN IS A SERIOUS WARNING THAT THEY SHOULD FOLLOW
 - HOW TO USE THEIR EPINEPHRINE, AND WHAT CONSTITUTES ANAPHYLAXIS (ANY MULTISYSTEM REACTION TO A KNOWN ALLERGEN FOR THAT PATIENT)
 - THAT EPINEPHRINE HELPS MOST WHEN DELIVERED EARLY, WHICH IS WHY THEY NEED TO CARRY IT EVERYWHERE ,KEEP IT IN DATE AND STORE IT CORRECTLY

The Impact of Food Allergy Diagnoses

- Risk of a severe anaphylaxis is just one of many concerns.
- **Financial Burden**
 - **Annual U.S. Direct Medical Costs: \$24.8 billion overall; \$4,184 per child⁸**
 - Clinician visits, ER visits, hospitalizations
 - The cost of special foods or diets
 - Lost productivity due to time off work
- **Nutritional Deficiencies**
 - Broad panel food testing at very young age can lead to **unnecessary avoidance** of foods
 - Can lead to poor weight gain and/or poor food choices due to limited options
- **Mental Health**
 - Mental health effects like restaurant, travel and camp anxiety are measurable
- **Death due to anaphylaxis** –highest in 15-25 year olds, 122/year in US
- **Sibling Effect**
 - If one child in the household is diagnosed with a food allergy, **the entire family often practices avoidance** even if they do not have a food allergy



3. POSITIVE IGE TESTING IS NOT A DIAGNOSIS OF FOOD ALLERGY

- PROVIDERS SHOULD ONLY ORDER TESTS TO CONFIRM A LIKELY TRIGGER AFTER AN EVENT, PRESCREENING OR SCREENING FOR MULTIPLE FOODS THE PATIENT ALREADY EATS IS RARELY HELPFUL , INCREASES HEALTH CARE COSTS AND CONFUSES THE FAMILY
- IN RARE CASES OF ATOPIC DERMATITIS SOME ALLERGEN SCREENING(MILK, SOY, EGG, WHEAT, PEANUT) MAY BE USED BUT SHOULD BE INTERPRETED BY A SPECIALIST WITH EXPERIENCE IN INTERPRETING SERUM IGE TO FOODS
- MANY OLDER PEDIATRIC PATIENTS WILL SHOW FOOD AND POLLEN CROSS-REACTIVITY ON IGE TESTING , AND TAKING AWAY A WELL TOLERATED FOOD BASED ON THIS MAY CAUSE WORSE SYMPTOMS ON RE-EXPOSURE(IE BIRCH POLLEN AND PEANUT/SOY CROSS REACT)

4. FOOD IMMUNOTHERAPY HAS OVER 20 YEARS OF RESEARCH HISTORY TO THIS POINT

- THE IMMUNE SYSTEM IS WELL DEVELOPED IN THE DIGESTIVE TRACT , WHERE ANTIGEN PRESENTATION MAY HELP WITH THE DEVELOPMENT OF PROTECTIVE IMMUNE RESPONSE TO THE FOOD, BUT MAST CELLS AND OTHER EFFECTOR CELLS ARE THERE ALSO THAT MAY TRIGGER ANAPHYLAXIS
- MANY FORMS OF IMMUNOTHERAPY FOR FOOD HAVE BEEN STUDIED DURING THE LAST 2 DECADES, AND OTHERS HAVE JUST BEGUN STUDY SO EXPECT AN EXPLOSION OF FOOD THERAPIES IN THE COMING YEARS
- THE MOST PROMISING AND RESEARCHED TO DATE INCLUDE :
 - ORAL, SUBLINGUAL AND EPICUTANEOUS

Epicutaneous Peanut IT (Viaskin® Peanut)



- **EPIT** allows immune system to be exposed to allergen by applying a patch to the skin.
- Phase IIb (JAMA2017) trial met primary efficacy endpoints so 171 patients - median cumulative reactive dose was 44mg -were rolled-over into the open label extended study for 2 more years to ascertain the effect of long-term treatment.
- 250 µg peanut patch determined to be the most effective dose, only in 6-11yr olds.
- After 3 years, 83.3% were able to tolerate more peanut protein
 - compared to 53.6% after the first year of the trial
 - after 3 years, reactive dose increased to 1,440mg (~6 peanuts), non reactive in 23%
 - 29 pediatric patients challenged after 36 months of 250mcg therapy and 2months off treatment with 80% sustained unresponsiveness with no change in pSIgE or IgG4

• Compliance was >95%, no serious adverse events reported

Peanut Sublingual IT-Kim EH, JACI2019:144(5)

- SLIT is a type of allergen immunotherapy administered under the tongue.
- Recent study: children 1-11 yrs old were treated with 2mg peanut SLIT for 3-5 yrs.
- Reacted to <300mg at baseline challenge. Out of 37 patients who completed the study, 86% were able to safely ingest >750mg of peanut and 32% were able to handle 5,000mg (20 peanuts).
- 12 patients who passed 5,000mg OFC were re-challenged 2-4 weeks after stopping SLIT.
 - 10/12 (27% of the total participants) passed the challenge without unresponsiveness.²⁷
 - Side effects minor and mostly local, none required epinephrine



PALFORZIA- FIRST FDA LICENSED FOOD ORAL IMMUNOTHERAPY FOR 4-18 YR OLDS WITH PEANUT ALLERGY

- PALISADE study- RDBPCT of 551 patients 4 -55 yrs with reactivity $<100\text{mg}$ peanut protein baseline DBPCFC and peanut $\text{sgE} > 0.35$ or wheat $> 3\text{mm}$, primary population 4-17 years old
- Escalation of daily oral peanut protein from 0.5 thru 6 mg day 1, then build q2q weeks to 300mg and continue for 24 weeks
- Exit DBPCFC, primary endpoint is tolerance to a 600mg dose (cumulative 1043mg), optional 1000mg dose could also be given- Primary endpoint met in 250/372 or 67.2% vs 5/124 in placebo arm. 50.3% tolerated the additional 1000mg dose (cumulative 2043mg) at exit challenge
- Considered treatment failure if not able to get to full dose by week 40
- Mild skin, GI or upper respiratory symptoms did not limit dose
- 25% of challenge symptoms were moderate, and in the placebo arm 59%. Severe symptoms were 5 and 11%
- Adults 18 -55 years did not show significant improvement in tolerance to 600mg
- 10% of participants used epinephrine at exit vs 53% of placebo arm

CLINICAL FOOD ORAL IMMUNOTHERAPY

- HAS BEEN DONE BY A SMALL BUT INCREASING GROUP OF ALLERGISTS IN THE US, ISRAEL AND OTHER COUNTRIES FOR 12-15 YEARS-CURRENTLY AROUND 300 PROVIDERS IN USA
- A LARGE SHARED DATABASE OF PROTOCOLS AND OUTCOMES HAS ALLOWED US TO LEARN FROM THIS
- USES FRESH COMMERCIALY AVAILABLE FOOD PRODUCTS THAT ARE PURCHASED FROM MANUFACTURERS WHO MAKE THEIR PRODUCTION SAFETY KNOWN TO THE GROUP
- PROTOCOLS ARE ONLY SHARED BY BOARD CERTIFIED ALLERGISTS , AFTER EDUCATION PROCESS INCLUDING A NATIONAL MEETING ANNUALLY

OIT options-Pros and cons

AllImmune Capsule

- Pharma cost, prior authorizations, and likely age limitations on use keeping it from younger patients
- Less fuss for office staff
- Only goes to 300mg protein, approximately 1 peanut dose so may not achieve full tolerance
- ONLY peanut

Peanut OIT FAST protocol

- Using 28% defatted peanut flour from Byrd Mill and weighing on in office scales- less expensive but requires staff time to prepare, some offices charge for this. Clean room and freezer storage!
- Patient transitions to raw peanut at 200mg (50mg protein)-this is more transportable
- Can also treat other serious food allergies

Social and Logistical

- ◆ One of most important factors to consider-
 - ◆ Always speak to both parents when there are divorced couples. Consent both of them
 - ◆ Ensure all children are up to date on immunizations
 - ◆ Ensure asthma is well controlled and patients/parents are compliant with your recommendations , get baseline PFT and use Peak Flow in OIT symptoms sheet
 - ◆ Consider starting AIT before OIT to see how schedules and compliance issues go, especially where pollen-food syndromes suspected
 - ◆ Make sure parents are able to attend visits, not a variety of caregivers

Exclusion/Inclusion Criteria

- Biological (Focus on Gastrointestinal)
 - Eosinophilic Oesophagitis
 - Irritable Bowel Syndrome
 - Dietary Inflexibility
 - Other Digestive Issues

- Psychosocial
 - Anxiety Disorders
 - Personality Disorders

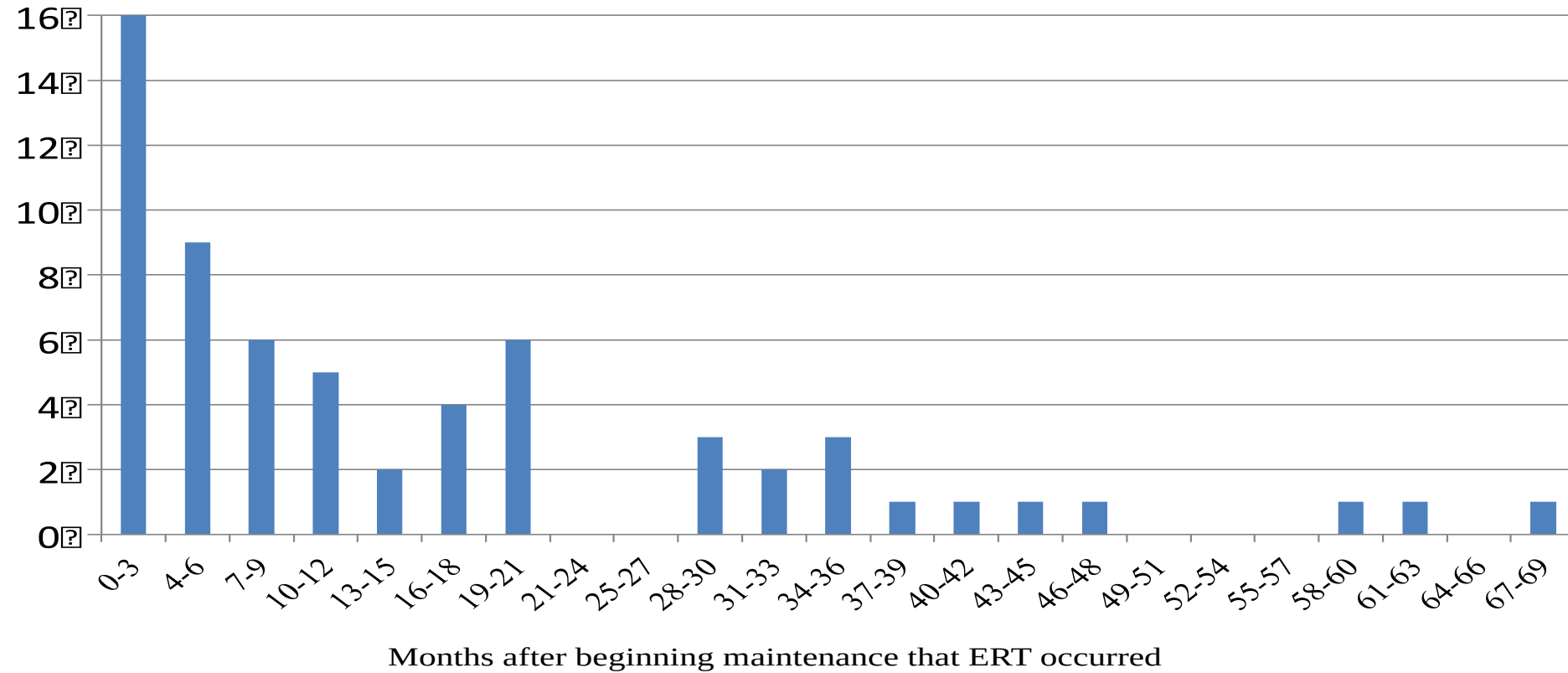


Maintenance- Food Allergy Support Team

- ◆ For peanut protocol, final step involves 12 g PN daily followed by 24 PN challenge (= 1 serving, ca. 8 g protein/ 2 Tbsp PB)
- ◆ After this, patients consume 8g PN or equivalent daily, but could consume more if desired (can “freely eat”)
- ◆ Dosing rules still apply with 45 minute post dose waiting
- ◆ Generally follow-up q6 months
- ◆ After 3 years maintenance, some kids appear to be truly tolerant (Dr. Wasserman published data)
- ◆ Not everyone wants/needs to “freely eat”
- ◆ Accidental protection conferred at 1g in most situations, 4 g virtually always
- ◆ Beware switching to other products without first analyzing content of pertinent allergen epitopes

Peanut OIT Maintenance ETRs

63 total ETRs in 214 Peanut Maintenance Patients



Eosinophilic Esophagitis Like, Related Syndrome (ELORS)

OIT-

- ◆ Vomiting more than 2 hours after dosing is the predominant symptom, also moderate dose related abdominal pain, clinically diagnosed

- ◆ 10.8% of treated patients

- ◆ Peanut 13.7%
- ◆ Milk 12.7%
- ◆ Egg 0%
- ◆ Cashew 6.3%
- ◆ Multi-food 8.1%

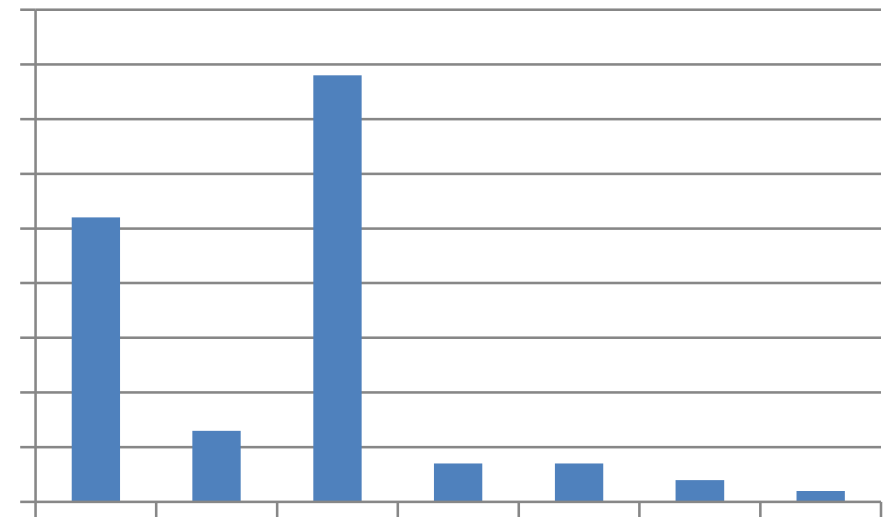
- ◆ 32/54 patients treated

- ◆ Dose reduction alone
- ◆ Some treated with a PPI
- ◆ 53% reached maintenance

- ◆ High pre-treatment IgE is the major risk factor

- ◆ Treated with dose reduction, rarely short course PPI

Symptoms in 54 ELORS Patients



Maintenance

Food	Source	Top dose
Peanut	Peanut PB, Bamba, M&M	3-10 peanuts (0.75-2.5 gm protein)
Milk	whole or 2% milk	120-240 ml milk (4-8 gm protein)
Egg	egg white liquid egg white powder egg whole	2-3 tbsp (3.3-5 gm protein) 4-6 gm (3.2-5 gm protein) 1 egg (3.4 gm protein)
Cashew	cashew milk cashews	60-120 ml (1-2 gm protein) 3-5 cashews (0.8-1.3 gm protein)
Walnut	walnut milk walnuts	100-170 ml (1.2-2.1 gm protein) 2-3.5 walnuts (1.2-2.2 gm protein)
Hazelnut	hazelnuts	7-10 hazelnuts (1-1.5 gm protein)
Almond	Elmhurst almond milk almonds	60-100 ml (1.2-2 gm protein) 5-8 (1.4-2 gm protein)
Sesame	seeds Tahini	5-7 gm (0.9-1.2 gm protein) same as above
Wheat	Whole wheat bread Dave's Awesome bagel	1 slice (4 gm protein) 1/3 to 1/2 bagel (4-6 gm protein)

Multiple Food OIT

- ◆ How many foods at once? Max number of foods?
- ◆ Is your staff prepared to handle the increased prep?
- ◆ Do you only do tree nuts? Other foods?
- ◆ Do you mix any combination of foods? Restrictions?
- ◆ Cross-protection? Do one food or a mix of both?
 - ◆ Walnut/pecan
 - ◆ Cashew/pistachio



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PEDIATRICS

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If you have patients who either need a clear diagnosis, more education around food avoidance or consideration of oral immunotherapy we welcome referral to Allergy/Immunology at UBMD Pediatrics

Phone: 716-323-0130

Fax: 716-323-0296

Please share any old labs you have at the time of referral

Thank You,
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