

# 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 child<sup>8</sup>**
  - 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.<sup>27</sup>
  - Side effects minor and mostly local, none required epinephrine



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

AR101 NEJM2018 Burks et al

- PALISADE study- RDBPCT of 551 patients ages 4 to 55 yrs with reactivity to <100mg peanut protein at baseline DBPCFC and peanut sIgE>0.35 or wheal >3mm, primary population 4-17yrs
- Escalation of daily oral peanut protein from 0.5 thru 6 mg day 1, then build q2weeks 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 placebo arm 59%. Severe symptoms were 5 and 11%
- Adults 18-55yrs 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 COMMERCIALLY 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



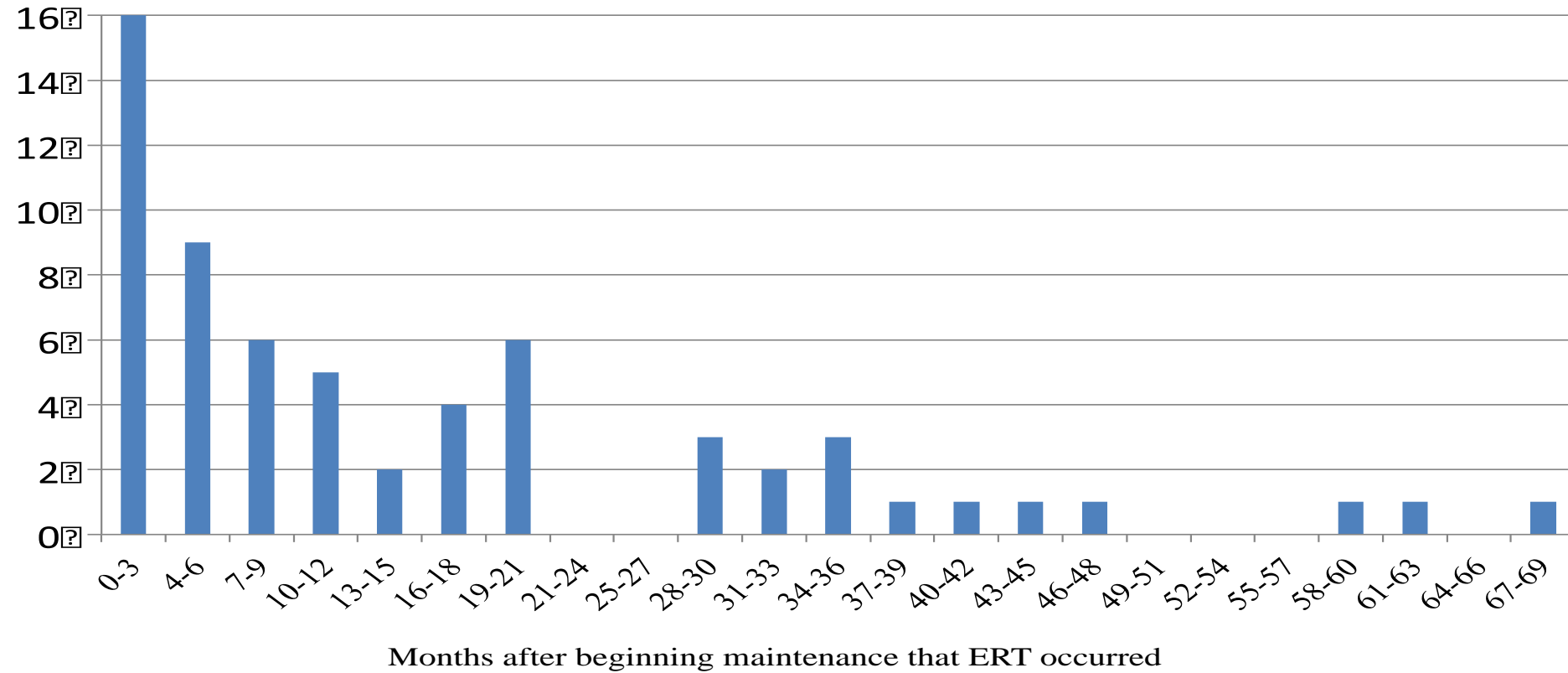


# Maintenance- Food Allergy Support Team

- ◆ 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%

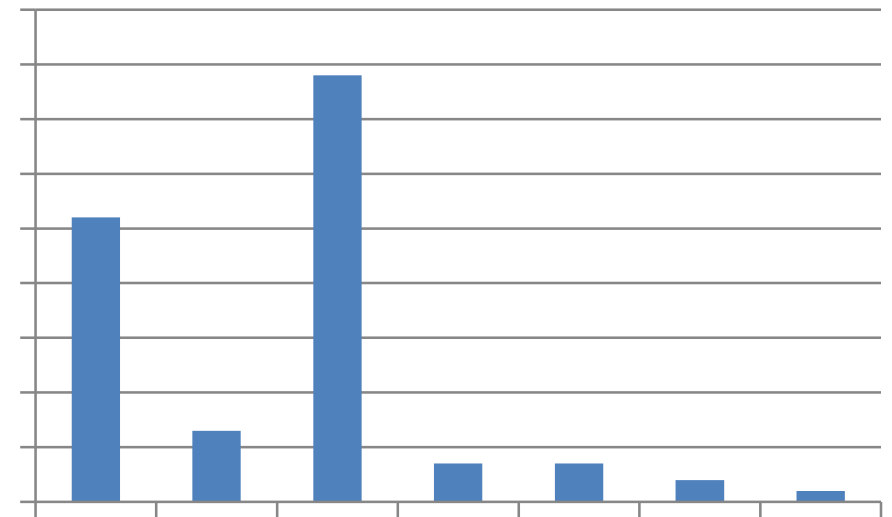
- ◆ 32/54 patients treated

- ◆ 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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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

716-323-0130/fax 716-323-0296

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

Thank You