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Food Allergy: Pearls and Pitfalls

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Disclosures

- None
- The opinions expressed are solely those of the author and do not represent an endorsement by or the views of the United States Air Force, the Department of Defense, or the United States government.

Objectives

- Review immune & non-immune mediated adverse food reactions
- Review epidemiology, pathophysiology and diagnosis of IgE mediated food allergy
- Associated conditions
- Updates on primary prevention, treatment and management options

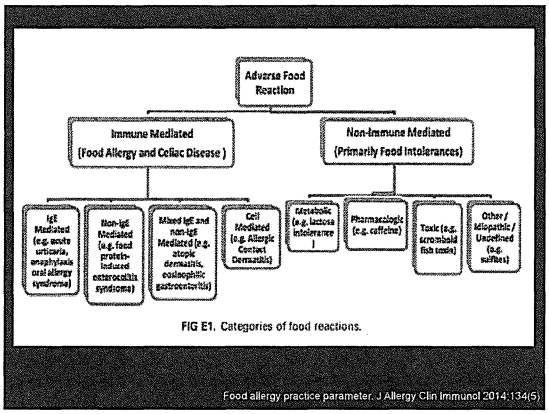

FIG E1. Categories of food reactions.

Food allergy practice parameter. J Allergy Clin Immunol 2014;134(5)

Food Intolerance

Toxic
- Bacterial food poisoning
- Scombroid fish poisoning
- Caffeine
- Alcohol
- Tyramine

Non-toxic
- Lactase deficiency
- Galactosemia
- Pancreatic insufficiency
- Gall bladder disease

Immune Mediated Food Intolerance

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Prevalence

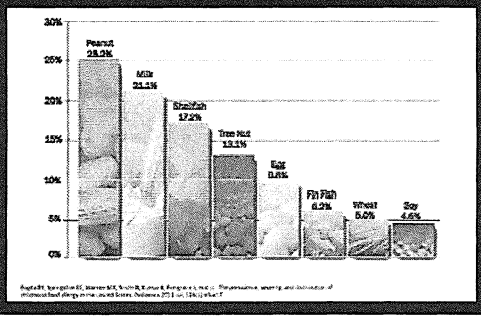
TABLE I. Estimated food allergy rates in North America

Prevalence	Infant/child	Adult
Milk	2.5%	0.3%
Egg	1.5%	0.2%
Peanut	1%	0.6%
Tree nuts	0.5%	0.6%
Fish	0.1%	0.4%
Shellfish	0.1%	2%
Wheat, soy	0.4%	0.3%
Sesame	0.1%	0.1%
Overall	5%	3% to 4%

- >20% of people *think* they have food allergy
- Only about 3-4% of adults and 5% of kids *have* a food allergy
- Higher in children with other atopic disorders

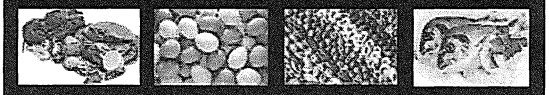
Sicherer et al. J Allergy Clin Immunol 2010;125(2)

Top Allergenic Foods

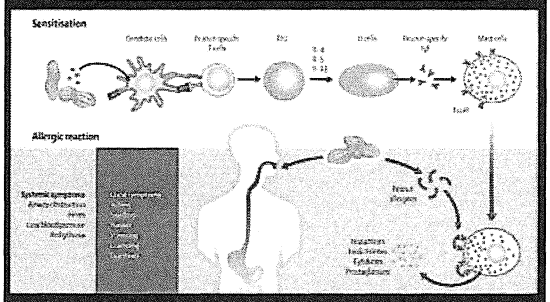


Epidemiology

- Children
  - Cow's milk, wheat, soy, egg, fish, and peanut
- Adults
  - Fruits and vegetables, peanuts, tree nuts, fish, and shellfish



Pathophysiology



Natural History

Food	Age of onset	Usual age of resolution
Egg	6-24 months	7 years (75% resolve)
Cow's milk	6-12 months	5 years (76% resolve)
Soybean	6-24 months	2 years (67% resolve)
Wheat	6-24 months	5 years (80% resolve)
Peanut	6-24 months	Persistent (20% resolve by 5 yo)
Tree nuts	1-7 years, Adulthood	Persistent (20% resolve by 7 yo)
Fish	Late childhood, Adulthood	Persistent
Shellfish	Adulthood	Persistent

Adapted from Lack, G. NEJM 2008;359:12

IgE Mediated Food Allergy

LEAST SEVERE → MOST SEVERE

Contact urticaria | Urticaria/Angioedema | Anaphylaxis

- Food accounts for 1/3 of all anaphylaxis seen in emergency rooms
- Onset of symptoms: immediate to within 4 hours
- Immediate treatment: **Epinephrine**

Food Allergy Diagnosis

History:

- Description of signs/symptoms
  - IgE mediated vs Intolerance
- Timing from ingestion to onset
- Quantity of food required to cause reaction
- Treatment received
- Reproducible symptoms
- Associated factors
  - Activity, medication, food preparation

Food Allergy Diagnosis

- If history suggests an IgE mediated process, look for food specific IgE
  - Skin prick tests vs serologic testing
  - Component testing
- If history does not suggest an IgE-mediated process, testing is likely to produce confusing results
  - Sensitization vs true allergy

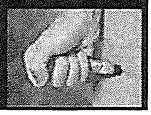
Difficulties in Diagnosis

- Correlate history and testing results
  - Targeted testing
- Food skin testing and serologic testing have fairly good sensitivity(>90%) but low specificity(50%)
  - Poor screening tests
  - Better tests when based on clinical suspicion
  - Some patients will still react to ingestion with negative skin test and serology

Chapman et al. Ann Allergy Asthma Immunol 2006;96

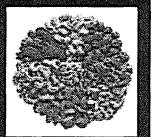
Food Allergy Management

- Emergency care plan – EPI, EPI, EPI
  - Injectable epinephrine
    - 0.3mg IM >30 kg (66lbs)
    - 0.15mg IM <30 kg
- Ready access to epinephrine autoinjector
  - Don't store in car
  - Ok to use even if expired…but please refill annually



Fatal Food-Induced Anaphylaxis

- Adolescents or young adults
- Known allergy to implicated food
  - 50% patients with known peanut allergy had an accidental ingestion of peanut within one year*
- History of asthma
- Peanuts and tree nuts most common
- Most occurred outside the home
- Epinephrine not given or given late
- ~150 deaths per year in the U.S.



*Bock J Allergy Clin Immunol 2001;107(1)

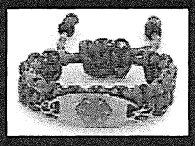
TABLE VI. Why epinephrine autoinjectors were not used*

An antihistamine was used	38%
Did not receive a prescription for epinephrine autoinjector	28%
The allergic reaction was mild	13%
An asthma puffer was used	8%
Did not have epinephrine autoinjector available	8%
Unsure when to give the epinephrine injection	8%
In previous reaction no treatment was needed	8%
Afraid to inject epinephrine	6%
Quick recovery time (reaction went away fast)	4%
Concern about possible side effects of epinephrine	4%
Did not think autoinjector was needed because trigger was being avoided	3%
Epinephrine autoinjector was past expiry date	2%
Could not afford to purchase epinephrine autoinjector	1%
Was given prescription for autoinjector but did not purchase it	0.1%

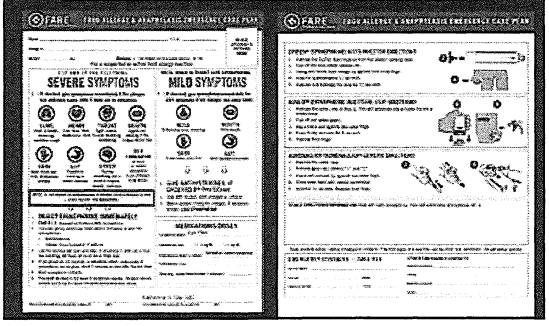
Simons et al. J Allergy Clin Immunol 2009;124 (2)

Food Allergy Management

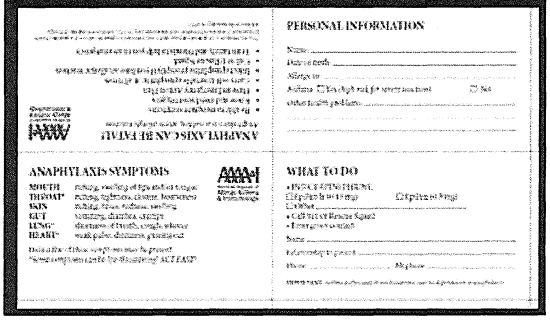
- Written anaphylaxis action plan
  - www.foodallergy.org
  - www.aaaai.org
- Medical alert jewelry



FARE www.foodallergy.org



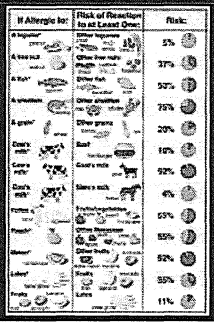
AAAAI: www.aaaai.org



Management Continued

- Strict avoidance
  - Careful consideration before eliminating foods which patient currently tolerates
  - Guidance on food label reading
    - "May contain…" = DOES CONTAIN
    - Can't just "pick it off"
  - Risk of cross reactivity or cross contamination

Cross Reactive Foods



Patient Resources

FARE
Food Allergy Research & Education

AllergyHome.org

KIDS WITH FOOD ALLERGIES FOUNDATION
kidswithfoodallergies.org

Follow Up Testing

- Allergen specific IgE can wane with time
  - Decrease in IgE can be associated with ability to tolerate a food
    - Less likely to occur in adults
- Recommend periodic re-evaluation

Follow Up Testing

- Certain foods (egg, milk, peanut) have specific cut off values for skin test/serology and risk of allergic reaction
  - Ex. Peanut serology of 15 kU/L ≈ 95% PPV for abnormal challenge
  - Ex. Peanut serology <2 kU/L ≈ 50% PPV for abnormal challenge

Oral Challenges

- Gold standard for diagnosis of food allergy
  - Confirm that food allergy exists
  - Confirm resolution of food allergy
- Protocols vary and depend on risk of reaction
- If challenge is passed then food needs to be consumed regularly in diet

Oral Challenges

- Carries inherent risk of reaction
  - Needs medical supervision
  - May defer if
    - High likelihood of reaction (50/50)
    - Other concurrent disorders (Ex. uncontrolled asthma, CV disease, recent anaphylaxis to suspected trigger food)
  - Practical considerations: age/maturity, desire to introduce food in diet

Peanut Challenge

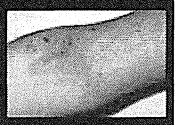
DATE:

STEP	TIME (write in actual time)	BP	HR	RR	POX	COMMENTS
Baseline	VS obtained -					Weight -
1. Buccal smear	0:00 -					
2. ½ tsp	0:10 -					
3. ½ tsp	0:25 -					
4. 1 tsp	0:40 -					
5. 2 tsp	0:55 -					
6. 1 tablespoon	1:10-					
7. Discharge	3:10-					

Associated Conditions

Atopic Dermatitis

- 1/3 of children with moderate to severe atopic dermatitis have food allergy
  - Cow's milk, hen's egg, soy, peanut most common
- Increased likelihood of food sensitization:
  - Younger age
  - More severe atopic dermatitis



Bergmann et al. J Allergy Clin Immunol In Practice 2013;1(1)

Atopic Dermatitis

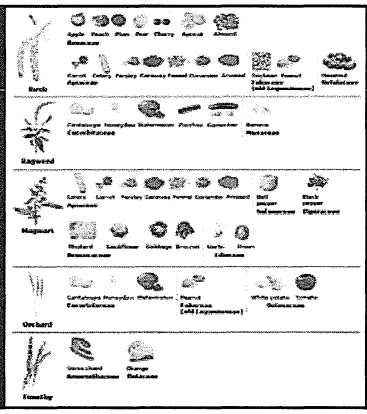
- IgE vs delayed-type (cell-mediated) reaction
  - Thus food allergy testing may not be helpful
    - Positive test has only 50% PPV
    - Negative skin test/serology have high NPV
  - May need to trial elimination diet to establish clinical reactivity
- Consider testing pts <5 yo with moderate-severe atopic dermatitis not controlled on meds

Oral Allergy Syndrome/ Pollen Food Allergy Syndrome

- Mild itching of tongue, palate, lips
- Caused by cross-reactive proteins between aeroallergen and food



Webber et al. Ann Allergy Asthma Immunol 2010;104

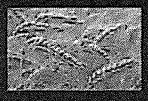


Pollen Food Allergy Syndrome

- Treatment
  - Avoid concerning food
  - Peeling fruit may be helpful
  - Heating or cooking food may alleviate symptoms
    - Denatures protein
  - Consider epinephrine autoinjector
    - 1-2% chance of anaphylaxis
  - May improve as a result of aeroallergen immunotherapy
    - Not an indication for immunotherapy but a bonus if it helps!

Food Dependent Exercise Induced Anaphylaxis

- Anaphylaxis after eating a certain food then exercising
  - Food without exercise – no problem
  - Exercise without food – no problem
  - Food + Exercise = Anaphylaxis
- Celery, wheat, shellfish most common


Food allergy practice parameter. J Allergy Clin Immunol 2014;134(5)

Food Dependent Exercise Induced Anaphylaxis

- Avoid the specific food for 4-6 hrs prior to exercise
  - Exercise with a buddy
  - Carry cell phone
  - Have epinephrine auto-injector
  - Wear medic alert jewelry

Food allergy practice parameter. J Allergy Clin Immunol 2014;134(6)

Chronic Urticaria

- Chronic urticaria (urticaria/angioedema lasting >6 weeks with no trigger)
  - NOT due to a food allergy
- You'll be tempted to order food serology…but please don't as it only complicates the picture
- Urticaria that occurs after ingestion of a food AND is reproducible could be a food allergy
  - Can order serology and/or refer

Updates on Primary Prevention, Treatment and Management Options

Prevention of Food Allergy

- Early feeding guidance ~2000
  - Dietary avoidance of certain antigens in pregnancy and while breastfeeding to prevent eczema and asthma
  - Use of partially hydrolyzed formula
  - Delay solid food introduction until 6 months of age
  - Delay introduction of high risk allergens

Prevention of Food Allergy

- Increased prevalence of food allergy
  - 1997 ~ 3.4%
  - 2000 ~ 3.6%
  - 2006 ~ 4.3%
  - 2009 ~ 5.1%

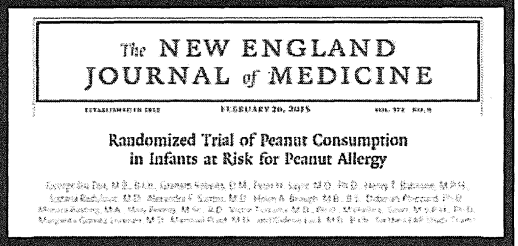
Observational Study

• Tel Aviv	• London
• 69% ate peanut by 9 mo • Median monthly consumption of peanut 7.1 g 8-14 mo	• 10% ate peanut by 9 mo
• Peanut allergy prevalence (0.17%)	• Peanut allergy prevalence (1.85%)

Adjusted risk ratio 9.8

Du Toit et al. J Allergy Clin Immunol 2008;122

LEAP: Learning Early About Peanut Allergy



The NEW ENGLAND JOURNAL of MEDICINE

FEBRUARY 26, 2015

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

LEAP

- Open label single center randomized control trial
- Trial of early (4-11 mo) v. delayed (60 mo) peanut introduction
- Inclusion:
  - Age 4-11 mo at screening
  - Have either (or both)
    - A. Severe eczema:
      - Frequent topical steroid/Calcineurin inhibitor use
      - "A very bad itchy rash in joints/creases" or " a very bad itchy, oozing, or crusted rash" reported by parent
      - SCORAD ≥ 40
    - B. Egg allergy
  - Screening peanut skin test wheal < 5 mm

Protocol

- All underwent skin testing
- Pts with SKT ≥ 5 mm were excluded (felt to already be 'likely' allergic)
- Randomized to 2 groups based on SKT size

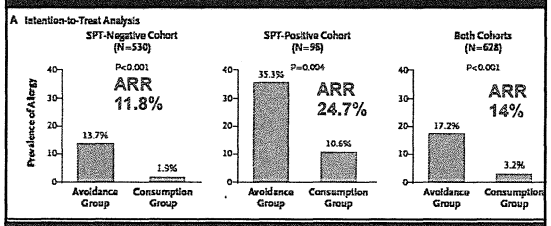
  0 mm v. 1-4 mm

- Randomized within each group to consume peanut (2g, 3x per week x 60 mo) v. avoid peanut
- All subjects underwent peanut challenge at 5 yo

Prevention

- Primary prevention: preventing peanut allergy from developing
  - Skin test negative person who has no baseline exposure to peanut
- Secondary prevention: preventing progression of allergy (from sensitization to reactivity)
  - Skin test positive but non-reactive person at baseline with no known peanut exposure

Results



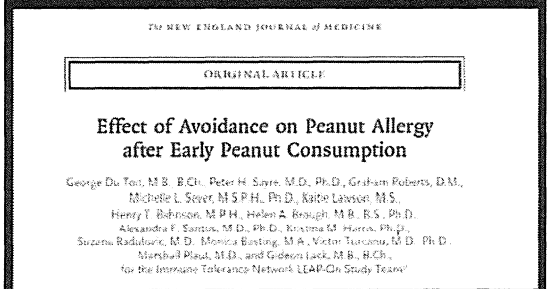
NNT 7.1 RRR 80%

Benefit was greater in the sensitized group (secondary prevention)

Unanswered Questions

- No placebo or low risk group
  - Can you apply to general population/low risk individuals?
- 'High risk' criteria differ
  - Some of the patients that were excluded may have just been sensitized
- Dose/duration not tested
- >96% retention at 5 years
  - ?Partial adherence
  - ?Long term outcome with discontinuation

LEAP-On



THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Avoidance on Peanut Allergy after Early Peanut Consumption

George Du Toit, M.B., B.Ch., Peter H. Sayre, M.D., Ph.D., Graham Roberts, D.M., Michelle L. Sever, M.S.P.H., Ph.D., Katie Lawson, M.S., Henry T. Bahnson, M.P.H., Helen A. Brough, M.B., B.S., Ph.D., Alexandra F. Santos, M.D., Ph.D., Rima M. Harris, Ph.D., Suzana Radulovic, M.D., Monica Basting, M.A., Victor Turcanu, M.D., Ph.D., Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the Immune Tolerance Network LEAP-On Study Team*

LEAP-On

- Patients that completed the initial LEAP trial enrolled in follow up study
  - Peanut consumption group
  - Peanut avoidance group
- All patients told to avoid peanut consumption for 12 months after LEAP
- Follow up food challenge at 12 months

LEAP-On

- After 12 months of avoidance, peanut allergy confirmed:
  - 18.6% of original peanut avoidance group
  - 4.8% of original peanut consumption group
- Statistically significant reduction in prevalence of peanut allergy associated with early introduction of peanut until 60 months of age persisted at 72 months of age despite 12 months of avoidance

Consensus Statement

- Interim policy from international consortium
- Recommend introducing peanut-containing products into the diet of "high-risk" infants early on in life (between 4 – 11 months of age)

AAP, AAAAI, ACAAI Published 2015

Consensus Statement

- Consider allergy referral for infants with early-onset atopic disease (severe eczema or egg allergy) in the first 4-6 months of life
  - Evaluation may consist of performing peanut skin testing and/or in-office observed peanut ingestion
    - Observed peanut challenge for those with evidence of a positive peanut skin test to determine if they are clinically reactive, before initiating at-home peanut introduction

AAP, AAAAI, ACAAI Published 2015

Consensus Statement

- "Of note, since children with lesser risk factors for peanut allergy were excluded from enrollment in LEAP, there are no prospective, randomized data investigating the benefit or risk of early peanut introduction in the general to low-risk populations"

AAP, AAAAI, ACAAI Published 2015

What is Not Addressed

- Use of alternative doses of peanut protein
- Minimal length of treatment necessary to induce the tolerogenic effect
- Potential risks of premature discontinuation or sporadic feeding of peanut
- Introduction of other foods…

EAT Study: Enquiring About Tolerance

- Randomized controlled trial
- Introduction of 6 allergenic foods (milk, peanut, sesame, fish, egg, wheat) in breastfed infants
  - Food allergy lower in the early introduction group (7.1% v 5.6%) but not statistically significant (p=0.32)
  - In the per protocol analysis, food allergy prevalence was significantly lower in the early introduction group (2.4% v 7.3%, p=0.003)
    - For peanut: 0% v 2.5%, p=0.003
    - For egg: 1.4% v 5.5%, p=0.009
    - No effects for wheat, milk, sesame, fish
- Early introduction of all 6 foods not easy but was safe

Perkin et al. NEJM 2016

Early Introduction of Egg

- Hen's Egg Allergy Prevention (HEAP)[1]
  - Early introduction not associated with prevention at 12 months of age
- Starting Time of Egg Protein (STEP)[2]
  - Early introduction in infants with high hereditary risk (maternal history of atopy) not associated with prevention of egg allergy at 12 months of age
- Beating Egg Allergy Trial (BEAT)[3]
  - Early introduction in infants with at least 1 first degree relative with allergic disease
  - ¼ had eczema
  - At 12 months, early introduction of egg associated with ARR 9.8%, NNT 11

[1-3] JACI May 2017

2010 NIAID Guidelines

Guidelines for the Diagnosis and Management of Food Allergy in the United States

Summary of the NIAID-Sponsored Expert Panel Report

Boyce et al. J Allergy Clin Immunol 2010;126(6)

2010 NIAID Guidelines

- Insufficient evidence exists to recommend routine testing prior to introduction of highly allergenic foods in children who are at high risk
  - High risk=children with history of severe allergic disease and/or family history of food allergy
- Do not recommend restricting maternal diet during pregnancy or lactation as a strategy to prevent food allergy

Boyce et al. J Allergy Clin Immunol 2010;126(6)

2010 NIAID Guidelines

- Exclusive breast feeding until 4-6 mo of age
  - Unless breastfeeding contraindicated
- Hydrolyzed formula may be considered as a strategy for preventing food allergy in at-risk infants
  - At risk defined as family history of rhinitis, asthma, eczema or food allergy
  - May reduce development of cow's milk allergy

Boyce et al. J Allergy Clin Immunol 2010;126(6)

2010 NIAID Guidelines

- Introduction of solid foods should not be delayed beyond 4-6 mo of age
- Potential allergenic foods may be introduced at this time as well

Boyce et al. J Allergy Clin Immunol 2010;126 (6)

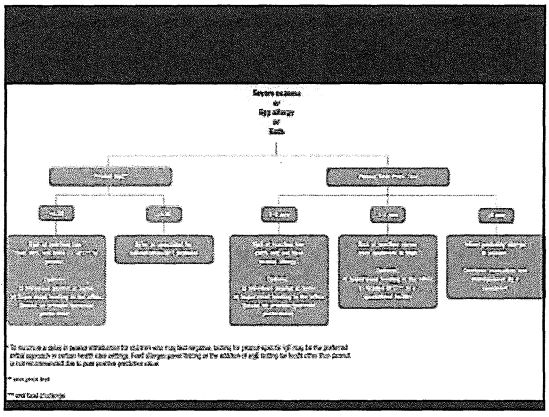
2017 NIAID Update

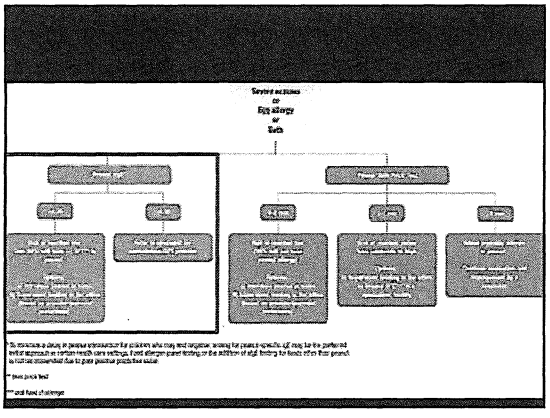
Addendum Guidelines for the Prevention of Peanut Allergy in the United States

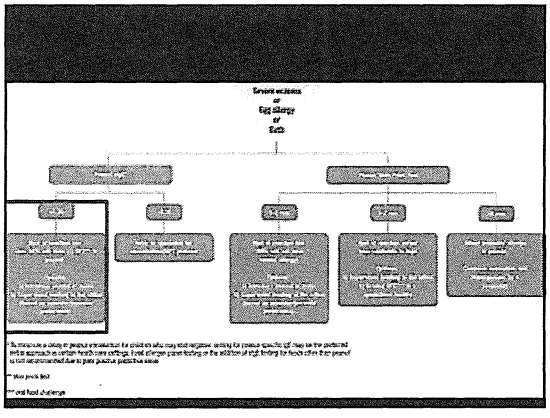
Report of the NIAID-Sponsored Expert Panel

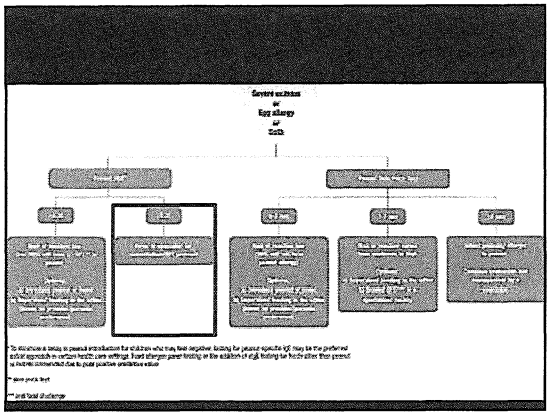
2017 NIAID Update

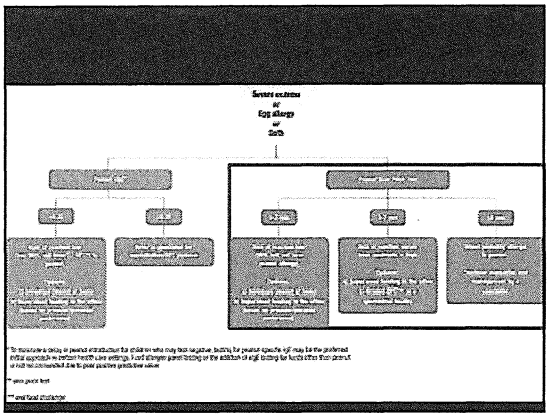
- In infants with severe eczema, egg allergy or both introduce age-appropriate peanut containing food as early as 4-6 months of age
  - Introduce other foods prior to peanut introduction to ensure infant developmentally ready
  - Evaluate with peanut serology and/or skin testing to determine if peanut introduction can occur and how
  - To minimize delay in peanut introduction, serology testing for peanut may be the preferred initial approach
    - Outpatient settings where skin testing is not routine











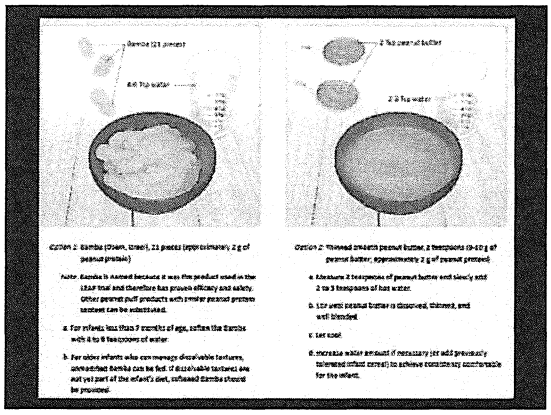
Peanut Introduction at Home

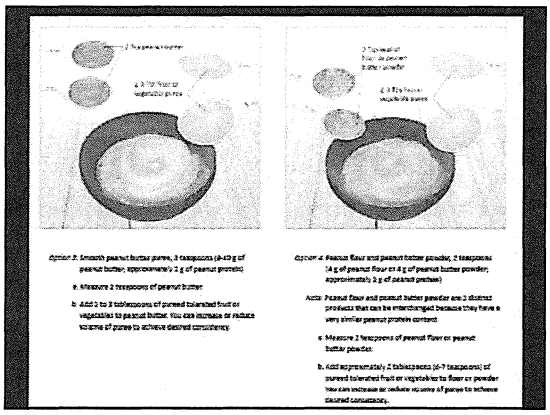
- Try when infant is healthy
- Give first dose at home
- Plan to observe for at least 2 hrs for signs allergic reaction
- Goal ~2 grams of peanut protein

Text Box 1: Examples of Peanut-containing Foods Utilized in the LEAP Trial

- Smooth peanut butter (2 teaspoons) mixed with milk or with mashed or pureed fruit
- *Bamba® snack (Osem; ~2/3's of 1 oz. (25 g) bag: 21 sticks of Bamba®)
  - for young infants (<7 months), softened with 20 – 30 ml water or milk and mixed with milk or with mashed or pureed fruit or vegetables
- Peanut soup
- Finely ground peanuts mixed into other foods such as yoghurt
- (*Other foods more customary to particular nations'/cultures may be substituted)

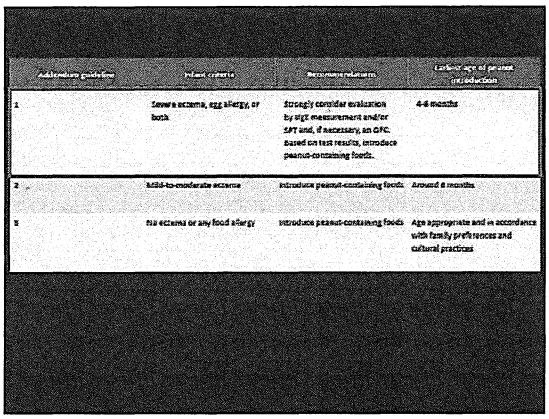
Whole peanut is not recommended for introduction as this is a choking hazard in children under the age of 4.



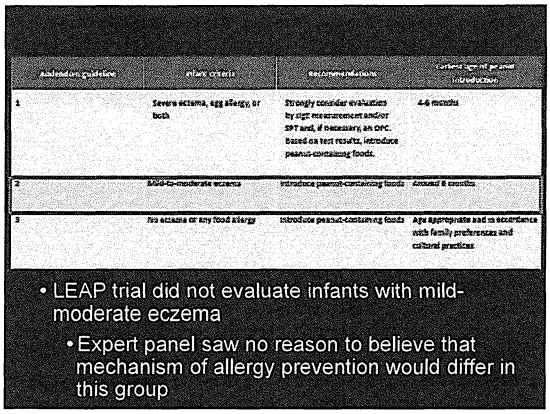


Infant Tolerated Peanut Introduction, Now What?

- Goal of regular and ongoing consumption of peanut
  - LEAP recommendation of 6 grams peanut protein (2 bags of Bamba or 5 tsp peanut butter) divided over 3 or more feedings per week



Addendum guideline	Infant criteria	Recommendation	Earliest age of peanut introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation by skin measurement and/or SPT and, if necessary, an OFC. Based on test results, introduce peanut-containing foods.	4-6 months
2	Mild-to-moderate eczema	Introduce peanut-containing foods	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods	Age appropriate and in accordance with family preferences and cultural practices



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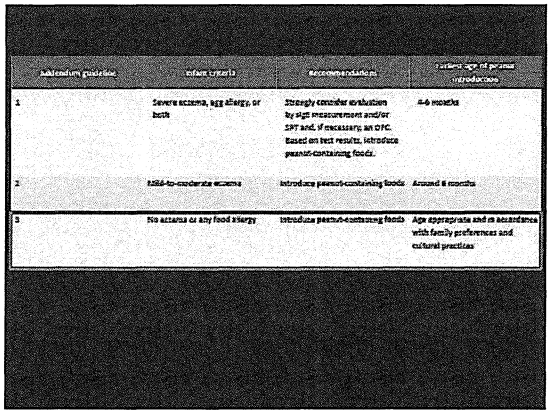
- LEAP trial did not evaluate infants with mild-moderate eczema
  - Expert panel saw no reason to believe that mechanism of allergy prevention would differ in this group



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Additional Considerations

- There is currently no cure for food allergies
- The current recommendation is to avoid the allergen
- Promising treatments on the way

Baked Egg and Baked Milk

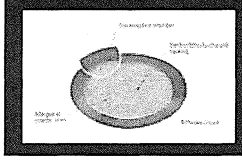
- Allergy to heat labile v heat resistant proteins
- Heat labile proteins change configuration with heating
  - Patient may be able to tolerate cooked version of food
- Evidence that introduction of 'baked' proteins in diet hastens resolution of milk and egg protein allergy
- Periodic evaluation is key to trend IgE values and offer families "baked" oral challenges

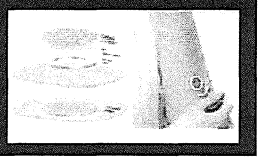
Immunotherapy

- Contact of an antigen induces tolerance
  - Patient is given increasing amounts of the allergen
- Sublingual immunotherapy (SLIT)
- Oral Immunotherapy (OIT)
  - May be effective during therapy (for egg, milk and peanut)
  - Side effects: GI (EoE), Anaphylaxis
- Ongoing research protocols investigating

Epicutaneous Immunotherapy (EPIT)

- Currently under investigation
  - Peanut, Milk (Egg in the works)
- Local reactions common





Food Allergy Summary

- History
  - IgE-mediated food allergy vs food intolerance
- Diagnosis can be tricky
  - When in doubt prescribe epinephrine auto injector & refer
- Education
  - Avoidance
  - Epinephrine is 1st line treatment
  - Written food allergy/anaphylaxis action plan
  - Medical alert jewelry
- Early peanut introduction in at risk infants recommended

Questions??