LET THEM EAT CAKE

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DISCLOSURE

A. I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity:

B. I do intend to discuss an unapproved/investigative use of a commercial product(s)/device in my presentation but I have no commercial interest.
HOW COMMON ARE FOOD ALLERGIES?

• More than 15 million Americans
• 8% of U.S. children have a food allergy
• 1 in 13 school-aged children, or 2 per classroom
• Of those with food allergy, 30% are allergic to multiple foods

HOW COMMON ARE FOOD ALLERGIES?

• Food allergy diagnosis among children increased approximately 50% between 1997 and 2011, according to a study released in 2013 by the CDC and Prevention
• Anaphylactic reactions to food have been increasing at a staggering pace, rising 377% percent from 2007 to 2016 according to a new report published by nonprofit FAIR Health private insurance claims


WHAT ARE THE MOST COMMON FOOD ALLERGIES AMONG THE 15 MILLION AMERICANS?

Specific labeling required by FALCPA to these foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanut</td>
<td>25%</td>
</tr>
<tr>
<td>Shellfish</td>
<td>17%</td>
</tr>
<tr>
<td>Eggs</td>
<td>9.8%</td>
</tr>
<tr>
<td>Fin Fish</td>
<td>6.2%</td>
</tr>
<tr>
<td>Milk/Dairy</td>
<td>21%</td>
</tr>
<tr>
<td>Tree Nuts</td>
<td>13%</td>
</tr>
<tr>
<td>Wheat</td>
<td>5%</td>
</tr>
<tr>
<td>Soy</td>
<td>4.6%</td>
</tr>
</tbody>
</table>
FAIR HEALTH: MOST COMMON FOODS FOR ANAPHYLAXIS

WHY THE INCREASE IN FOOD ALLERGY?

- Genetic make up?
- Public health changes?
- "Hygiene Hypothesis" - immune system is bored (vaccines, antibiotics, hygiene)
- Environmental exposures?
- Too much testing? Not real?
- Waiting too long to introduce foods?
- Changes during pregnancy and delivery?
- Vitamin D deficiency?
- Epigenetic Changes?
- Gut Flora
AGE OF ONSET OF ALLERGY AND RESOLUTION

Savage, Jessica et al. The Natural History of Food Allergy. JACI: In Practice. 2016; 4, 196 – 203

17 years ago the American Academy of Pediatrics Committee on Nutrition recommended:

- Infants with a positive family history of any allergy are considered “high risk”
- Breast feeding generally protective of allergy
- If “high risk” infant then peanut avoidance during lactation
  - also wise to skip tree nuts, shellfish, and fish
- Delay introduction of solid foods >6mo
  - Cow milk/dairy not until age 1 year
  - Egg not until age 2 year
  - Peanut, tree nut, seafood not until age 3
MISTAKES

• Guidelines were for “high risk but embraced by general population
• Parents and the public began thinking peanut causes allergies and all children should not eat peanut until the age of 3.
• Then a spike in disease prevalence and questions as to why?

RECANT: AAP 2008

• No evidence that maternal dietary restrictions during pregnancy or lactation prevents atopic disease.
• No evidence that delaying introduction of solid food beyond age 4-6 months prevents atopic disease
• But no recommendations as to when to introduce so most parents held off

 FOOD ALLERGY PREVENTION FOR AT-RISK INFANTS: NIAID-SPONSORED EXPERT PANEL 2010

► Insufficient evidence exists that maternal diet during pregnancy or lactation affects the development or clinical course of food allergy.
► Exclusive breast-feeding or feeding with hydrolyzed infant formula until age 4-6 months is recommended for all “at risk” infants.
► Insufficient evidence exists for delaying the introduction of solid foods including potentially allergenic foods beyond age 4 to 6 months.

Boyce JA, et al. JACI 2010;126:S1-S58

How important is allergen exposure during infancy?
THE BURDEN OF PEANUT ALLERGY

- Peanut allergy growing public health concern
- In 1999 peanut allergy affected 0.4% of children in the US, rose to 2% in children in 2010.
- Peanut allergy leading cause of death related to food induced anaphylaxis
- Fear of anaphylaxis contributes significantly to medical and psychosocial burden of disease
- In the majority of patients, peanut allergy begins early in life and persists as a lifelong problem
- “Cost effective measures to prevent peanut allergy would have a high effect in terms of improving public health, reducing personal suffering, decreasing health care use and costs”

Togias et al. J Allergy Clin Immunol 2017;139:29-44

PIVOTAL OBSERVATION: TURNING THE TIDE

- Prevalence of peanut allergy determined by clinically validated questionnaire among Jewish school children
  - 5171 in the United Kingdom
  - 5615 in Israel
- Prevalence of peanut allergy in the UK was 1.85%
- Prevalence in Israel was 0.17% ($P < .001$) despite accounting for atopy
- Peanut was introduced earlier, more frequently and in larger quantities in Israel than in the UK
  - 70% of Israeli infants by 7 mo.
  - 10% by English infants 7 mo.
- Jewish children in the UK have a prevalence of PA that was 10-X higher than Jewish children in Israel

LEAP (LEARNING EARLY ABOUT PEANUT ALLERGY)

- Dr. Gideon Lack and colleagues published in New England Journal of Medicine February 2015
- Hypothesis: Early introduction (before 11 months) of peanut based products would lead to the prevention of peanut allergy in “high risk” infants
- Eligibility:
  - Infants at 4 months < 11 months old (median 7.8 mo.)
  - Severe eczema and/or egg allergy
  - Skin test ≤ 4 mm
- First prospective randomized controlled trial


LEAP “HIGH RISK DEFINITIONS”

**Definition of Egg allergy**
- Skin prick wheal diameter ≥ 6 mm to raw hen’s egg white without previous egg tolerance
- Skin prick test wheal diameter of ≥3 mm to pasteurized hen’s egg white and allergic symptoms related to exposure to hen’s egg

**Definition of severe eczema**
- A rash that
  - Been reported by parent to be “very bad in joints and creases” or a very bad itchy, dry, oozing, or crusted rash
  - Currently or previously scored by SCORAD scale >40
  - Requires topical steroid creams, ointments, calcineurin inhibitors
**STUDY GROUPS**

- **Randomization:**
  - **Sensitized** SPT 1-4 mm (N=98)
  - **Not Sensitized** SPT 0 (N=540)

- **Consumption:** 2 g of peanut protein 3x/week
  - Peanut snacks or peanut butter from infancy
  - Whole peanuts could be added after 3 years of age

- **Avoidance:** Avoid all peanut consumption

- Study groups until age of 5

Du Toit G et al. NEJM 2015;372(9):803-813

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**LEAP RESULTS**

**LEAP RESULTS**

86% Relative Reduction  
70% Relative Reduction  
81% Relative Reduction
ONE YEAR LATER LEAP-ON

• Enrolled 88.5% from the primary trial
• Now everybody doesn’t eat it for 12 months
• Peanut allergy at 72 months in peanut-avoidance group was 18.6% (52 of 280) compared to original peanut-consumption group 4.8% (13 of 270), P<0.001
• 3 new cases of allergy developed in each group
• After 12 months of avoidance, no significant increase in the prevalence of allergy among participants in the consumption group
• Fewer participants in the peanut-consumption group than in the peanut-avoidance group had high levels of Ara h2, peanut component (component associated with more severe allergy)

Du Toit G et al. NEJM Mar 4, 2016

CONSENSUS COMMUNICATION ON EARLY PEANUT INTRODUCTION AND THE PREVENTION OF PEANUT ALLERGY IN HIGH-RISK INFANTS

• Level 1 evidence providers should recommend introducing peanut-containing products into the diet of high risk infants between 4-11 months because delayed introduction can be associated with increased risk of peanut allergy
• Screen by skin test
  – Infants with early-onset eczema
  – and/or egg allergy
  – Peanut allergic siblings***

ADDENDUM GUIDELINES FOR THE PREVENTION OF PEANUT ALLERGY IN THE UNITED STATES: REPORT OF THE NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES-SPONSORED EXPERT PANEL

TOGIAS ET AL. J ALLERGY CLIN IMMUNOL 2017;139:29-44

WHEN TO INTRODUCE PEANUT

- Infants with severe eczema, egg allergy or both: Test First. Not studied but guidelines suggest early introduction could be good.
- Infants with no eczema or food allergy: Age appropriate time, no different than any other food.
- Infants with mild to moderate eczema: Not studied but guidelines suggest early introduction could be good.
Algorithm for peanut introduction

Severe eczema or egg allergy or both

Peanut serum IgE
- <0.35 kU/L: Introduce home or office
- ≥0.35 kU/L: Refer to specialist

Peanut SPT
- 0-2 mm: Introduce home or office
- 3-7 mm: Risk mod-high Supervised feeding in office or OFC
- ≥8 mm: Most likely true peanut allergy

"Expert panel does not recommend food allergen panel testing or the addition of serum IgE testing for foods other than peanut because of their poor positive predictive value, which could lead to misinterpretation, over-diagnosis of food allergy, and unnecessary dietary restrictions."

Togias et al. J Allergy Clin Immunol 2017;139:29-44
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Peanut SPT

- 0-2 mm
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- 3-7 mm
  - Risk mod-high
  - Supervised feeding in office or OFC

- > 8 mm
  - Most likely true peanut allergy

INSTRUCTIONS FOR HOME FEEDING

1. • Make sure you have a 2 hour block of time
2. • Change to higher end, feed remainder at infant’s pace
3. • Repetitive cough, change in skin color (pale, blue), sudden tiredness/lethargy/limp
**RECIPES OPTIONS FOR 2 GRAMS OF PEANUT PROTEIN**

- **Bamba**
  - 21 pieces
  - < 7 months: soften with water or breast milk
  - > 7 months: finger food

- **Smooth PB Thinned**
  - 2 teaspoons of PB slowly added to 2-3 teaspoons of hot water
  - Stir until blended
  - Let cool
  - Add more H2O for good consistency

- **Smooth PB Puree**
  - 2 teaspoons of PB
  - Add 2-3 tablespoons of tolerated pureed fruit or vegetable

- **Peanut flour or PB powder**
  - 2 teaspoons of peanut flour or PB powder
  - Add 2 tablespoons of tolerated baby food
  - Thin as needed

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**ARALYTE**

- **What is it?** all-natural distilled peanut extract and complete doses of essential vitamins like vitamin D
- **Advantages of Aralyte?**
  - Premeasured dose that allows first dose in the presence of a physician
  - Easy to administer and safe to swallow
  - Non-messy and sterile single use.
  - Each contains 1 gram of peanut protein
  - Dosed daily instead of 3 times per week
  - Low risk of cross contact if other peanut allergic sibling
  - Not FDA approved

[www.aralyte.com](http://www.aralyte.com)
Hello, Peanut!

- New product
- Introduction Kit contains 8 packets
  - First day’s packet contains 200mg of peanut
  - Each consecutive day gradually increases the amount of peanut
  - Maintenance packet which contains 2 grams (3 ½ peanuts)
- First product to have FDA qualified health claim to prevent peanut allergy recognized
- Introduction kit $25, Maintenance kit (8) $20

www.hello-peanut.com

Simply Peanut™

- Simply Peanut™ provides 2 grams of peanut protein to help build infant and children immune systems
- Simply Peanut™ is 100% is organic and natural
- Simply Peanut™ can be mixed with breast milk, formula or any volume of baby food
- THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT DISEASE.
- 1 month (24 packets) $20

www.simply-peanut.com
LOADS OF NEW QUESTIONS

- How much allergen exposure is enough to prevent food allergy?
- Does changes in the timing of peanut introduction have an impact on prevention?
- Is there a non-specific effect of peanut early introduction on the prevention of other allergies like tree nut?
- Impact of significant parental skepticism, “but I ate PB during pregnancy or breastfeeding”?
- Is there a more critical window of time when the peanut protein should be introduced than 4-11 months?

Allen, KJ. Clin Experimental Allergy 2015; 46:42-47

IS THERE A MORE CRITICAL WINDOW OF TIME WHEN THE PEANUT PROTEIN SHOULD BE INTRODUCED THAN 4-11 MONTHS?

Birth-3-4 months

8-12 months

>12 months

Resolution

Factors that influence the capacity for tolerance
- optimal colonization
- genetic predisposition
- allergen properties (dose, interval, timing, preparation)
- gut permeability/maturity/pH
- continued breast-feeding
- other immunomodulatory factors (fatty acids, stress, antioxidants)

CRITICAL WINDOW FOR EARLY PEANUT INTRODUCTION


INSPIRED START

• Introduce all allergens early!
• The only baby food for early introduction of 8 common allergens
• Each pouch contains 1 gram of allergen protein, except for our Banana & Tree Nut pouches which contain 1 gram of each tree nut protein (almond, walnut, and cashew) for a total of 3 grams.
• Pack 1: introduces peanut, egg, tree nut, and soy (2 pouches of each)
• Pack 2: introduces wheat, sesame, shrimp, and cod (2 pouches of each)
• Variety Pack: contains 1 pouch of each of “our delicious recipes”
• $23 per pouch

www.inspired-start.com
CAN THIS DATA BE APPLIED TO OTHER FOODS?

TIMING OF ALLERGENIC FOOD INTRODUCTION TO THE INFANT DIET AND RISK OF ALLERGIC OR AUTOIMMUNE DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

- Meta-analysis of prevention trials
- 16,289 titles, 51 studies identified
- Moderate certainty evidence from five trials (1915 participants) that are early egg introduction at 4-6 months was associated with reduced egg allergy. (Risk ratio RR 0.56; 95%CI 0.36-0.87; 12=36%; P=.009).
  - Absolute risk reduction for a population with 5.4% incidence of egg allergy was 24 cases per thousand population.
- Moderate certainty evidence from two trials (1550 participants) that early peanut introduction at 4 to 11 months was associated with reduced peanut allergy (RR 0.29; 95%CI 0.11-0.74; 12=66%, P=.009)
  - Absolute risk reduction for a population with 2.5% incidence of peanut allergy was 18 cases per 1000 population
- Timing of egg and peanut introduction was not associated with risk of allergy to other foods
- There was low to very low certainty evidence that early fish introduction was associated with reduced allergenic sensitization and rhinitis.
- There was high certainty evidence that timing of gluten introduction was not associated with celiac disease risk and timing of allergenic food introduction was not associated with other outcomes

Ierodiakonou ,D et al. JAMA 2016; 316:1181-1192
RANDOMIZED TRIAL OF INTRODUCTION OF ALLERGENIC FOODS IN BREAST-FED INFANTS (EAT STUDY - ENQUIRING ABOUT TOLERANCE)

- **Population**: based randomized controlled trial of exclusively breastfed infants
- **Hypothesis**: early introduction of multiple allergenic foods starting at 3 months will reduce prevalence of food allergy
- **Primary outcome**: prevalence of challenge-proven IgE-mediated food allergy to 1 or more of the 6 intervention foods between 1-3 years of age


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EAT TRIAL - ONGOING

- Exclusively breastfed infants
  - n=1303
  - 3 months old
- Early introduction starting 3 mo.
  - SPT to 6 intervention foods introduce if neg SPT or neg OFC
  - 2 gm per week
  - n=652
- Standard introduction after 6 mo.
  - n=651
  - 3 yr.

EAT STUDY

- Prevalence of any food allergy was significantly lower in the early introduction group than in the standard introduction group (7.3% versus 2.4%, P = 0.01)
- Prevalence of peanut allergy was 0% versus 2.5%, (P = 0.003) and egg allergy 1.4% versus 5.5%, (P = 0.009)
- There was no effect with respect to milk, sesame seed, fish, or wheat
- Conclusion: Maybe the effect is dose dependent?


SUMMARY

- Don’t delay food introduction to infants
- Sensitization and food allergy can develop early
- Early introduction to high risk infants appears to prevent peanut allergy
- Pediatricians should now screen high risk infants to prevent peanut allergy
- More data is needed regarding early introduction of other food allergens, other prevention approaches, and which groups of infants to target