Disclosures

- NIH-NIAID Funding for studies
- Food Allergy Initiative Consultant and funding for studies
- Food Allergy & Anaphylaxis Network Medical Advisor
Learning Objectives

• Understand the current data on atopy prevention through infant diet
• Advise families on dietary approaches with regard to food allergy prevention

Suggested References:
and
Prevention Through Diet

- Prevention of...
  - Sensitization
  - Inflammation
  - Disease
- Through “ingestion”...
  - Pregnancy
  - Breast feeding
  - Breast feeding-with Maternal diet alteration
  - Choice of breast milk substitution
  - Complementary foods When/what
What are “normal” feeding practices?

- Breast feed
- Weaning
- Solids that are easily managed by an infant
- Progression as teeth erupt
Breast Feeding (focus on eczema)

• **18 prospective studies** (Gdalevich JAAD 2001; 45:520-7)
  - Atopic (OR 0.58; 95% CI, 0.41-0.92)
  - Non-atopic (OR 0.84; 95% CI, 0.59-1.19)

• **21 studies** (Yang YW BJD 2009;161:373-383)
  • Overall: OR 0.89 (95% CI 0.76-1.04)
  • vs. formula OR 0.7 (95% CI 0.50-0.99)
    • (but p=NS removing Chandra)

• **ISAAC Study** (Flohr C BJD 2011;165:1280-9)
  • 51,119 children. No evidence of overall protection.

• Recent studies suggest genetic differences affect risk
  (Hong et al JACI 2011;128:374-81)
META-ANALYSIS: MATERNAL DIET RESTRICTION WHILE BREAST FEEDING

• Insufficient evidence that maternal allergen avoidance prevents atopic disease
• Possible exception for atopic dermatitis
• 2 studies
  Kramer Kakuma Cochrane database 2006
• 2010 Food Allergy Guidelines: Not recommended to reduce FA
The German Infant Nutritional Intervention Study

• “At risk” for atopy (one 1st degree)

• Randomized to study formula (within context of instruction to breast-feed)
  – Cow’s milk formula (CMF)
  – Extensively hydrolyzed casein (eHF-C)
  – Extensively hydrolyzed whey (eHF-W)
  – Partially hydrolyzed whey (pHF-W)

Von Berg A JACI 2003; 111:533

Von Berg JACI 2007
Von Berg JACI 2008
The German Infant Nutritional Intervention Study

- Lesson #1: Cannot assume a formula’s effect (e.g., eHF-W)
- Lesson #2: Impact on subtypes of risk*

*Trends
Randomized Trial of 3 Formulas if Weaning

- 620 infants positive family history atopy
- Cow’s milk vs. soy vs partially hydrolyzed whey at weaning
- Followed age 2 years (93%) and age 7 (80%)
- 50% exposed ~5 months, ~75% 1 year
- No differences in AD, food skin tests, asthma, rhinitis

Lowe et al JACI 2011;128:360-5
Prevention Formulas

- Soy not recommended for “prevention” (AAP, NIAID)
- “Hydrolyzed infant formulas” recommended over whole cow’s milk protein for “at risk” (NIAID Guideline) and some evidence for reduced atopic dermatitis (slight advantage of extensive casein hydrolysate versus partial whey hydrolysate weighed by cost (AAP))
Dietary Prevention Program, US

- Randomized, prospective, 288 subjects, one parent with atopy and sensitization
- Program:
  - Pregnancy, 3rd trimester-no milk, egg, peanut, reduced soy/wheat
  - Lactation, avoid same, supplement casein hydrolysate
  - Solids at 6 mo, 12 mo-CM, wheat, soy, 24 mo-egg, 36 mo-peanut, fish
- Followed to age 7 years

Dietary Prevention Program, US Period Prevalence of Disorders


Asthma

Atopic dermatitis

Food Allergy

“Prevention”
AAP Committee on Nutrition, 2000

• Breast feed 1 year
• If supplement, “hypoallergenic formula”
• Solids delay to age 6 mo
• Should eliminate Peanut, Tree nuts, and consider eliminate egg, milk, fish “others” while nursing
• No Cow’s milk to 12 mo
• No Egg to age 2 yr
• No Peanut, Tree Nuts, fish to 3 yr
• Pregnancy: consider peanut exclusion

Suggestions aimed at “high risk”
Solid Foods

Rate of Eczema

Age of Solid food Introduction

3 months
6 months

Fergusson et al. *Clin Allergy* 1981


Veg (>4 mo)
Egg (>8 mo)

Atopic Dermatitis OR (95% CI)

Zutavern et al. *ADC* 2004
Solid Food Post 2000

- **Germany** (Filipiak J Pediatr 2007;151:352)
  - 4753 infants (birth cohort): Among “at risk” atopy if waited on giving egg (RR 1.8, 95% CI: 1.2-2.6)

- **Belgium** (Sariachvili PAI 2010;21:74)
  - Case Control: Solids before 4 months, less eczema (OR 0.49; 95% CI 0.3-0.7)

- **Finland** (Nwaru Pediatrics 2010;125:50)
  - Cohort 994: Later introduction of solid foods associated with higher food sensitization

- **Netherlands** (Tromp Arch Pediatr Adolesc Med 2011;165:933)
  - Cohort 6905: No relationship of eczema/wheeze to receiving milk, egg, soy, nut, wheat prior to age 6 months
Complementary feeding and food sensitization: Detroit

- Enrolled 1258 women, 44.9% parental atopy
- Dietary inclusion of complementary foods at < 4 months versus food sensitization at age 2-3 years
- 74.2% with data for this analysis

<table>
<thead>
<tr>
<th>Family Atopy</th>
<th>IgE &gt; 0.7 kUA/L E/M, &gt;0.35 peanut</th>
<th>Adjusted odds ratio</th>
<th>P-value</th>
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<tbody>
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<td>Egg/milk</td>
<td>0.5 (0.3-0.9)</td>
<td>0.023</td>
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<tr>
<td>Yes</td>
<td>Peanut</td>
<td>0.2 (0.1-0.7)</td>
<td>0.007</td>
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<td>No</td>
<td>Egg/milk</td>
<td>1.0 (0.6-2.0)</td>
<td>0.894</td>
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<tr>
<td>No</td>
<td>Peanut</td>
<td>1.3 (0.6-2.7)</td>
<td>0.544</td>
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</tbody>
</table>

Joseph et al JACI 2011;127: 1203-10
“HealthNuts” study, 2589 infants population-based, cross-sectional study

- Effects seen in high-risk and low-risk infants with cooked egg introduction
- Adjusted for confounding factors
- Confirmed egg allergy

Koplin et al JACI 2010
Cereal Grain Introduction and Wheat Allergy

“Daisy” study (US), 1612 infants, birth cohort observational study

- Parent reported wheat allergy in 1%, 4 with positive wheat-IgE
- Adjusted for parental allergic diseases and any food allergy < 6mo of age
- Designed to investigate natural hx of diabetes and celiac disease in a HLA-predisposed population

Poole et al Pediatrics 2006
Cow’s Milk Introduction and Milk Allergy

Prospective feeding study of 13019 infants in Israel, telephone interview, encourage to breast feed

- Low prevalence of IgE-mediate allergy 0.5%, which confirmed milk allergy
- Regards parental atopy as a potential confounding factor
- Nursery milk exposures not considered

Katz et al JACI 2010
Introduction of milk/milk products and atopy outcomes

- KOALA Birth cohort (n=2558, Netherlands)
- Followed to age 2: Delayed milk/milk products associated with eczema; delayed “other foods” with atopy, prolonged BFing-protective.

Adjusted Odds Ratio
Eczema

Snijders et al
Pediatrics
2008;122:e115-22
Government and Pediatric Society Response To Peanut Allergy “Epidemic”

• Avoid peanut during pregnancy, lactation and wait to age 3 years to feed it

• American Academy of Pediatrics 2000

• Committee on Toxicology (UK) 1999
Ingestion is bad...Uh oh...?

Maybe if you don’t eat it, you touch it, have accidental periodic ingestions that are all sensitizing?

Peanut Allergy:

Genetic predisposition to peanut allergy

Atopic Dermatitis

Dietary & Environmental Exposures

Use of Antacids

Ingestion of cross-reactive proteins (soy)

Maternal ingestion during pregnancy

Maternal ingestion during breast feeding

Frequency of ingestion

What are “normal” feeding practices?

- Breast feed
- Weaning
- Solids that are easily managed by an infant
- Progression as teeth erupt
Weaning Foods

- Thailand: coconut, chilis, tamarind, lemon grass
- Africa: meats
- China: rice, fish, vegetables, meat
- India: wheat, rice, milk, egg, fish, legumes
- Japan: rice, soy, fish

What are “normal” feeding practices?

- Breast feed
- Weaning
- Solids that are easily managed by an infant via pre-mastication
- Progression as teeth erupt
Characteristics Mothers Completing the Questionnaire Asking Whether They Have Ever Given Pre-masticated Food to Their Children

- Anonymous survey
- 90, HIV infected mothers
- Brooklyn, NY
- Overall, 18% pre-masticated

<table>
<thead>
<tr>
<th>N=90</th>
<th>Yes, Premasticates</th>
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<tbody>
<tr>
<td>Born US</td>
<td>18%</td>
</tr>
<tr>
<td>Born Carribean or Central America</td>
<td>13%</td>
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<tr>
<td>Born Africa</td>
<td>29%</td>
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<tr>
<td>Hispanic</td>
<td>7%</td>
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<tr>
<td>African American</td>
<td>38%</td>
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<td>29%</td>
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<tr>
<td>Mother Pre-masticated</td>
<td>42%</td>
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<tr>
<td>Mother did not Pre-masticate</td>
<td>12%</td>
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</table>

ENDS: MEANS

• Prevention of...
  - Sensitization
  - Inflammation
  - Disease

• Through ingestion...
  - Pregnancy
  - Breast feeding
  - Breast feeding-with Maternal diet alteration
  - Choice of breast milk substitution
  - Complementary foods When/what
ENDS: MEANS

- Prevention of...
  - Pregnancy
  - Breast feeding
  - Maternal diet alteration
  - Choice of breast milk substitution
  - Complementary foods

- Through ingestion...
  - No obvious Effect (?)
  - Good for everyone, exclusive to 4-6 mo
  - Certain Hydrolyzed formulas, not soy, not cow’s milk
  - No, but for high risk maybe (AD)
  - Nothing special (exceptions?)
  - When/what
Thank You!