Feed those babies some peanut products!!!
Edward Brooks

Case presentation
5 month old male with severe eczema starting at 3 months of age. He was breast fed exclusively for 3 months and then supplemented with Similac. Solid foods (rice cereal, fruits, vegetables, meats) were introduced at 4 months with no apparent reactions, but with an urticarial reaction to eggs last week. Parents have not yet introduced nuts or seafood.

He gets a bath with Aveno daily and mother uses topical moisturizers for the eczema. He has a 4 y/o sister with egg allergy, a 7 y/o brother with asthma and “lactose intolerance.” Both had eczema for the first 3 years of life. His mother has peanut allergy (hives and lip swelling) and allergic rhinitis. There is a maternal uncle with asthma and shrimp anaphylaxis.

Mother is concerned about food allergies and wants advice on whether or not to introduce eggs, nuts or seafood.

WHAT DO YOU RECOMMEND????
You prescribe topical steroids and order an “allergy test.”

Immunocap

Allergen fixed to solid phase matrix – sponge-like with high surface area

Patient serum IgE placed onto Cap, and binds to allergen

Enzyme conjugated anti-IgE placed on Cap binding to patient IgE

Fluorescent substrate bound to enzyme

Fluorescence intensity measured

IgE quantified against standards

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You prescribe topical steroids and order an “allergy test.”

TEST POSITIVE FOR EGGS, COW’S MILK AND PEANUTS

NOW, HOW WOULD YOU COUNSEL THE MOTHER????
2000 AAP Recommendations – high risk infants

Mother should consider excluding peanuts and nuts from diet while breastfeeding.

Breastfeeding for 6 months: "... exclusive breast-feeding may promote the development of oral tolerance and prevent some food allergy and atopic dermatitis."

Delayed introduction of solid foods until 6 months of age.

Hyposalergenic formula for supplementation (not soy).

Peanuts, nuts, and seafood should be avoided until 3 years of age, eggs avoided until age 2, and milk avoided until age 1.

2008 AAP Recommendations – high risk infants

No restrictions on maternal diet.

There is lack of evidence that maternal dietary restrictions during pregnancy or lactation plays a significant role in the prevention of atopic disease in infants, with the exception of cow’s milk during lactation, although more data are needed to substantiate this conclusion.

Exclusive breastfeeding for 4 months for high risk infants.

For infants at high risk of developing atopic disease, there is evidence that exclusive breastfeeding compared with intact cow’s milk protein formula decreases the cumulative incidence of atopic dermatitis and cow’s milk allergy.

Hyposalergenic formula for high risk infants.

Hydrolyzed formula for high risk infants. There is no convincing evidence that delaying their introduction beyond this period has a significant protective effect.

Solid food introduced at 4-6 months.

Solid food introduced at 4-6 months. There is no convincing evidence that delaying their introduction beyond this period has a significant protective effect.

No dietary restrictions after 4-6 months.

For infants after 4-6 months of age, there are insufficient data to support a protective effect of any dietary intervention for the development of atopic disease.

Eliminate identified food allergens from diet.

For a child who has developed an opercular disease that may be precipitated or exacerbated by ingested proteins (e.g., human milk, infant formula, or specific complementary foods), treatment may require specific identification and restriction of causal food proteins.

How did we get there?

- Focus on prevention of severe reactions in "high risk" infants
- Breast feeding reduces risk
- Increased allergen exposure increases risk in "high risk" infants
- Uncertainty in predictive value of testing and widespread access to testing (and misinterpretation)
- Delay in early feeding (>4 mo.) increases the risk for food allergy in high risk populations, so
- Increased reactions in high risk infants to breast feeding

PARADOX: Allergen immunotherapy (100 years experience) reduces risk of allergic reactions i.e. "give them what they're allergic to"

- Question: DID THE 2000 GUIDELINES INCREASE THE RISK FOR THE PREVALENCE OF FOOD ALLERGY?

Consequences of Guidelines

- 2000: Parents of "high risk" infants avoided high risk foods (egg, peanut, seafood) and protected high risk infants from severe reactions.
- 2008: Despite the change in the guidelines, behavior changed little
- Continued focus on "exposure" as the major risk factor
- Philosophy likely spread to "low risk" infants

RESULT: Increased prevalence of food allergy sensitization and reactions, "the more we avoided, the worse it got"

ALTERNATIVE HYPOTHESIS: delayed feeding of "highly allergic foods" increases the risk for sensitization

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5 month old male with severe eczema starting at 3 months of age. He was breast fed exclusively for 3 months and then supplemented with Similac. Solid foods (rice, cereal, fruits, vegetables, meats) were introduced at 4 months with no apparent reactions, but with an unexplained reaction to eggs last week. Parents have not yet introduced nuts or seafood.

He gets a bath with Aveeno daily and mother uses topical moisturizers for the eczema.

He has a 4yo sister with egg allergy, a 7yo brother with asthma and "lactose intolerance." Both had eczema for the first 3 years of life. His mother has peanut allergy (hives and lip swelling) and allergic rhinitis. There is a maternal uncle with asthma and shrimp anaphylaxis.

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You prescribe topical steroids and order an "allergy test."

TEST POSITIVE FOR EGG, COW’S MILK AND PEANUTS

SO BASED ON THE 2008 GUIDELINES, HOW WOULD YOU COUNSEL THE MOTHER????

PROBLEM: SHOULD INFANTS SENSITIVE TO ONE FOOD AVOID ALL FOODS???

Now for a LEAP of Faith

Learning About Peanut Allergy

- Background:
  - Israeli infants routinely fed peanuts (Bamba)
  - Rate of peanut allergy 10x greater in UK Jewish children
  - 6 to 11 months
  - Severe eczema, egg allergy or both
  - Peanut SPT + (1-4 mm) or neg
  - Baseline peanut challenge (2 g) negative
  - Protocol:
    - 6 gms peanut proteine/week in 3-4 meals – Bamba or peanut butter
    - 60 months

Toit et al, NEJM Feb 2015, 372:9
Not perfect

- Safety
  - No severe reactions
  - Increased reactions in consumption group
- Consumption group
  - 9 discontinued due to reactions
    - 6/9 with + OFC at 60 months
    - 2 with + initial OFC – avoidance
    - 4/7 with + OFC at 60 months

**Oral Challenge**

**OFC – Oral Food Challenge Protocol**

![Graph showing oral food challenge protocol](image)

**TABLE 1: Oral food challenge**

<table>
<thead>
<tr>
<th>Food Product</th>
<th>0.1 mg</th>
<th>1 mg</th>
<th>10 mg</th>
<th>100 mg</th>
</tr>
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<tbody>
<tr>
<td>Peanut</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheat</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Egg</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Casein</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cow's milk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

![Reprinted with permission from Niggemann et al.](image)
Prediction of Eliciting Dose during OFC

Blumchen 2014, JACI 134:2

OFC prediction using sIgE/total IgE ratio

Gupta 2014 JACIP 2:3

Summary

- Early feeding of highly allergenic foods can induce tolerance even in "high risk infants"
- Avoidance increases the risk for food allergen sensitization

Development of Food Allergy

- Atopy
- Innate Immunity
- Environmental factors
The Atopic March

In utero
- Genetic predisposition
- Maternal influence-fetal programming
- Environmental factors
- TH2 predominance/TREG dysfunction?

Infancy
- Eczema
- Food Allergy

Toddler
- Asthma

School Age
- Asthma
- Allergic rhinitis

Can genetics explain the rise in Atopy?

Clear evidence for genetic predisposition to atopy, but insufficient to explain the rapid rise in atopic disease.

“Genes load the gun, but... the environment pulls the trigger”

The Hygiene Hypothesis

protective effect with exposure to:
- farms
- pets
- day care
- large family size
- endotoxin exposure
- frequent infections (fewer antibiotics)
- Microbiota diversity
- Dietary diversity
- Diets rich in vegetables

Immune mechanisms under the surface (mucosa)

Cells of Allergic Inflammation
Microflora diversity – bacterial AHR ligands
Presence of “bad” AHR ligands (PAHs)
Dietary diversity
Presence of “good” dietary ligands for AHR (crucifers)
Epithelial cell integrity (Filagrin, IL-22)
Maturation of protective immunity and tolerance

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Now, how would you counsel the mother?

Allergy Testing/Challenge

Food

Sensitized

Clinical reaction

Re-exposure

Sensitized

No IgE

No reaction

Natural History of egg allergy

Recent Statement from the experts

Up to date Apr 07, 2015

It is possible for an allergic reaction to occur the first time a child eats a particular food. We recommend giving highly allergenic foods to high-risk children in the following manner:

Your infant can be given an initial taste of one of these foods at home, rather than at day care or at a restaurant.

If there is no apparent reaction, the food can be introduced in gradually increasing amounts.

Consult your child’s healthcare provider if your child has signs of an allergic reaction after eating a food, has moderate to severe atopic dermatitis that is difficult to control, or has a sibling with a peanut allergy. An allergy evaluation may be suggested in these cases.

Treatment

Education
Patient
Family / caregivers
School
Medications
Epinephrine
Antihistamines
Emergency access
911
Emergency room

Anaphylaxis:
More epinephrine
More antihistamine
Steroids
IV fluids
Breathing assistance
Blood pressure support
Future Therapies

- Oral desensitization
- Sublingual immunotherapy
- Humanized anti-IgE antibody therapy

Peanut IgE Results


Mean Threshold Dose of Peanut Eliciting Symptoms with anti-IgE therapy

Summary

**Diagnosis of food allergy**
- History / physical / a priori reasoning
- Laboratory tests
- Elimination / oral challenge

**Treatment**
- Earlier introduction of allergenic foods
- Global dietary management
- Reverse hygiene therapy
- Elimination / treatment for accidental ingestion

**Future**
- Improved diagnostic strategies
- Improved therapeutic strategies