Nutrition First
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Food Allergy Updates

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Disclosures
• No financial relationships to disclose
• Community physician
• Participate in regional and national allergy organizations
• Volunteer clinical faculty at UW
• Try to keep up with new developments!

Background
• Food allergies have been on the rise in recent years, though it's unclear why.
• There has been a sharp upswing in food allergy awareness, anxiety, and testing.
• Food allergy guidelines have been in flux, sometimes with contradictory information.
• Currently there are no official means of preventing or treating food allergy.

Today’s objectives
• Review common food allergies and epidemiology
• Diagnosis, testing, and management
• Early food introduction
• Can we prevent or treat food allergies?
• When to refer to an allergist
• Case
• Time for questions

Definitions
Adverse food reaction: any untoward reaction to ingesting food or a food additive

• **Food allergy/hypersensitivity**: adverse food reaction due to an immunologic mechanism
  – e.g. IgE “allergic” antibodies
  – symptoms can include: immediate hives, swelling, difficulty breathing, vomiting/diarrhea, loss of consciousness
  – reaction occurs with every exposure

• **Food intolerance**: adverse reaction due to a physiologic or non-immunologic mechanism
  – lactose intolerance

• **Food sensitivity**: highly subjective
  – variable symptoms: fatigue, headache, behavior change, “inflammation”
  – no validated testing to rule in or rule out
  – empiric food elimination may be the best approach
**Immunologic (Allergic) Adverse Food Reactions**

- **IgE-Mediated**
  - Systemic (Anaphylaxis)
  - Oral Allergy Syndrome
  - Immediate gastrointestinal allergy
  - Asthma/rhinitis
  - Morbilliform rashes and flushing
  - Eosinophilic esophagitis (EoE)
  - Eosinophilic gastritis
  - Eosinophilic gastroenteritis
  - Atopic dermatitis

- **Mixed IgE/Non IgE**

- **Non-IgE Mediated Cell-Mediated**
  - Food Protein-Induced Enterocolitis
  - Food Protein-Induced Enteropathy
  - Food Protein-Induced Proctocolitis
  - Dermatitis herpetiformis
  - Contact dermatitis

**Non-Immunologic Adverse Food Reactions**

- **Toxic / Pharmacologic**
  - Bacterial food poisoning
  - Heavy metal poisoning
  - Scombroid fish poisoning
  - Caffeine
  - Alcohol
  - Histamine

- **Non-Toxic / Intolerance**
  - Lactase deficiency
  - Galactosemia
  - Pancreatic insufficiency
  - Gallbladder / liver disease
  - Hiatal hernia
  - Gustatory rhinitis
  - Anorexia nervosa
  - Idiosyncratic
  - Carbohydrate malabsorption

**Estimated Prevalence of Food Allergy**

<table>
<thead>
<tr>
<th>Food</th>
<th>Children (%)</th>
<th>Adults (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow’s milk</td>
<td>2.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Egg</td>
<td>1.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Wheat, Soy</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Peanut</td>
<td>2.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Sesame</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Tree nut</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Crustacean</td>
<td>0.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Fish</td>
<td>0.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Overall</td>
<td>6.0%</td>
<td>2-3.5%</td>
</tr>
</tbody>
</table>

**Cross-reactivity**

Cow/goat milk (92%)
- tree nut, sesame
  - Among tree nuts (37%)
    - cashew/pistachio together
    - walnut/pecan together
  - almond allergy less common
    - Among shellfish (75%)

**Natural History of Food Allergy**

- ~80% of milk, soy, egg, and wheat allergy remit by teenage years
  - Declining/low levels of specific-IgE may help predict resolution
  - >70% of children tolerate extensively heated egg, prior to tolerating partially-cooked versions

- Allergies to peanut, tree nuts, seeds, seafood are typically lifelong
  - More often associated with severe reactions
  - Epinephrine autoinjector for all nut, seed, and seafood allergies
  - ~150 food allergy deaths/yr (especially peanut and tree nut anaphylaxis)

**Natural history of Food Allergy**

<table>
<thead>
<tr>
<th>Food</th>
<th>Typical Onset/Resolution of IgE mediated allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>Develops: usually first 6-12 months of life</td>
</tr>
<tr>
<td></td>
<td>Resolves: ~30% by age 12 yrs, 70% by 16 yrs</td>
</tr>
<tr>
<td>Egg</td>
<td>Develops: 1-2 yrs</td>
</tr>
<tr>
<td></td>
<td>Resolves: 40% by age 12 yrs, 60% by 16 yrs</td>
</tr>
<tr>
<td>Wheat</td>
<td>Resolves: 65% by age 12 yrs</td>
</tr>
<tr>
<td>Peanut</td>
<td>Develops: most before age 2 yrs</td>
</tr>
<tr>
<td></td>
<td>Resolves: 20% overall, ~9% relapse rate</td>
</tr>
<tr>
<td>Tree Nuts</td>
<td>Develops: ages 1-7 yrs, or as adults</td>
</tr>
<tr>
<td></td>
<td>Resolves: in ~10% overall</td>
</tr>
<tr>
<td>Fish/Shelfish</td>
<td>Fish in late childhood or adulthood</td>
</tr>
<tr>
<td></td>
<td>Shellfish (shrimp) often adulthood (60%)</td>
</tr>
<tr>
<td></td>
<td>Resolution: uncommon or rare</td>
</tr>
</tbody>
</table>
Common food reactions: **Infants/Toddlers**

- **Food Protein-Induced Allergic Proctitis/Proctocolitis**
  - often cow’s milk/soy protein
  - blood in stool + other symptoms, usually well-appearing infant
  - usually negative skin/blood testing
  - dairy/soy avoidance until 1-2 years of age

- **Atopic Dermatitis** (aka eczema)
  - discuss later

- **Classic food allergy** (IgE-mediated)
  - egg, dairy, nuts, seeds, seafood, wheat, soy
  - rapid-onset hives, swelling +/- respiratory (cough, wheeze) or GI (vomiting, diarrhea) symptoms
  - allergy testing can be helpful

- **Repeated vomiting 2-4 hours after eating certain solids for the first time**
  - cow’s milk, soy, rice, oat, poultry, sweet potato…
  - often more than 1 food (e.g. milk + soy)

- **Can be severe, but usually self-limited**
  - may see watery/bloody diarrhea several hours later
  - severe cases: hypovolemia, leukocytosis, thrombocytosis, metabolic acidosis, methemoglobinemia

- **Differential** is broad:
  - infectious gastroenteritis, sepsis, NEC, anaphylaxis, inborn errors of metabolism, lactose intolerance, GER, Hirschprung disease, eosinophilic esophagitis/enteritis, celiac, malrotation/volvulus

**Common food reactions: Infants/Toddlers**

- **Avoid trigger foods, watch for others**
- **Testing** (sIgE) is usually negative
- **Spontaneous resolution in 1-4 years**
  - 80% outgrown by 4 years
  - rare in teens, adults?
- **When to oral food challenge??**
- **Also consider chronic FPIES**
  - intermittent vomiting/diarrhea, poor weight gain, FTT
  - resembles many other conditions (GE reflux?)
  - resolves upon elimination of trigger food(s)

**Current Food Allergy Management**

1. Make an accurate diagnosis
2. Eliminate trigger foods
3. Be prepared for food allergy reactions
4. Consider oral food challenge

**Food Protein-Induced Enterocolitis Syndrome (FPIES)**

- Repeated vomiting 2-4 hours after eating certain solids for the first time
  - cow’s milk, soy, rice, oat, poultry, sweet potato…
  - often more than 1 food (e.g. milk + soy)

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**Common food reactions: all ages**

- **Classic food allergy** (IgE-mediated)

- **Oral Allergy Syndrome**
  - pollens/food cross-reactivity
  - e.g. birch pollen → celery, carrot, pitted fruit
  - primarily oral symptoms (itch, tingle), resolve with cooking
  - can improve with allergy shots

- **Eosinophilic Esophagitis (EoE)**
  - infants: vomiting, FTT, food refusal, “reflux”
  - adults: food impaction, painful swallowing, “bad reflux”
  - food often a trigger (e.g. dairy)
  - food allergy testing has limited benefit

**Food Allergy Evaluation and Diagnosis**

- **History, History, History!**
  - food, timing, symptoms, reproducibility

- **Skin or blood testing if indicated**
  - detect food-specific IgE antibodies
  - skin and blood testing are roughly equivalent
  - high false-positive rate (“cries wolf”)
    - “sensitized” vs. true clinical allergic reactions
  - experienced interpretation is critical to making an accurate diagnosis
Food allergy tests

- **Skin prick tests**
  - looks for pre-formed allergic IgE antibodies
  - same day, takes 15-20 minutes to complete
  - reliability:
    - helpful for ruling IN a food allergy (specific)
    - excellent at ruling OUT a food allergy (sensitive)
  - may test at 4-6 months of age

- **Blood tests**
  - IgE antibody levels in the blood ("RAST", "ImmunoCAP")
  - requires a needle stick, days to weeks for results
  - similar reliability, not as sensitive as prick testing
  - may test at 4-6 months of age

Other food allergy tests

- **Skin patch tests**
  - takes 3-5 days
  - questionable utility in food allergy diagnosis/management

- **Intradermal food skin tests**
  - injection under skin, look for food-specific IgE antibodies
  - NOT recommended for food allergy testing

- **Unproven/Experimental tests to avoid**
  - food-specific IgG/IgG4 levels
  - provocation-neutralization
  - cytotoxic tests
  - applied kinesiology (muscle response testing)
  - hair analysis
  - electrodermal testing

Food allergy at school

- **Dietary Elimination**
  - **Complete avoidance** (e.g. peanut) vs. **partial avoidance** (e.g. avoid whole egg but eat baked egg products if tolerant)
  - **FALPCA**¹ (effective 1/1/06) requires labeling for the 8 major food allergens.
  - **Advisory warning labels** (May contain..., Processed in a facility...). For peanut, <10% of products had peanut.²
  - **Cross contact issues**: share equipment, fried foods
  - **Dietary counseling**

Food Avoidance

- **Skin prick testing**

Dietary Elimination

Hypoallergenic Infant Formulas for Cow's Milk Allergy (CMA)

- **Soy based formulas** For IgE-CMA, soy co-allergy is 0-14%. For non-IgE CMA, soy co-allergy 0% to 60%.
- Partial hydrolysates (e.g. Good Start, Peptamin Jr, Pediasure Peptide) are not recommended for CMA
- **Extensively hydrolyzed formulas (EHF)** Alimentum, Nutramigen: >90% tolerance in IgE-CMA
- **Elemental amino acid based formulas** (Neocate, Elecare): CMA, FPIES intolerant of EHF, EoE


Anticipating food allergy reactions

- Food allergic reactions can sometimes develop into life-threatening reaction
  - variable triggers: quantity, route, state of health
  - reaction severity cannot be predicted using test results or previous reaction history
- **Treatment**
  - antihistamines for “minor” reactions
  - self-injectable epinephrine (adrenaline) for “severe” or “systemic” reactions (aka anaphylaxis)

Managing Anaphylaxis

- Written Anaphylaxis Emergency Action Plan
- Emergency identification bracelet
- Epinephrine: drug of choice for systemic reactions
  - 2 doses of self-injectable epinephrine available on hand at all times (in case of biphasic reaction)
- Antihistamines: WILL NOT STOP ANAPHYLAXIS


Common questions

- **Can we prevent food allergy?**
- **What should I feed my baby?**
- **Is food allergy causing my baby’s eczema?**

Can we prevent food allergy?

- No official means of preventing food allergy
- Early food introduction may be protective
  - prior observation: 1/10 prevalence of PN allergy in Israel
- **LEAP study:** early peanut exposure may reduce the risk of developing peanut allergy...

Learning Early About Peanut (LEAP 2015)

- Landmark RCT, 640 infants, 4-11 months of age at high risk for developing PN allergy
  - High risk = severe eczema, egg allergy, or both
  - skin tested, placed into 3 groups, +/− peanut, and later assessed at 5 years of age
- **Group 1:**
  - skin test: >4 mm wheal = “peanut allergic”
  - excluded from study
- **Group 2:**
  - skin test: negative
    - ate peanut ~6 grams per week (3 rounded teaspoons peanut butter)
    - avoided peanut
- **Group 3:**
  - skin test: 1-4 mm wheal
    - ate peanut: ~6 grams per week
    - avoided peanut


LEAP: PN allergy prevalence at 5 years of age

• **Group 1**: (“allergic”, did not enroll)

• **Group 2**: (negative skin test group)
  – ate peanut: 1.9% allergic
  – avoided peanut: 13.7% allergic (p<0.001; 86% RRR)

• **Group 3**: (skin test 1-4 mm wheal)
  – ate peanut: 10.6% allergic
  – avoided peanut: 35% allergic (p=0.004; 70% RRR)

2017 addendum guidelines for prevention of peanut allergy in the US

• **Guideline #1** (severe eczema and/or known egg allergy)
  – PCP may check peanut specific IgE
    – If undetectable (<0.35), then try peanut at home
      – If positive (≥0.35), then refer to an allergist for further evaluation
  – Or refer to an allergist for skin prick testing
    – If SPT 0-2 mm wheal, then try peanut in the office, or at home
      – If SPT 3-7 mm wheal, then supervised feeding in specialist office
      – If SPT ≥8 mm wheal, then probably allergic to peanut

• **Guideline #2** (mild-moderate eczema)
  – No testing necessary, try peanut at home around 6 months, “in accordance with family preferences and cultural practices”
  – May consider referral to an allergist for testing and in-office peanut introduction
  – Avoid choking hazards (unthinned peanut butter, peanut pieces)

• **Guideline #3** (no eczema or food allergy)
  – No testing necessary
  – Introduce peanut “freely” into the diet together with other solids, and in accordance with family preferences and cultural practices

Early Peanut Introduction

• Initial peanut introduction:
  – 2 g peanut protein = 2 tsp (9-10 g) thinned peanut butter (e.g. hot water, apple sauce, vegetable puree), or 1 bag of Bamba

• If tolerated, then continue eating 2 g peanut protein 3 times per week until age 5
  – 2 g = 1 bag (28 g) Bamba, peanut butter on bread or toast (16 g), 2.5 tsp ground peanuts (8 g)
  – Avoid choking hazards (unthinned peanut butter, peanut pieces)
Evolving food introduction guidelines
2000 (AAP)
- All mothers: consider restricting peanut during pregnancy
- For "high risk" infants (= parent or sibling with allergies)
  - breast feeding moms eliminate peanut, tree nuts
  - also consider avoiding eggs, cow’s milk, and fish
  - *delay introduction of dairy until 12 months, eggs until 2 years, and peanut/tree nuts/fish until 3 years
- Based on expert consensus, and not intended for all infants

Evolving food introduction guidelines
2008 (AAP), 2010 (NIAID)
- No convincing evidence to delay introduction of highly allergenic foods like dairy, egg, nuts, or seafood
- Did not specifically encourage introducing complementary foods (e.g. cow’s, egg, soy, wheat, peanut, tree nuts, fish, shellfish) or when

What should I feed my baby?
- Exclusive breastfeeding is recommended until 4-6 months of age
  - may reduce risk of milk allergy, eczema, wheezing
- For infants at high-risk who cannot be exclusively breastfed for first 4-6 months
  - hydrolyzed formula may prevent eczema
- Maternal avoidance diets during pregnancy and lactation are not recommended based on current data

Is food allergy causing my baby’s eczema?

Atopic Dermatitis (aka Eczema)

- Atopic Dermatitis is common
  - non-allergic and allergic (food, environmental) triggers
  - managing allergic triggers will not “cure” AD
  - diligent skin care: frequent bathing, non-soap cleansers, emollients, as-needed topical steroids, +/- bleach baths, wet wraps
  - AD often resolves before school age

- Common allergic triggers in AD
  - foods: egg, milk, peanut, tree nuts, wheat, soy, seeds, seafood
  - (indoor) environmental triggers often overlooked: dust mites, cat, dog

Eczema and food sensitization/allergy

- General population (no eczema):
  - 28% of US children are sensitized to foods (i.e. positive skin or blood test, but no clinical reaction)
  - 8% have a positive peanut test (sensitized)

- Infants/children with eczema
  - elevated total IgE is common
  - 50-80% test positive (sensitized) to at least one food
  - e.g. milk, egg, and peanut; often wheat or soy
  - 84-93% of food were being avoided unnecessarily

- Of food allergy “Treatments”

Effect of Cooking & Digestion on Food Proteins

Children who “outgrow” milk (or egg) allergy will often tolerate baked-milk products first

BAKED GOODS
Changing from Avoidance to Limited Diet

- 70% of children with egg allergy tolerate in baked goods
- 75% of children with milk allergy tolerate in baked goods
- Regular ingestion of these proteins is associated with less positive test results
- Regular ingestion may result in more rapid resolution of milk/egg allergy

Food Desensitization

- Desensitization: change in the threshold dose of food needed to cause an allergic reaction while therapy is continued
- Sustained Unresponsiveness: allergy has resolved
- Oral immunotherapy (OIT)
  - consume (eat) increasing amounts of allergenic food daily
  - drops or tiny pieces of food
- Epicutaneous immunotherapy (EIT)
  - patch/sticker with small amount of allergenic food
  - daily application

OIT/EIT Progress

• Oral immunotherapy
  – most patients on OIT achieve desensitization, but very few achieve “sustained unresponsiveness”
  – may see more success in infants and young children
  – chronic GI side effects lead to poor adherence
  – occasional/unpredictable systemic reactions

• Epicutaneous immunotherapy
  – well tolerated, relatively safe
  – skin rash, itching are common
  – currently in FDA phase III study, approval in 1-2 years?

Gernez et al. JACI In Practice 2017

Other news

Influenza

• Fever, cough, body aches
• 294,128 influenza hospitalizations per year in US1-2
  – 21,156 are children under 5 years old
• 23,607 deaths per year
  – 124 children

• Vaccines
  – IIV (inactivated influenza vaccine, trivalent or tetravalent)
  – LAIV (live attenuated intranasal influenza vaccine)
  – Flumist® nasal spray NOT approved for 2017/2018 season3.


Influenza vaccination and egg allergy

• CDC guidance for 2017-2018 season1 (unchanged from last year)
  – if mild egg allergy (e.g. hives only), then may receive any licensed, age-appropriate flu vaccine
  – if history of severe reaction to egg, patients should receive influenza vaccine in a supervised medical setting

• 2018 and beyond
  – give influenza vaccine to all egg-allergic patients (no matter their reaction history)
  – inactivated or live attenuated vaccines
  – no need for testing, split dosing, or supervised administration
  – “Vaccine providers should not ask about the egg allergy status of recipients of influenza vaccine.”


Influenza vaccination and egg allergy

• Most influenza vaccines grown in fertilized chicken eggs
  – trace amounts of egg protein (ovalbumin)

• Egg-containing influenza vaccines were contraindicated in patients with egg allergy
  – used to defer vaccination, split dosing, or arcane skin testing

Growing evidence egg allergy may not be a problem..

New FDA peanut labeling

“For most infants with severe eczema and/or egg allergy who are already eating solid foods, introducing foods containing ground peanuts between 4 and 10 months of age and continuing consumption may reduce the risk of developing peanut allergy by 5 years of age. FDA has determined, however, that the evidence supporting this claim is limited to one study.

If your infant has severe eczema and/or egg allergy, check with your infant’s healthcare provider before feeding foods containing ground peanuts.”

• A “Qualified Health Claim”, supported by credible scientific evidence
• vs. “Authorized Health Claim”, supported by significant scientific agreement

https://www.fda.gov/food/newsevents/constuentupdates/ucm575001.htm, accessed 10/18/17
**When to refer to Allergy**

- Known or suspected food allergy reaction
- Infants with moderate/severe eczema refractory to management
- "Allergic" families (with infants, or expecting)
  - counseling about maternal and infant diets
  - testing, if indicated
- Child with older food-allergic sibling
  - 7% increased risk of peanut allergy vs. avoiding testing?


**Case: eczema & food allergy in 1975**

- 7 month old boy with mild eczema on cheeks, inner elbows
  - responds to moisturizer and occasional topical steroid
- Breastfed for first 6 weeks, then cow’s milk formula
- Around 6 months, tried scrambled egg on 2 occasions:
  - hives and worse eczema both times
- How to proceed?
  - Need allergy testing?
  - Avoid other foods?
  - Will egg allergy go away?

**The Allergist’s Role**

- Use focused, evidence-based testing to confirm a known or suspected food allergy
- Assist in food allergy test interpretation
- Patient education:
  - identification of causative food, elimination diet
  - education on the signs and symptoms of allergic reactions and anaphylaxis, and appropriate treatment including correct epinephrine autoinjector technique
- Assist in formulation of individual health plans, particularly for child-care and educational settings
- Evaluate for and conduct food challenges
  - may rule-out food allergy


**Case: Eczema in 2000-2007**

- 7 month old with mild eczema on cheeks, inner elbows
  - breastfed for first 6 months
  - has tried fruit, veg, grains, but no “high-risk” foods
- Parents: “tell us which foods are causing eczema”
  - testing revealed multiple positives: egg, milk, wheat, soy, peanut, tree nuts
  - anxiety, numerous food eliminations
  - resolution of egg, milk, wheat, soy allergy by school age
  - lifelong nut allergy

**Case: Eczema in the future**

- 7 month old with mild eczema on cheeks, inner elbows
  - breast feed for first year, watch for food triggers in breast milk
  - extensively hydrolyzed formula if CM allergy or CMPI
  - if CMPI, may consider soy formula if tolerated
  - elemental formula if completely dairy intolerant
- around 6 months
  - offer baked egg/milk proteins (bread, muffins, cakes) before uncooked/partially-cooked (pancakes, waffles; fried, scrambled, or boiled egg)
  - if no eczema or mild/moderate eczema, try peanut at home
  - see an allergist if moderate/severe eczema, known egg allergy, or both
  - otherwise, may introduce other foods

Summary: food allergy

• Food allergies have been on the rise
• More allergy testing, diagnosis, and anxiety
• Evolving food introduction recommendations from experts
• No official means to prevent or treat food allergies
• History is key in making an accurate food allergy diagnosis
• Food allergy testing can be unreliable (especially if there’s eczema) and result in incorrect diagnosis

Summary: food allergy

• No evidence for maternal food avoidance during pregnancy/lactation
• At 6 months, encourage introduction to a wide range of foods — may help prevent food allergies
• Most infants should try peanut protein for the first time at home
• If severe eczema, egg allergy, or other suspected food allergy, then refer to an allergist for evaluation
• If eczema, consider restricting egg first, then dairy (mom + infant’s diets) before referral or testing
• Later consider maternal restriction of nuts, seafood, wheat, soy
• Younger sibling of food-allergic child: consider prophylactic testing

Summary: food allergy

• If there is milk or egg allergy, exposure to baked milk/egg proteins (when tolerated) probably speeds up resolution of milk/egg allergy
• Future treatments (OIT, EIT) may have limited benefits and probably will not cure food allergy
• If egg allergy, may receive flu vaccine without special testing or precautions.
• May refer for supervised administration if family wants reassurance

Food Allergy: Future Goals

• Manage children and adults with a known food allergy
• More responsible food allergy testing
• With early food introduction, hope to see a drop in food allergy prevalence
• Create a less fearful, and healthier relationship with food

Food allergy prevalence

• 20-25% of American claims to have a food allergy (actual ~2-3%)
• Increasing prevalence
• Increased peanut
• Studies question the increased prevalence

Studies from p223 of In Practice
n=7896, 6-19 yo 1998-1994 (11.2% sensitized, sIgE >0.35 to milk, egg, peanut, and shrimp) vs 2005-2006 (6.1% sensitized) National Health and Nutrition Examination Surveys. No change in prevalence of sensitization. Improved diagnosis/recognition? Delayed introduction converts from sensitized to clinical reactions? Another study: “treating” AD with food elimination may lead to more clinical food allergies. 30% included anaphylaxis. Younger siblings of food-allergic children. 66.6% were sensitized, but only 13.6% were clinically reactive/allergic. Discourage screening of younger siblings (due to high false-positive rate?). Compared to other children, maybe these kids only have a modestly increased rate of allergy.