Food Allergy and Atopic Dermatitis: Common, Co-Morbid, Confusing

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Disclosures

• Employment: Pediatric Institute of Emory University + Children’s
• Consultant/Advisor: Aimmune Therapeutics; AllerGenis, LLC; Aravax (pending); Food Allergy Research and Education (FARE); Reacta Biosciences
• Grant support: NIH-NIAID; FARE
• Clinical investigator: Aimmune; DBV Technologies; Genentech; Regeneron
• Equity interests/stock ownership: none
Learning Objectives

• Discuss the mechanistic role of the skin in contributing to food allergy development.

• Describe the appropriate use of allergen testing modalities in making a food allergy diagnosis.

• Summarize an updated recent statement from the American Academy of Pediatrics regarding complementary feeding, breastfeeding, infant formulas, and other interventions in the prevention and management of allergic disease.
Sensitization and Allergy Exist On a Continuum

Food

Sensitized

Sensitized

No IgE

Clinical reaction

Re-exposure

No reaction

Children's Healthcare of Atlanta | Emory University
A Real Case From my First Year of Fellowship

• 15 month old Caucasian child of married middle class parents
• History of moderate to severe eczema and poor weight gain
• Some mild developmental delay
• Pediatrician diagnosed multiple food allergy based on *in vitro* IgE measurements
• Saw outside allergist before presenting to A/I clinic for further evaluation / second opinion
A Real Case From my First Year of Fellowship, cont

• Obviously malnourished, with weight << 3%ile, temporal/gluteal wasting, sparse hair, protuberant abdomen
• Lethargic & irritable with impressive eczema
• Treatment: organic skin balm
• Diet: highly restricted based on parental “skin testing” method:
  
  **GRAPEFRUIT, DANDELION “TEA,” AND PUREED ROASTED RED PEPPER**

• Serum [Na⁺] = 122
Case cont.

• What to do now?
  – Corrected electrolytes in hospital
  – Introduced elemental diet and established good wt gain
  – Instituted appropriate therapy for atopic dermatitis
  – Added lamb, spinach, sweet potato, squash prior to discharge w/ plans to add 2-5 more foods as outpt

• Family meeting, Nutrition, SW, education, close f/u

Take Home Points:
1. The proper diagnosis of food allergy can be tricky
2. This is especially true in patients with atopic dermatitis, which is highly comorbid
3. IgE testing is probability-based and often requires confirmation with challenge
<table>
<thead>
<tr>
<th>Test Name</th>
<th>Full Name</th>
<th>Concentration</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>f25</td>
<td>Tomato</td>
<td>3.13 kUA/l</td>
<td>II</td>
</tr>
<tr>
<td>f7</td>
<td>Oat</td>
<td>32.0 kUA/l</td>
<td>IV</td>
</tr>
<tr>
<td>f9</td>
<td>Rice</td>
<td>4.08 kUA/l</td>
<td>III</td>
</tr>
<tr>
<td>f49</td>
<td>Apple</td>
<td>2.80 kUA/l</td>
<td>II</td>
</tr>
<tr>
<td>f92</td>
<td>Banana</td>
<td>2.74 kUA/l</td>
<td>II</td>
</tr>
<tr>
<td>f40</td>
<td>Tuna</td>
<td>3.21 kUA/l</td>
<td>II</td>
</tr>
<tr>
<td>f41</td>
<td>Salmon</td>
<td>&lt;0.35 kUA/l</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Flag/Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barley IgE</td>
<td>14.80</td>
<td>2</td>
</tr>
<tr>
<td>Beef IgE</td>
<td>27.20</td>
<td>4</td>
</tr>
<tr>
<td>Broccoli IgE</td>
<td>0.97</td>
<td>2</td>
</tr>
<tr>
<td>Carrot IgE</td>
<td>6.47</td>
<td>3</td>
</tr>
<tr>
<td>Chicken IgE</td>
<td>31.50</td>
<td>4</td>
</tr>
<tr>
<td>Cucumber IgE</td>
<td>1.98</td>
<td>2</td>
</tr>
<tr>
<td>Peach IgE</td>
<td>0.15</td>
<td>0/1</td>
</tr>
<tr>
<td>Pear IgE</td>
<td>0.24</td>
<td>0/1</td>
</tr>
<tr>
<td>Potato Sweet IgE</td>
<td>0.96</td>
<td>2</td>
</tr>
<tr>
<td>Potato White IgE</td>
<td>0.43</td>
<td>1</td>
</tr>
<tr>
<td>Rabbit Meat IgE</td>
<td>1.85</td>
<td>2</td>
</tr>
<tr>
<td>Turkey IgE</td>
<td>13.00</td>
<td>3</td>
</tr>
</tbody>
</table>
Which of the following statements is true regarding serum specific IgE testing?

A. Serum IgE tests are more accurate than skin tests.
B. Clinical severity is associated with the IgE level.
C. Reactions can still occur in patients with undetectable IgE.
D. Component IgE levels should sum to the total allergen-specific IgE level.
Food Allergy Diagnostic Toolbox

1. History: ~50% sensitivity
2. Prick Skin Test: high NPV, poor PPV
3. In vitro allergen- or component-specific IgE: High PPV
   – But only for a few foods & when supported by an appropriate history
4. Elimination Diets/rechallenge: ~ 2 to 4 weeks
   – Can be very useful in the evaluation of AD food triggers
5. Gold Standard: food challenge, aka “swallow test”
   – Natural exposure at home: often can get with a careful history
   – Deliberate exposure in office: open OFCs with real foods (DBPCFCs usually research-only)
Two Common Scenarios When an OFC is Especially Helpful

1. The patient has a positive test but never knowingly ingested the food.
   - The only way to distinguish between a true- and false-positive is with an OFC

2. An exposure did occur but what happened next is unclear:
   - the exposure was small/sub-threshold (e.g. terminated by spitting out, occult / contamination)
   - details are vague (e.g. unwitnessed, poor historian / limited health literacy, confounded by anxiety)
In These Scenarios, OFCs are Commonly Passed

Table II. OFC results on foods avoided due to immunoassay or PST

<table>
<thead>
<tr>
<th>Food group</th>
<th>Avoiding on admission</th>
<th>OFC positive result</th>
<th>OFC negative result</th>
<th>Avoiding on discharge</th>
<th>% Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg</td>
<td>10</td>
<td>1</td>
<td>9</td>
<td>1</td>
<td>90%</td>
</tr>
<tr>
<td>Fruits</td>
<td>10</td>
<td>2*</td>
<td>8</td>
<td>2</td>
<td>80%</td>
</tr>
<tr>
<td>Meats</td>
<td>13</td>
<td>0</td>
<td>13</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Milk</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Oats</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Peanut</td>
<td>7</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>86%</td>
</tr>
<tr>
<td>Shellfish</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Soy</td>
<td>19</td>
<td>1</td>
<td>18</td>
<td>1</td>
<td>95%</td>
</tr>
<tr>
<td>Vegetables</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Wheat</td>
<td>13</td>
<td>3</td>
<td>10</td>
<td>3</td>
<td>77%</td>
</tr>
<tr>
<td>Other</td>
<td>18</td>
<td>0</td>
<td>18</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Totals</td>
<td>111</td>
<td>8</td>
<td>103</td>
<td>8</td>
<td>93%</td>
</tr>
</tbody>
</table>

- N=125 children with AD aged 1-19 evaluated at National Jewish
- Offered OFC unless: (1) a history of life-threatening anaphylaxis or (2) a convincing reaction within 6-12 mo
  - Note some patients were challenged despite IgEs > 95% PPV levels

In all, 325 of 364 (89%) of OFCs were negative; 0 challenges were positive with sIgE < 95% PPV
Co-Morbid Atopic Dermatitis Poses Several Problems in Food Allergy

1. Fact: AD is strongly associated with, and may be a risk factor for, true IgE-mediated food allergy (estimated prevalence ~30%; many more are sensitized)
   – Implication: these patients, especially infants, will present clinically and need careful evaluation

2. Fact: AD is strongly associated with abundant polyclonal IgE production
   – Implication: the interpretation of serology may be especially challenging in this population (?)

3. Fact: delayed/ill-defined symptoms can occur following food exposure in some AD patients
   – Implication 1: many parents will bring their children to a pediatrician and/or an allergist seeking testing to identify the trigger(s), convinced of a causal relationship
   – Implication 2: it is easier and faster to order a test than it is to take a careful history and explain why testing is not indicated
   – Implication 3: avoidance may cause harm: (1) aversion & allergy can develop to a previously tolerated food; (2) risks of malnutrition / vitamin deficiency / poor growth; (3) unnecessary psychological suffering

Robison and Singh, JACI : In Pract 2019
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Robison and Singh, JACI: In Pract 2019
AD Severity and Timing Associate With Food Allergy

50.8% with early-onset AD and high-potency steroids had challenge-proven food allergy

• Prevalence of food allergy at 12 months of age is most closely associated with:
  – Time of onset
  – Potency of topical steroids (likely a proxy for severity)
  – Both effects appear to be dose-dependent
• FLG mutations are strongest known genetic risk for peanut allergy

"We postulate that scratching from pruritus likely damages the skin and increases local release of TSLP, IL-33, and other type 2 cytokines to enhance TEWL responses and support environmental peanut allergen penetration through the skin, due to the loss of skin barrier function from immune activation."

Leung et al Sci Transl Med 2019
IL-33 is a Druggable Epithelial Alarmin That Acts on Highly Relevant Targets...
…Which Circulates After Skin Injury, Activates Allergic Gut Inflammation, & Worsens Anaphylaxis in Mice
**NIAID Guidelines: Consider Screening Tests, but Only for Peanut and Only in Certain Circumstances**

2016 NIAID Addendum Guidelines

**TABLE I. Summary of addendum guidelines 1, 2, and 3**

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

“It is possible that an FA evaluation prior to introduction of a food could potentially prevent allergic reactions. However, widespread SPTs and sIgE tests are not recommended because of their poor predictive value. These tests would lead to many clinically irrelevant results and unnecessary dietary restrictions, especially if unconfirmed by oral food challenges.”

Togias et al. JACI 2016
Boyce et al JACI 2010
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<table>
<thead>
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<th>4-6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severe eczema is defined as persistent or frequently recurring eczema with typical morphology and distribution assessed as severe by a healthcare provider and requiring prescription-strength topical corticosteroids, calcineurin inhibitors, or other anti-inflammatory agents despite appropriate use of emollients.</td>
<td>4-6 months</td>
</tr>
<tr>
<td>2</td>
<td>Introduce peanut-containing foods.</td>
<td>Around 6 months</td>
</tr>
<tr>
<td>3</td>
<td>Age appropriate and in accordance with family preferences and cultural practices.</td>
<td>Around 6 months</td>
</tr>
</tbody>
</table>

Guideline 34: The EP suggests that the general population of children not be tested for FA to highly allergenic foods if the population of children do not have a family history of allergic disease.

“It is possible that an FA evaluation prior to introduction of a food could potentially prevent allergic reactions. However, widespread SPTs and sIgE tests are not recommended because of their poor predictive value. These tests would lead to many clinically irrelevant results and unnecessary dietary restrictions, especially if unconfirmed by oral food challenges.”

Togias et al. JACI 2016
Boyce et al JACI 2010
Don’t rely on antihistamines as first-line treatment in severe allergic reactions.

Epinephrine is the first-line treatment for anaphylaxis. Data indicate that antihistamines are overused as the first-line treatment of anaphylaxis. By definition, anaphylaxis has cardiovascular and respiratory manifestations, which require treatment with epinephrine. Overuse of antihistamines, which do not treat cardiovascular or respiratory manifestations of anaphylaxis, can delay the effective first-line treatment with epinephrine.

Epinephrine should be administered as soon as the diagnosis of anaphylaxis is suspected. Antihistamines are second-line supportive therapy for cutaneous non-life-threatening symptoms (hives), but do not replace epinephrine as the first-line treatment for anaphylaxis.

Fatalities during anaphylaxis have been associated with delayed administration of epinephrine.

Don’t perform food IgE testing without a history consistent with potential IgE-mediated food allergy.

False or clinically irrelevant positive allergy tests for foods are frequent. Indiscriminate screening results in inappropriate avoidance of foods and wastes healthcare resources. IgE testing for specific foods must be driven by a history of signs or symptoms consistent with an IgE-mediated reaction after eating a particular food. Ordering IgE testing in individuals who do not have a history consistent with or suggestive for food allergy based on history frequently reveals positive tests that are unlikely to be clinically relevant. Testing, when done, should be limited to suspected foods.

The diagnostic utility of IgE testing for specific foods is optimal when a history compatible with or suggestive for the diagnosis of food allergy is present. In the absence of a compatible or suggestive history, the pre-test probability for a diagnosis of food allergy is low and a positive skin or in vitro IgE test does not establish a diagnosis of food allergy. Skin testing or serum testing for specific-IgE to food antigens has excellent sensitivity and high negative predictive value, but has low specificity and low positive predictive value.

Considering that 50 to 90 percent of presumed cases of food allergy do not reflect IgE-mediated (allergic) pathogenesis and may instead reflect food intolerance or symptoms not causally associated with food consumption, ordering panels of food tests leads to many incorrectly identified food allergies and inappropriate recommendations to avoid foods that are positive on testing.

Don’t routinely order low- or iso-osmolar radiocontrast media or pretreat with corticosteroids and antihistamines for patients with a history of seafood allergy, who require radiocontrast media.
6. Don’t prescribe high-dose dexamethasone (0.5mg/kg per day) for the prevention or treatment of bronchopulmonary dysplasia in pre-term infants.

High dose dexamethasone (0.5 mg/kg day) does not appear to confer additional therapeutic benefit over lower doses and is not recommended. High doses also have been associated with numerous short- and long-term adverse outcomes, including neurodevelopmental impairment.

7. Don’t perform screening panels for food allergies without previous consideration of medical history.

Ordering screening panels (IgE tests) that test for a variety of food allergens without previous consideration of the medical history is not recommended. Sensitization (a positive test) without clinical allergy is common. For example, about 8% of the population tests positive to peanuts but only approximately 1% are truly allergic and exhibit symptoms upon ingestion. When symptoms suggest a food allergy, tests should be selected based upon a careful medical history.

8. Avoid using acid blockers and motility agents such as metoclopramide (generic) for physiologic gastroesophageal reflux (GER) that is effortless, painless and not affecting growth. Do not use medication in the so-called “happy-spitter.”
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Robison and Singh, JACI : In Pract 2019
Specific IgE testing: Caveats

1. Derived from populations with high pre-test probability of IgE-mediated symptoms
   - May not be applicable to unexposed
2. Do not offer any information about severity
3. Only preclude the need for OFC if above threshold
4. Only pertain to major allergens: milk, egg, peanut, tree nut, fish, (soy/wheat)
## 95% PPV Decision Points
(in Dr. Sampson’s Clinic, In Baltimore, 15 Years Ago)

<table>
<thead>
<tr>
<th>Allergen</th>
<th>95% predictive level (kU_A/l)</th>
<th>Positive predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg</td>
<td>7</td>
<td>98</td>
</tr>
<tr>
<td>Infants ≤ 2 years (34)</td>
<td>2</td>
<td>95</td>
</tr>
<tr>
<td>Milk</td>
<td>15</td>
<td>95</td>
</tr>
<tr>
<td>Infants ≤ 2 years (33)</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>Peanut</td>
<td>14</td>
<td>95</td>
</tr>
<tr>
<td>Fish</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>Tree nuts (42)</td>
<td>~15</td>
<td>~95</td>
</tr>
<tr>
<td>Soybean</td>
<td>30</td>
<td>73</td>
</tr>
<tr>
<td>Wheat</td>
<td>26</td>
<td>74</td>
</tr>
</tbody>
</table>

Note: not Class IV
Interpreting Serology: Your Mileage May Vary

• “Diagnostic cutoff values can vary widely in different studies. For instance, the 95% PPV cutoff to diagnose PA was 15 kU/L in US and UK studies, but was 24.1 kU/L, 34 kU/L, and 57 kU/L in studies performed in the Netherlands, Australia, and France, respectively... 

• These differences can result from the patient population (eg, prevalence of FA, comorbidities) and/or from the research study where the cutoffs were determined...these factors need to be taken into account when comparing studies and when extrapolating cutoffs from published studies into daily clinical practice...

• ...PPVs are a function of the sensitivity and specificity of the test and the prevalence of the disease; therefore, they are only valid for patients who have the same pretest probability of disease as the population in which the PPV was established.”

• This is true for components too!

<table>
<thead>
<tr>
<th>Foods</th>
<th>Components associated with clinical allergy</th>
<th>Cutoffs for specific IgE to main components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanut</td>
<td>Ara h 1</td>
<td>Ara h 2 sIgE: 0.35 to 42.2 kU/L had 90%-95% PPV&lt;sup&gt;16,24,27&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Ara h 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ara h 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ara h 9 (in Southern Europe)</td>
<td></td>
</tr>
<tr>
<td>Hazelnut</td>
<td>Cor a 9</td>
<td>Cor a 9 sIgE: 1 kU/L had 83% accuracy&lt;sup&gt;28&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Cor a 14</td>
<td>Cor a 14 sIgE: 0.72 to 47.8 kU/L had 87%-90% accuracy&lt;sup&gt;27,31&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
### TABLE V. Factors modulating the interpretation of allergy test results

<table>
<thead>
<tr>
<th>Factors identified in the clinical history</th>
<th>Effect on the probability of clinical allergy for a given specific IgE level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported immediate allergic reaction to the specific food</td>
<td>A history of reacting to the tested food supports the clinical relevance of detected IgE.</td>
</tr>
<tr>
<td>(Younger) Age</td>
<td>Lower levels of allergen-specific IgE have increased clinical relevance in young children.</td>
</tr>
<tr>
<td>(Black) Ethnicity</td>
<td>Black race is associated with higher levels of allergen-specific IgE with decreased clinical relevance.</td>
</tr>
<tr>
<td>Atopic eczema</td>
<td>Polyclonal IgE response can be non-allergen-specific and thus decrease clinical relevance of a given specific IgE level.</td>
</tr>
<tr>
<td>Concomitant inhalant allergies</td>
<td>Pollen sensitization can cause false-positive results of specific IgE to plant food extracts.</td>
</tr>
<tr>
<td>Atopic population</td>
<td>Positive predictive value of a given specific IgE level increases with the increase in the prevalence of the disease in the population.</td>
</tr>
<tr>
<td>Geographical location</td>
<td>Variable</td>
</tr>
</tbody>
</table>

These factors affect the pretest probability and therefore influence the resulting post-test probability.
IgE testing can predict food allergy status in patients with moderate to severe atopic dermatitis

Pamela A. Frischmeyer-Guerrero, MD, PhD †; Marjohn Rasooly, MSN ‡; Wenjuan Gu, MS †; Samara Levin, BA †; Rekha D. Jhamnani, MD †; Joshua D. Milner, MD †; Kelly Stone, MD, PhD †; Anthony L. Guerrero, MD, PhD ‡; Joseph Jones, MS §; Magnus P. Borres, MD ‡; Erica Brittain, PhD ‡

• 78 patients 2 – 20 y (median 10.7 y) with mod-severe AD recruited at NIH – unselected for FA
• Assessed for historical reactions (no OFCs) to milk, egg, peanut, wheat, and soy & SCORAD
• Serum taken for these 5 foods plus wheat & soy: slgE, CRD, total IgE w/ dilutions PRN
• Wilcoxon/M-W, logistic regression with bootstrapping, and multivariate prediction algorithms

Results
• 91% sensitized to ≥ 1/5 foods; 51% reported convincing allergic reactions by PRACTALL guidance
• Total IgE: median 8430 (IQR 3946 – 19,095) in those allergic ≥ 1 food vs. 3323 (1076 – 9140) tolerant to all; p = 0.0165
• In those allergic vs. tolerant: SCORAD not different; slgE to milk, egg, PN were significantly higher; specific-to-total IgE not helpful; components did add value
### Food IgE

<table>
<thead>
<tr>
<th>Food IgE</th>
<th>50% NPV from logistic model</th>
<th>Decision point (max sens + spec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>42.8 (23.2 – 116.7)</td>
<td>27.4</td>
</tr>
<tr>
<td>Egg white</td>
<td>28.0 (11.4 – 103.8)</td>
<td>16.7</td>
</tr>
<tr>
<td>Peanut</td>
<td>36.4 (19.8 – 66.7)</td>
<td>35.6</td>
</tr>
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</table>

### Bottom Line:

slgE can identify FA even in mod-severe AD when total IgE is high; but we need to be more aggressive with offering OFC to sensitized patients.
Co-Morbid Atopic Dermatitis Poses Several Problems in Food Allergy

1. Fact: AD is strongly associated with, and may be a risk factor for, true IgE-mediated food allergy (estimated prevalence ~30%; many more are sensitized)
   - Implication: these patients, especially infants, will present clinically and need careful evaluation

2. Fact: AD is strongly associated with abundant polyclonal IgE production
   - Implication: the interpretation of serology may be especially challenging in this population (?)

3. Fact: delayed/ill-defined symptoms can occur following food exposure in some AD patients
   - Implication 1: many parents will bring their children to a pediatrician and/or an allergist seeking testing to identify the trigger(s), convinced of a causal relationship
   - Implication 2: it is easier and faster to order a test than it is to take a careful history and explain why testing is not indicated
   - Implication 3: avoidance may cause harm: (1) aversion & allergy can develop to a previously tolerated food; (2) risks of malnutrition / vitamin deficiency / poor growth; (3) unnecessary psychological suffering

Robison and Singh, JACI : In Pract 2019
Co-Morbid Atopic Dermatitis Poses Several Problems in Food Allergy

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Robison and Singh, JACI : In Pract 2019
Establishing Pre-Test Probability: Ask Specific, Probing Questions

• Suspected culprit food protein:
  – Which was it (egg vs. red Gatorade)?
  – What form did they eat? Had they eaten it before?
  – How much?
  – Have they eaten it again - ask about other forms - since the episode?

• What happened then?
  – Timing & sequence of symptoms?
    • Yes: Hives, swelling, abd pain, vomiting, wheezing/coughing, significant and typical flare of known AD, anaphylaxis following known exposure
    • No: significant delay between exposure & onset of symptoms (ie next day); headaches, fatigue, flat nonpruritic red rash on face or bottom; changes in color/consistency of stool; vague behavioral change
  – Did the episode require treatment?

• THEN decide if you want to test or just have them eat the food again
Guideline 22: In individuals without documented or proven FA, the EP does not recommend avoiding potentially allergenic foods as a means of managing AD, asthma, or EoE.

“No conclusive evidence exists to suggest that avoiding food allergens reduces the severity of AD, asthma, or EoE in individuals who are not sensitized and have not demonstrated specific clinical reactivity to foods.”

– 2 high-quality Cochrane reviews evaluated the effect of dietary exclusion for treating AD; both negative

2010 NIAID Food Allergy Guidelines

Guideline 35: The EP suggests that children less than 5 years old with moderate to severe AD be considered for FA evaluation for milk, egg, peanut, wheat, and soy, if at least one of the following conditions is met:

- The child has persistent AD in spite of optimized management and topical therapy.
- The child has a reliable history of an immediate reaction after ingestion of a specific food.

5.2.4. Testing in Infants and Children With Persistent Atopic Dermatitis
What I Do in My Practice

1. Describe the chronic waxing-waning nature of AD with a parent (gain trust)
2. Establish the possibility that within this context, cause-effect associations could be spurious
3. Shift the discussion from foods to skin
4. Review the family’s approach to daily skin care, which is quite often missing one or more steps.

All patients should have:

- Daily soaking bath at least 15 minutes in length
- Plain, unscented cleansers with neutral pH
- Liberal application of a cream/ointment (not lotion) immediately after bath and again another time if possible
- Use of an appropriate potency topical steroid PRN (address any steroid phobia directly)
- Consideration of adjunctive therapies like wet wraps / bleach baths / topical or oral antimicrobials
- Fingernails cut short
- Written / online instructions to refer to

see Boguniewicz et al: AD Yardstick in Annals January 2018
Child with moderate to severe AD and no history of immediate-type allergic reactions to regularly ingested foods

No improvement with optimal skin care

Positive tests: Diagnostic elimination test diet for 4 weeks*

Allergy work-up to most common food allergens in AD

Negative tests: No elimination diet

No improvement: Food allergy not a trigger
Stop elimination test diet

No improvement: Food allergy not a trigger
If strong suspicion, aggressive AD treatment and reconsider OFC

Improvement: Consider food allergy

Negative OFC: Reintroduce food into diet

Improvement: Consider food allergy

Positive OFC (with an immediate or delayed skin reaction): Confirms food allergy. Institute an elimination diet, organize follow-up visits.

Standardized OFC
Editorial

Elimination Diets in Eczema—A Cautionary Tale

Michael C. Young, MD  Boston, Mass

• Retrospective chart review of 298 AD patients at Lurie Children’s referred for evaluation of FA
• 19% with likely food-triggered AD & no history of immediate reaction developed new IgE-mediated FA after an average of 1 year of observation
• 24 of 31 (77%) of new reactions were to foods being avoided
• 30% of these reactions were anaphylaxis
• Retrospective review of 442 at Riley Children’s: 13% “conversion” from trigger food to failed OFC
• Similar findings from case series in Dallas, Netherlands, Israel, elsewhere

Chang et al JACI: In Pract 2016
Eapen et al Annals 2019
Which of the following statements is true regarding the evaluation of AD patients who present with FA concerns?

A. Specific IgE levels are clinically meaningless when the total IgE is high
B. It is appropriate to test patients whose AD management regimen is sub-optimal
C. Most AD patients who are sensitized to foods but have no history of clinical reaction will pass an OFC to the food, even with elevated sIgE
D. The prevalence of IgE-mediated FA is the same in AD and non-AD populations
Maternal Diet in 2019 AAP Report

• Summary: Lack of evidence to support maternal dietary restriction during pregnancy or lactation
• No change from prior report
• Since last report, considered 1 new meta-analysis and 2 new systematic reviews
  – One systematic review noted diet rich in fruits, vegetables, fish, and foods rich in Vitamin D and “Mediterranean dietary patterns” were associated with lower risk of allergic disease.
## Effect of Breastfeeding on Allergic Outcomes

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<th>Conclusion</th>
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Greer et al Pediatrics 2019
## Conclusion

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**Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. Cochrane Database Syst Rev. 2012(8):CD003517**


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Greer et al Pediatrics 2019
Which of the following statements is true regarding infant feeding and food allergy development?

A. Maternally ingested food allergens do not pass into breastmilk
B. Exclusive breastfeeding in infancy helps with eczema but does not affect FA development
C. Mothers should be encouraged to strictly avoid peanut consumption during pregnancy and lactation
D. All infants with eczema should be tested for peanut allergy prior to introduction
Putting It All Together
Pretest probability case #1:
A clear peanut allergy diagnosis

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<td>Child recently had 2 episodes of anaphylaxis to isolated ingestion of peanut</td>
<td>Almost obvious peanut allergy, 98% by history</td>
<td>PST 4 mm, LR ~2</td>
<td>Posttest probability &gt; 99%, confirms allergy</td>
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<tr>
<td>B</td>
<td>Child has no medical illnesses, but never ate peanut and sibling has peanut allergy</td>
<td>Epidemiologic risk is 7%</td>
<td>PN-IgE 2 kU/L, LR~3</td>
<td>Posttest probability 25%, consider another test, such as OFC</td>
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<td>C</td>
<td>Child with milk allergy and atopic dermatitis has not eaten peanut</td>
<td>Epidemiologic risk ~30%</td>
<td>PN-IgE 35 kU/L, LR ~ 30</td>
<td>Likely allergy (95%)</td>
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<tr>
<td>D</td>
<td>Child with allergic rhinitis ate peanut but stopped 2 months ago after a blood test was performed</td>
<td>Chance of becoming allergic since test was performed, &lt; 1%</td>
<td>PN-IgE 15 kU/L, LR~8</td>
<td>Unlikely to be allergic (~2%), could perform OFC</td>
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Pretest probability case #2: Sensitized (Low IgE), never eaten: needs OFC

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Pretest probability case #3: Sensitized (High IgE), never eaten, +risk: likely allergic

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Pretest probability case #4: Sensitized but clinically tolerant: OFC ASAP!

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Summary

1. If an IgE-mediated food allergy is suspected, take a thorough history to establish pre-test probability
   – If the child can eat the food, there is no need to do a test
   – If the child has never eaten the food, there is also no need to do a test *possible exception: hi-risk infant
   – If the child has not eaten the food since the episode, and allergy is suspected:
     – Perform skin tests &/or ImmunoCAP to only specific foods in question
       • “Positive:” Indicates presence of IgE antibody (sensitization), not necessarily clinical reactivity
       • “Negative:” Generally useful but reactive patients with negative tests (even to Ara h 2) have been reported – importance of history
   – Oral food challenge as indicated: have low threshold to offer in AD patients even if IgE high

2. Resist the urge to test to many foods either on skin or in serum: not recommended

3. In AD patients, optimize skin care before testing (per AD yardstick); then consider only milk/egg/peanut/wheat; Components might be helpful if sIgE ↑↑
   – rely on serial 2/4-wk elimination/re-challenge method. Be sure to put foods back in!

4. The ones that come in with long list of foods (“he/she is allergic to EVERYTHING”): these are the ones we can really help the most!!
Thank You - Q&A / Discussion

bpvicke@emory.edu

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