Allergy and Infection: What’s the Deal? What’s Real?
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DISCLOSURES

Lawrence F. Eichenfield, MD

• Anacor/Pfizer
• Genentech
• Lilly
• Regeneron/Sanofi;
• Medimetriks
• Otsuka
• Galderma Laboratories
• Novan
• Valeant Pharmaceuticals

Discussion is based on evidence-based recommendations and published or scientifically vetted, well designed studies

None relevant to this talk
Guidelines of care for the management of atopic dermatitis

Section 1. Diagnosis and assessment of atopic dermatitis

Work Group: Co-chair, Lawrence F. Eichenfield, MD, a Wynnis L. Tom, MD, a Sarah L. Chamlin, MD, MSCI, b
Steven R. Feldman, MD, PhD, c Jon M. Hanifin, MD, d Eric L. Simpson, MD, d Timothy G. Berger, MD, e
James N. Bergman, MD, f David E. Cohen, MD, g Kevin D. Cooper, MD, h Kelly M. Cordoro, MD, c
Dawn M. Davis, MD, i Alfons Krol, MD, d David J. Margolis, MD, PhD, j Amy S. Paller, MS, MD, k
Kathryn Schwarzenberger, MD, l Robert A. Silverman, MD, m Hywel C. Williams, PhD, n Craig A. Elmets, MD, o
Julie Block, BA, p Christopher G. Harrod, MS, q Wendy Smith Begolka, MBS, q and
Co-chair, Robert Sidbury, MD r

Section 2. Management and treatment of atopic dermatitis with topical therapies

Work Group: Lawrence F. Eichenfield, MD (Co-chair), a,b Wynnis L. Tom, MD, a,b Timothy G. Berger, MD, c
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Guidelines of care for the management of atopic dermatitis

Section 3. Management and treatment with phototherapy and systemic agents

Robert Sidbury, MD (Co-chair), Dawn M. Davis, MD, David E. Cohen, MD, Kelly M. Cordoro, MD, Timothy G. Berger, MD, James N. Bergman, MD, Sarah L. Chamlin, MD, MSCI, Kevin D. Cooper, MD, Steven R. Feldman, MD, PhD, Jon M. Hanifin, MD, Alfons Krol, MD, David J. Margolis, MD, PhD, Amy S. Paller, MD, Kathryn Schwarzenberger, MD, Robert A. Silverman, MD, Eric L. Simpson, MD, Wynnis L. Tom, MD, Hywel C. Williams, DSc, Craig A. Elmets, MD, Julie Block, BA, Christopher G. Harrod, MS, Wendy Smith Begolka, MBS, and Lawrence F. Eichenfield, MD (Co-chair)

Food Allergy: Definitions

- Food allergy food ≠ intolerance
- *Food allergy* is defined as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food

**Food allergens**: specific components of food or ingredients within food (typically proteins, but sometimes also chemical haptens) that are recognized by allergen-specific immune cells and elicit specific immunologic reactions, resulting in characteristic symptoms.

Food allergy: Conditions

Cutaneous reactions to foods --

• Acute urticaria
  – Angioedema
  – Increase in atopic dermatitis (AD) symptoms
  – Allergic contact dermatitis
  – Contact urticaria
  – Respiratory manifestations
  – Heiner syndrome
Food allergy: Conditions

• Food-induced anaphylaxis

• GI food allergies and specific syndromes
  – Immediate GI hypersensitivity
  – Eosinophilic esophagitis (EoE)
  – Eosinophilic gastroenteritis
  – Food protein-induced allergic proctocolitis (AP)
  – Food protein-induced enterocolitis syndrome (FPIES)
  – Oral allergy syndrome (OAS)
• Family history and AD are risk factors for sensitization and food allergy
• Medical history and Physical Exam are important in diagnosis of food allergy

Individuals can develop **allergic sensitization** (as evidenced by the presence of allergen-specific IgE [sIgE]) to food allergens without having clinical symptoms on exposure to those foods.

*Sensitization alone is not sufficient to define FA*

# Diagnostic Tests: Sensitivity

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<tr>
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<th>Pos</th>
<th>Neg</th>
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<tr>
<td>Pos</td>
<td>a</td>
<td>b</td>
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<tr>
<td>Neg</td>
<td>c</td>
<td>d</td>
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**Reference “Gold Standard”**

**Study Test**

Sensitivity = Proportion of patients with the condition that the test identifies: $\frac{a}{a+c}$
### Diagnostic Tests: Specificity

**Specificity** = Proportion of patients **without** the condition that the test correctly identifies:

\[
\text{Specificity} = \frac{d}{b+d}
\]

<table>
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<td><strong>REFERENCE “GOLD STANDARD”</strong></td>
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\[
\text{Specificity} = \frac{d}{b+d}
\]
### Positive Predictive Value

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<tr>
<td><strong>Pos</strong></td>
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<td>a+b</td>
</tr>
<tr>
<td><strong>Neg</strong></td>
<td>c</td>
<td>d</td>
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</table>

Proportion of those with positive tests who actually have the condition \[ \frac{a}{a+b} \]
Challenges in food allergy Testing:
Skin Prick or sIgE (RAST):

Example: Cow’s Milk Allergy
Mehl et al. 2006:
• Assessed 437 children
• 169 tested positive for milk allergy with DBPCFC

SPT: sensitivity of 0.85
specificity of 0.75
Milk Allergy Testing in a General Population

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Estimated prevalence of 5%
## Milk Allergy Testing in a General Population

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Sens. = 0.8   Spec. = 0.75
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<td>Pos</td>
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<td>Neg</td>
<td>8</td>
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Sens. = 0.8   Spec. = 0.75  
PPV = 42/280 = 15%

238 of 1000 tested will have false + tests
Two year old with eczema had specific IgE Ab testing performed at the parent’s request. It’s POSITIVE (mid-high) for MILK. What is your estimate of the positive predictive value?

A. 85%+
B. 50-65%
C. 35%
D. 15-20%
E. 0%

So…only 15% of the time!
Similar values for other foods
Is IgE testing predictive of future allergy?

Study of infants with AD: 3-18 mths

• Pimecrolimus vs. Vehicle, TCS rescue trial)
• 36 mth trial; up to 33 mth open label phase
• sIgE: Baseline, End DB, end OL phase
• 15.9% had at least 1 food allergy
  – Peanut 6.6%; Cow’s milk 4.3%; Egg white 39%

• Positive tests had poor predictive value!

  Spergel JM et al. Pediatrics 2015(Dec)136:e1530-8
Atopic Dermatitis in Children With Other Atopic Diseases

Children With Atopic Disease During the Prior Year, %

- No atopic dermatitis
- Atopic dermatitis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Atopic Dermatitis</th>
<th>Asthma</th>
<th>Hay fever</th>
<th>Food allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>7.9</td>
<td>19.8</td>
<td>34.4</td>
<td>15.1</td>
</tr>
<tr>
<td>Hay fever</td>
<td>14.3</td>
<td>34.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food allergy</td>
<td>3.6</td>
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Patients with severe AD were more likely to have asthma, severe allergic rhinitis, and/or food allergies.

How common is food allergy in children with AD?

Older figures: 30-50%

Mild to moderate AD: ABOUT 15-16%

Spergel JM et al. Pediatrics 2015(Dec)136:e1530-8
Food Allergy Guidelines

“suggest that children less than 5 years of age with moderate to severe AD be considered for FA evaluation for milk, egg, peanut, wheat and soy, if at least one of the following is met:

- Persistent AD in spite of optimized management and topical therapy
- History of an immediate reaction after ingestion of a specific food

Food Avoidance and Getting the Foods Back!

• 125 children: 1-19 yrs (median: 4 yrs); National Jewish Medical Center

• Jan 2007- Aug 2008 evaluated for IgE-mediated food allergy Retrospective chart review

• History, prick skin tests, and serum-specific IgE test results were obtained

• Underwent oral food challenges

Food Avoidance and Getting the Foods Back!

- 100% Negative food challenges to (n=34)
  - Meat, Egg, Oat, Shellfish, Vegetables
- Positive challenges
  - 23% wheat; 20% fruit; 14%peanut; 10% egg
- 93% of food challenges overall were negative!
- Depending on the reason for avoidance, 84%-93% of the foods being avoided were returned to the diet after an oral food challenge,

Peanut Consumption: Prevents Allergy!

- Negative skin-prick test @ baseline
  - Prevalence of peanut allergy at 60 mths:
    - 13.7% in the avoidance group
    - 1.9% in the consumption group (P<0.001)
- Initially positive skin prick at baseline:
  - 35.3% avoidance group
  - 10.6% consumption group

New Food Allergy Guideline: NIAID

2017 Addendum to the 2010 guidelines for Diagnosis and Management of Food Allergy

‘Severe eczema’: defined as persistent or frequently recurring eczema with typical morphology and distribution, assessed as severe by a health care provider and requiring frequent need for prescription-strength topical corticosteroids, TCI, or other anti-inflammatory agents despite appropriate use of emollients.
New NIAID Food Allergy Guidelines

 Recommends that infants with severe eczema, egg allergy or both have introduction of age-appropriate peanut-containing food as early as 4-6 months of age to reduce the risk of peanut allergy

• Direct referral to allergy or

• Serum IgE screen (if negative, feed); if + referral to allergy
Food allergen panel testing or sIgE for other than peanut: not recommended
Mild to Moderate Eczema

• Introduce peanut-containing food as early as 4-6 months of age

• ...in accordance with family preferences and cultural practices, to reduce the risk of peanut allergy.

• Peanut should not be the initial solid food

• Peanut introduced at home without an in-office evaluation.

• However, the EP recognizes that some caregivers and health care providers may desire an in-office evaluation
Infants without eczema or food allergy

• Age-appropriate peanut-containing foods freely introduced in the diet, together with other solid foods, and in accordance with family preferences and cultural practices.
Patch Testing in Atopics

• Considered with persistent/recalcitrant disease and/or a history or physical examination findings consistent with allergic contact dermatitis

Sidbury R et al. Part 4, JAAD 2014;71:1218-33
Contact Allergy in the Guidelines: Diagnosis and Assessment

Allergic contact dermatitis:

• alternative diagnosis

• and/or exacerbator

Eichenfield LF et al, Part 1, JAAD, 2014;70:338-51
When are oral antibiotics advised for AD?

A. Only when iv forms are used for systemic infection
B. When topical bleach baths have failed
C. When there is skin oozing in inflamed areas
D. When there is clinical impetigo or pustules
E. They are contraindicated due to concerns about bacterial resistance
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Clinical Infection

- Impetiginized AD
- Pustules
- Abcesses
- Rare: Cellulitis, sepsis, osteomyelitis, others
- Colonization, without infection
Topical antimicrobials: Guidelines and ? Beyond

• Except for bleach baths with intranasal mupirocin, no topical antistaph treatment has been shown to be clinically helpful: NOT routinely recommended

• Moderate to severe AD and signs of bacterial infection: bleach baths and i.n. mupirocin may be recommended