Skin Test Workshop

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Disclosures

• None
Objectives

• Discuss selection of appropriate skin test devices
• Demonstrate correct skin prick test technique
• Discuss appropriate interpretation of skin prick tests
Why Test For Specific IgE? 
Isn’t the Clinical History Good Enough?

- History alone is insufficient to diagnose specific allergen sensitivity
- Allergy tests help direct and optimize management
  - If non-atopic: results will allow you to focus on other etiologies
  - If atopic: will provide guidance for appropriate treatment
- Inappropriate treatment recommendations may result if allergen sensitivity is based on history alone
- This may cause unnecessary environmental controls and patient costs or failure to implement appropriate environmental controls
When Should Allergy Diagnostic Tests be Performed?

Allergy diagnostic tests should be used in clinical practice to:

• Assist in confirming or excluding IgE sensitization in support of a clinical history based diagnosis of stinging insect hypersensitivity, drug allergy, food allergy or aeroallergen allergy

• Determine the need for environmental control recommendations to reduce exposure to outdoor or indoor aeroallergens

• Demonstrate sensitization to inhalant occupational allergens, which may cause occupational asthma or rhinitis

• Guide the selection of aeroallergens for inclusion in allergen immunotherapy extracts
The Importance of “Prior Probability”

The test result to egg is moderately positive and in various studies indicates a 50% risk of reaction

- HISTORY #1: Patient eats egg and test was done to evaluate hyperactivity → prior probability was zero, conclusion → not allergic (no reason to test)
- HISTORY #2: Patient reacted to egg ingestion with hives and wheezing 3 weeks ago and 6 months ago → prior probability was extremely high, test is now “diagnostic” → Avoid egg
- HISTORY #3: Patient has recalcitrant atopic dermatitis → prior probability and test moderate → elimination diet/oral food challenge to secure a diagnosis
Diagnostic Algorithm for the Assessment of Human Allergic Disease

Clinical History & Physical Examination

- Are there symptoms with exposure?
  - Yes
    - Perform Diagnostic test for Specific IgE (skin test/In-vitro test)
      - Positive Test?
        - Yes
          - IgE-mediated Reaction Confirmed
            - No
          - Non IgE-mediated Reaction
            - No
          - Consider provocation challenge
            - Yes
            - Not allergic to that exposure
  - No
    - Not allergic to that exposure
  - Uncertain
    - Perform Diagnostic test for Specific IgE (skin test/In-vitro test)
      - Positive Test?
        - Yes
          - IgE-mediated Reaction Confirmed
            - No
          - Non IgE-mediated Reaction
            - No
Foods - When to Test/What to Test

IgE associated clinical disorder?

Yes

No

Alternative tests/advice

Determination of potential triggers
- Requires careful history, consideration of epidemiology, pathophysiology
- Foods tolerated (should not be tested)
- Foods not often ingested, more likely triggers
- Foods commonly associated with severe reactions:
  - Peanut, nuts from trees, fish, shellfish, seeds
  - Common allergens for children with moderate-severe atopic dermatitis:
    - Egg, milk, wheat, soy

Selection of serological or skin tests
- select tests to confirm/exclude suspicions
- avoid “panels” of food allergens
- avoid testing tolerated foods
Additional Pearls for Food Testing

- Egg white is the major egg allergen (typically no need to test yolk, whole egg)
- Cow milk is a good test for cow milk allergy, no advantage to test milk proteins (alpha lactalbumin) or foods (cheese)
- There are no reliable tests for IgE antibody to additives/colors
- Clinical cross reactivity rates are often lower than test results would indicate (e.g., a peanut allergic individual often [>50%] tests positive to multiple legumes but reaction rates are ~5%)
- Persons with pollen allergies may test positive to numerous fruits/vegetables that may induce no or mild (oral) symptoms, but only rarely severe reactions
- Fresh extracts are very helpful for certain allergens (ex. Fresh fruits and vegetables)
Allergy Skin Testing

- Skin testing remains the central test to confirm allergic sensitivity when it can be performed \(^1\)
- Skin testing is fast (15-30 minutes), safe, sensitive and a minimally invasive procedure which can be cost effective
- When performed correctly, skin testing is reproducible
- Skin testing has demonstrated good correlation with results of nasal challenge\(^2\) and bronchial challenges \(^3\)
- Results of skin test should always be used as an adjunct to the clinical history and physical examination when making the diagnosis of allergic disease

1. Oppenheimer et al, Ann Allergy 2006;S1:6-12
Skin Testing Results Correlate with Nasal Challenge Results

Relationship between grass-pollen nasal challenges with and skin prick test end-points in patients allergic to grass: skin test reactivity correlated with sensitivity during allergen challenge.

Bousquet et al, Clin Allergy 1987;17:529-38
Food-specific IgE Antibody Concentrations or Skin Test Size Correlate with Risk of Clinical Reactivity

Curve varies by:
- Food
- Disease
- Age
- Assay (brand)

At certain high IgE values, the chance of a clinical reaction approaches certainty.

One study, one test brand, children age 5: Egg - 7 kIU/L, Milk 15 kIU/L, Peanut 14 kIU/L

Negative test is not zero risk

Clinical Sensitivity & Specificity of Skin Tests

- Prick skin tests may be positive in individuals who are without respiratory symptoms:
  - 42% with a positive family history for asthma or rhinitis may have + SPT and no disease
  - 29% of those with a negative family history for asthma or rhinitis may have +SPT
- Always use caution when interpreting skin tests; skin tests are a confirmatory diagnostic tool reflecting sensitization and do not make the diagnosis of clinical allergy, which is based on:
  - Diagnosis of clinical allergy = history and confirmatory allergy diagnostic tests.

Sensitivity and Specificity - Foods

- Sensitivity is >90%
- Specificity is approx. 50%
- These values use oral challenge as the standard for food allergens

Food Allergy: A Practice Parameter, Chapman, et al, March 2006
Sensitivity and Specificity - Inhalants

• Sensitivity is 85%-87%
• Specificity is 79%-86%
• These values use nasal provocation challenge as the standard for inhalant allergens

Allergy Skin Tests: General Rules

• The technician performing the skin tests and the clinician ordering and interpreting skin tests must understand the characteristics of the tests they are administering.

• These include:
  • type of skin testing (intradermal vs percutaneous)
  • device used (single vs multiple puncture)
  • placement of tests (location and adjacent testing)
  • the quality and potency of the extracts being used
  • potential confounder of medications that may suppress skin test response.
Skin Testing Mechanics

• Test is applied and read in 15-20 minutes
• Wheal and flare should be measured in millimeters
• No standard on mean wheal diameter \((D+d/2)\) or longest diameter
• Positive result is considered wheal 3mm larger than the negative control

Appropriate Prick Technique

• Prick at a 45-60° angle to the skin
• The skin should be gently lifted creating a small break in the epidermis
Appropriate Puncture Technique

- Puncture at a 90° angle to the skin
- The device should have a shoulder to prevent penetration too deep into the dermis

Skin Test Devices

• Numerous studies have directly compared the performance of the multiple percutaneous devices.

• Percutaneous skin test devices vary in the degree of trauma they impart to the skin. Therefore they differ in the size of positive reactions and in the likelihood of inducing a false positive reaction at the site of the negative control.

• Different devices require different criteria for what constitutes a positive reaction.
**Comparisons of Four Different Skin Prick Test Devices in Allergic and Non-Allergic Subjects**

Timothy Campbell, MD; Kathy Caruso, RN; Susan Golubski, LPN; Stephanie Slattery, RN; Sarah Worley, MS;

Alton Melton, Jr., MD The Respiratory Institute
Cleveland Clinic, Cleveland, OH

**Introduction**

- Skin prick testing (SPT) remains the most cost effective, sensitive and efficient way to screen patients for allergies to Aeroallergens and foods.
  - A liquid allergen is introduced to the skin of the patient with the use of a SPT device.
  - Several different devices are currently utilized for epicutaneous allergy SPT and results can be quite variable between patients and devices.
  - When choosing a device, many considerations must be made including cost, ease of use, reproducibility and rate of false positive and false negative reactions.
  - Correlation of results with different SPT devices would be useful when comparing SPTs utilizing different devices.

**Methods**

- A randomized, prospective study on 64 atopic and 36 non-atopic volunteer subjects off antihistamines for at least 48 hours was performed.
  - Subjects provided informed consent and self-reported whether they exhibited allergic symptoms.
  - Three allergy nurses were trained on each of the four SPT devices and performed all testing which was interpreted by a single physician.
  - Each subject underwent epicutaneous testing in duplicate using 4 different devices
    - Quintest® (Bayer Corporation, Spokane, Washington)
    - Bifurcated Needle (Allergy Laboratories of Ohio, Columbus, Ohio)
    - DermaPIK® (Greer Laboratories, Lenoir, North Carolina)
    - Duotip® (Lincoln Diagnostics, Decatur, Illinois)
  - Each subject was tested to three allergens (Dermatophagoides farinae 30,000 Au/ml, Timothy Grass 1:20, short ragweed 1:20) and two control substances, albumin saline negative control and histamine (6 mg/ml) positive control.
  - Testing sites were randomized to one of four quadrants on the back.
  - Epicutaneous reactions were measured after 15 minutes using crossed-wheel and flare diameter in millimeters.
  - Responses in which wheal diameter <3mm to histamine control were considered false negative and wheal diameter reactions ≥3mm to saline control were considered false positive.
  - Immediately after SPT, subjects rated preference for skin testing method with one being most preferred and four being least preferred method.

**Results**

**Patient Preference for SPT Device**

<table>
<thead>
<tr>
<th></th>
<th>Most Preferred (%)</th>
<th>Least Preferred (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bifurcated Needle</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>DermaPIK®</td>
<td>29</td>
<td>21</td>
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<tr>
<td>Duotip®</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>Quintest®</td>
<td>16</td>
<td>23</td>
</tr>
</tbody>
</table>

**Discussion**

- Mean wheal diameters showed significant differences between devices, especially with positive and negative controls.
  - False positive saline control reactions were higher for the Duotip and DermaPIK® SPTs indicating that these may be more traumatic testing methods compared to Quintest and bifurcated needle.
  - Frequency of false positive saline reactions between skin test technicians varied suggesting that individual SPT techniques may affect results. Back position did not affect false positive/negative rate.
  - Quintest and bifurcated needle were the most preferred testing modalities, while Duotip was the least preferred.
  - There was no significant difference between correlation and agreement data after correcting for the saline-adjusted wheal diameters.
  - Correlation and agreement for histamine and saline responses between different SPTs was particularly poor.
  - Very high correlation coefficients would be necessary to generate an equation to compare results of different SPT devices. The correlation coefficients achieved in this study averaged 0.90, equivalent to an R-squared of 0.81, which was not sufficient to allow accurate predictions when making comparisons between SPT devices.

**Conclusion**

- There exist significant differences between SPT devices regarding positive and negative control reactions and false positives and false negative rates.
  - Attempts to find a strong correlation between the SPT device data were unsuccessful.
  - Skin test technicians should be trained with the specific device used to establish consistent positive and negative criteria.
  - Test device differences must be considered when comparing results from different SPT methods.

**References**

Recording Skin Test Response

- A record of skin testing should indicate a minimum amount of information that will allow another physician to interpret the results, avoiding the need to repeat skin testing.

- This should include:
  - the concentration of extract employed - consider including manufacturer
  - method of testing - ID or PST including device
  - location of where testing was performed
  - size of the positive and negative control reactions - preferably actual measurement or tracings, but if a score is used include the grading system
Allergy Skin Testing

As a members-only benefit, the forms can be edited and customized for individual practices. Be sure to click on the version with the.

- Allergy Skin Test Documentation Guidelines
- Allergy Skin Test Documentation Guidelines
- Allergy Skin Test Report Form
- Allergy Skin Test Report Form
- Allergy Skin Test Report Form - Completed Example
- Allergy Skin Test Report Form - Completed Example
- Patient Skin Test Instruction and Consent Form
- Patient Skin Test Instruction and Consent Form

The Allergy Skin Test Report Form is based on the AAAAI’s Guidelines for Reporting Immediate Skin Test Results.

By accepting the Terms of Use on preceding pages, you agree that these forms are being provided for educational and informational purposes only and are not intended to be a substitute for your independent medical judgment. The AAAAI is not liable for any decision made, or action taken by you or anyone else, in reliance upon the information contained within these forms.
Variables That Affect Skin Test Results

Controllable
- Medications:
  - H1 Antihistamines
  - H2 Antihistamines
  - Antidepressants
  - Corticosteroids
- Immunotherapy
- Relation to adjacent positive reactions
- Extract quality
- Skin testing devices

Uncontrollable
- Chronobiology:
  - Diurnal
  - Seasonal
  - Menstrual Cycle
  - Age:
    - Specific IgE
    - Histamine Reactivity
- Location on Body:
  - Variations on Back
  - Back vs. Forearm
# Allergen-Specific IgE

**In vitro (lab) and In-Vivo (skin tests)**

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<tr>
<th></th>
<th>In-vitro</th>
<th>In-vivo</th>
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<tbody>
<tr>
<td>IgE Antibody Serology</td>
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<td></td>
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<tr>
<td>High sensitivity*</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>High specificity*</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>High reproducibility</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Quantitative results in kIU/L^</td>
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<td>No</td>
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<tr>
<td>WHO Standard calibrated</td>
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<tr>
<td>Quality assurance test program</td>
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<tr>
<td>Can be used independently of pharmaceutical treatment</td>
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<td>No</td>
</tr>
<tr>
<td>Can be used independently of patient skin status</td>
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<td>No</td>
</tr>
<tr>
<td>Time factor</td>
<td>1-7 days</td>
<td>15-30 minutes</td>
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<tr>
<td>Cost factor</td>
<td>more expensive</td>
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</tr>
<tr>
<td>Usefulness in motivating patients</td>
<td>obscure</td>
<td>dramatic</td>
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</tbody>
</table>

*Results may vary between specific bioassays
^Although all are expressed with same units, cannot compare results between different bioassays
### Allergen Concentration: Extract Manufacturer *

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Concentration</th>
<th>Extract Manufacturer</th>
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<tr>
<td></td>
<td></td>
<td>Alternaria Termitis (HS 1:10)</td>
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<td></td>
<td></td>
<td>Fusarium moniliforme (GR 1:10)</td>
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<tr>
<td></td>
<td></td>
<td>Aspergillus fumigatus (HS 1:10)</td>
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<td></td>
<td></td>
<td>Penicillium chrysogenum (GR 1:10)</td>
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<td></td>
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<td>Hormodendrum cladosporioides (HS 1:10)</td>
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<td></td>
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<td>Whole Chicken Egg (GR 1:10)</td>
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<td>Cows Milk (HS 1:20)</td>
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<td>Black Walnut (GR 1:20)</td>
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<td></td>
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<td>Pecan (GR 1:20)</td>
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<td></td>
<td></td>
<td>GS Fish Mix (GR 1:20)</td>
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<td></td>
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<td>GS Shellfish Mix (GR 1:20)</td>
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<tr>
<td></td>
<td></td>
<td>Cow's (GR 1:40)</td>
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<tr>
<td></td>
<td></td>
<td>Latex Glove Extract (Created in offices)</td>
</tr>
</tbody>
</table>

### Comments:
- Grass Mix = Kentucky Bluegrass, Orchard, Redtop, Timothy, Sweet Vernal, Meadow Fescue, Perennial Rye
- Fish Mix = Codfish, Pionder, Halibut, Macareted, Tuna
- Shellfish Mix = Clam, Crab, Oyster, Scallops, Shrimp
### General Information about Skin Test Protocol

1. **Percutaneous Location**: back
2. **Device**: Single Use Greer Pick
3. **Intradermal**: 0.05ml injected
4. **Location**: Left / Right arm
5. **Extracts**: All extracts are 1000 PNU by Hollister-Stier unless otherwise indicated.
6. **Results**: Longest diameter of wheal (W) and erythema (F) measured in millimeters at 15 minutes.

### Allergen Concentrations

<table>
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<th>Allergen</th>
<th>Concentration</th>
<th>Control (Extraction)</th>
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</thead>
<tbody>
<tr>
<td>Mine Ferrite (GR 10,000 BU)</td>
<td>3 1/2</td>
<td>A</td>
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<tr>
<td>Mine Ferrite (HS 15,000 BU)</td>
<td>4 1/2</td>
<td>B</td>
</tr>
<tr>
<td>Cashew AP (HS 10,000 BAU)</td>
<td>10 2/0</td>
<td>C</td>
</tr>
<tr>
<td>Dog Hair-Dander AP (HS 1/50)</td>
<td>5 2/5</td>
<td>D</td>
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</tbody>
</table>

### Controls

- Negative: HSA w/ Phenol (G)
- Positive: Histamine non-med. base (FS)

### Comments

- Grass Mix: Kentucky Bluegrass, Orchard, Redtop, Timothy, Sweet Vernal, Meadow Fescue, Perennial Rye
- Fish Mix: Codfish, Flounder, Halibut, Flounder, Tuna
- Shellfish Mix: Clam, Crab, Oyster, Scallops, Shrimp
The Allergy & Asthma Center, P.C.

900 N. Orange Suite 207
Missoula, MT 59802
(406)-721-4540
fax (406)-721-1838

Patient name: [name redacted]
Date of Test: 3-27-13
Testing Technician: KBailey

Last use of antihistamine (other med affecting response to histamine): 7 days medication

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   * Extract manufacturer abbreviations: O=Greer, AL=Alergy Labs, K=ALK Abell, HS=Hollister-Stier, AG=Antigen, AM=Allermed

<table>
<thead>
<tr>
<th>Allergens</th>
<th>Concentration</th>
<th>Exctract Manufacturer*</th>
<th>W (mm)</th>
<th>W (mm)</th>
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<tbody>
<tr>
<td>Mine-Ferrite (GR 10,000 AL)</td>
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<td>Mite-Poreovoximus (HS 10,000 AL)</td>
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<td>Cat Hair AF (HS 10,000 BAU)</td>
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<td>Horse Hair-Dander AP (HS 1-50)</td>
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<td>Cow Epithelium (GR 1-20)</td>
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<td>Rabbit Epithelium (GR 1-20)</td>
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<td>GS Feather Epithelium (GR 1-10)</td>
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<td>Sed Grass Mix (HS 100,000 BAU)</td>
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<tr>
<td>Mosquito (AG 1-20)</td>
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</tbody>
</table>

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<tbody>
<tr>
<td>Crab (GR 1-20)</td>
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<td>Maine Lobster (GR 1-20)</td>
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<td>Salmon (GR 1-20)</td>
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<td>Shrimp (GR 1-20)</td>
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<td>Beef (GR 1-20)</td>
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<td>Chicken (GR 1-20)</td>
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<td>Turkey (GR 1-20)</td>
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<tr>
<td>Pork (GR 1-20)</td>
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<td>Chocolate (GR 1-20)</td>
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<td>Sunflower Seed (AL 1-20)</td>
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<td>Almond (GR 1-20)</td>
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<td>Cashew (GR 1-20)</td>
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<td>Pecan (GR 1-20)</td>
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<td>Filbert (HA) (GR 1-20)</td>
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<td>Bakers Yeast (GR 1-20)</td>
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<td>Whole Grain Rice (GR 1-20)</td>
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Comments: Grass Mix = Kentucky Bluegrass, Orchard, Redtop, Timothy, Sweet Vernal, Meadow Fescue, Perennial Rye
          Fish Mix = Codfish, Flounder, Halibut, Mackerel, Tuna
          Shellfish Mix = Clam, Crab, Oyster, Scallops, Shrimp
Pearls and Pitfalls of Allergy Diagnostic Testing Summary

- Allergy skin testing and specific IgE serology are effective tests for confirming sensitization in:
  - Eczema, urticaria, angioedema
  - Food allergy, eosinophilic gastroesophagitis
  - Rhinitis, otitis, conjunctivitis, sinusitis
  - Asthma, cough, dyspnea
  - Insect sting allergy
  - Drug allergy (some i.e.. Beta-lactams and local anaesthetics)
  - Occupational allergy (some)
  - Anaphylaxis
Conclusion

Selection of allergy diagnostic tests and interpretation of specific IgE antibody results MUST be directed, guided, and viewed within the context of the patient’s clinical history.