Allergy Testing – Test Request and Result Interpretation

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Learning Objectives

By the end of this presentation you will:

• Know which test to request for allergy testing and the process

• Be confident with your interpretation of allergy test results
Allergy Testing Challenges in Alberta

- Increased prevalence of atopic disorders and shortage of allergy specialists
  - Difficult to diagnose and treat
  - Primary care, self diagnosis and treatment
- Processes, procedures, and policies for allergy testing outdated and not in-line with new/updated guidelines
- Inappropriate test use and variation in clinical practice
- Suboptimal performance of some allergy tests
- Significant impact on patients
- Financial burden to the healthcare system

<table>
<thead>
<tr>
<th>Send Out Test Audit for Allergen Specific IgE</th>
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<tbody>
<tr>
<td><img src="image" alt="Table" /></td>
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<table>
<thead>
<tr>
<th></th>
<th>Number of tests</th>
<th>% Number of Tests</th>
<th>% Negative Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>319</td>
<td>100%</td>
<td>72%</td>
</tr>
<tr>
<td>Allergist Clinical Immunologist</td>
<td>94</td>
<td>29%</td>
<td>46%</td>
</tr>
<tr>
<td>Other</td>
<td>225</td>
<td>71%</td>
<td>83%</td>
</tr>
</tbody>
</table>
Classification of Adverse Reactions to Food

ADVERSE FOOD REACTION

- Toxic
- Non-Toxic

Food Allergy (Immune)
- IgE
- Mixed
- Non IgE-mediated

Food Intolerance (Non-Immune)
- Pharmacological
- Metabolic
- Psychological
- Idiosyncratic

Food allergy, allergic rhinitis
Oral allergy syndrome
Anaphylaxis
Eosinophilic esophagitis
Atopic dermatitis
Celiac disease

Most Common Food Allergies

- 8 foods are responsible for 90% of all food allergies

Infants and Young Children (6-8%)
- Cow’s Milk
- Egg White
- Peanut (legume)
- Tree Nuts
- Wheat
- Soy (legume)

Teens and Adults (2-4%)
- Shellfish - Mollusca - Crustacea
- Peanut
- Tree Nuts
- Fish

Food Reactions:
- Food Allergy 10%
- Food Intolerance 15%
Natural History of Allergies

**Atopic March** *(World Allergy Organization)*

**Co-existing IgE diseases:** food allergy, atopic dermatitis, eosinophilic esophagitis, allergic rhinitis, asthma

Children often outgrow food allergies (develop **tolerance**) to milk, egg, soy and wheat. Food allergies to peanuts, tree nuts, shellfish and fish often persist.

Immunotherapy may alter the natural history of allergic rhinitis

Avoidance of triggers and medications help manage persistent food allergies and asthma

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**Diagnosis of IgE Mediated Allergy**

- Medical history and physical examination
  - Identify causative allergen
  - Multiple symptoms occur within minutes to hours, anaphylaxis
  - Co-existing atopic disorder
  - Guides diagnostic test selection
- Test identifies causative allergen (**sensitization**, IgE-mediated)
  - skin prick test (SPT), rarely intradermal test
  - serum allergen specific IgE antibody (sIgE)
  - SPT or sIgE alone are not diagnostic
- Confirmatory diagnostic tests
  - spirometry (asthma)
  - oral food challenge (food allergy)
  - elimination diet, skin or GI biopsy, histology (mixed or non-IgE)

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*National Institute of Allergy and Infectious Disease Guidelines for Food Allergy Diagnosis 2010, CSACI Position Statement on Food-Specific IgG*
Serum Allergen Specific IgE (sIgE)

1972 RadioAllergoSorbent Test (RAST)
   - term used incorrectly, abandon
1980's Automated fluoroenzyme immunoassays

• Indirect measurement of circulating IgE antibodies to specific allergens, more specific than total IgE
• Edmonton (DL) and Calgary (CLS) use the same platform and numeric cut-off

Test Menu, Performance and Cost

• Multi-allergen sIgE screens (qualitative, $17.16 per screen)
  – Inhalant screen
    • Allergic symptoms but causative allergen unknown, order once
    • Good rule-out test (93% sensitivity, 89% specificity)
    • Positive screen reflexes to inhalant panel
  – Food screen (>20,000 per year) and reflex food panel discontinuation
    • Poor sensitivity and specificity (high false positive rate)
    • Broad screening for foods is not supported by guidelines

• Individual allergen sIgE (quantitative, $17.16 per allergen)
  – Inhalant, antibiotic and insect venom panels
  – Specific food, inhalant, and latex allergens
  – More sensitive and specific than multi-allergen screens
Clinical Utility of Serum Allergen Specific IgE

- Indicates sensitization to a particular allergen not clinical allergy
- Good performance for most foods, pollen, dust mite and latex
- Complimentary to skin tests for animal dander, molds, insect venoms and drugs
- Levels correlate with an increased likelihood of clinical allergy not allergic severity
- Monitor for development of tolerance
  - High initial sIgE associated with lower rate of resolution of clinical allergy
  - Monitor every 6 months to a year

Reporting/Interpretation of sIgE Results

- **Negative (<0.35kU/L)**
  - A negative allergen specific IgE antibody test should not be used alone to reject a diagnosis of allergy. It is possible for a patient to have significant allergy yet have a negative test. Results must be interpreted within the clinical context of the patient.

- **Positive**
  - Detection of IgE antibodies in the serum (sensitization) indicates a greater likelihood of clinical allergy and identifies the allergens that may be responsible for symptoms. Clinical correlation is required. Consider referral to an allergist.

- **Insufficient information provided on the requisition. Test cancelled.**
  - Guidelines recommend selection of individual allergens based on patient history.

Serum Allergen Specific IgE Testing

**Strengths**
- Available in primary care office
- One sample, many results
- Less invasive
- Quantitative, reproducible
- Antihistamines are ok
- No risk of reaction
- Patients with skin condition
- Young child or geriatric patient

**Limitations**
- Often non-allergists order test
- Test selection requires patient history
- Broad screening - expensive
- Delayed results
- Challenge interpreting results (sensitization vs. clinical allergy)
- Sensitivity/specificity varies by allergen
- Cross reactivity
Future Directions

- Family physician and pediatrician feedback on requisition
- Audit for test utilization and performance
- Provincial allergy testing working group
  - Educational materials
  - Guidelines
  - Policy
- Component resolved diagnostics
  - Allergen extract quality
  - Cross-reactivity
  - Allergic severity

Acknowledgements

- *DynaLIFE*<sub>Dx</sub>
  - Allergy testing working group

- Allergists/Clinical Immunologists/Respirologists
  - Dr. Stuart Carr, Dr. Tim Vander Leek, Dr. Per Lidman, Dr. Harissios Vliagoftis, Dr. Joel Doctor, Dr. Dilini Vethanayagam

- Medical laboratory science students
  - Ms. Agnes Tan and Ms. Raluca Maries

- Alberta Health Services and Calgary Laboratory Services
- Somagen, General Practitioners, Dieticians and Families
Clinical Utility of Serum Total IgE

- **Non-specific** and not recommended by guidelines for use as a screen or diagnostic test for atopic disorders

- Screen and diagnosis of Allergic Bronchopulmonary Aspergillosis

- Omalizumab dose for treatment of persistent severe asthma
  - Baseline serum total IgE (30-700kU/L) and patient’s body weight

- Parasite infections

- Cancer

- Immunodeficiency

### sIgE Levels & Probability of Clinical Allergy

<table>
<thead>
<tr>
<th>Allergen</th>
<th>95% Predictive level (kU/L)</th>
<th>PPV</th>
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<tbody>
<tr>
<td>Egg</td>
<td>7</td>
<td>98</td>
</tr>
<tr>
<td>Infants ≤2 y</td>
<td>2</td>
<td>95</td>
</tr>
<tr>
<td>Milk</td>
<td>15</td>
<td>95</td>
</tr>
<tr>
<td>Infants ≥2 y</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>Peanuts</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>Fish</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td>Tree nuts</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>
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### Allergen Cross Reactivity

**Table 3** Oral allergy syndrome: cross reaction between proteins in pollen and fresh fruits and vegetables [6]

<table>
<thead>
<tr>
<th>Pollen</th>
<th>Fresh fruit/vegetable/nuts</th>
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