Serum Allergy Testing

The Role of the Clinical Laboratory in Allergy Diagnosis
What is Allergy?

Allergy = Atopy
Atopy = IgE mediated allergy only

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What is Atopy?

Rhinitis
What is Allergy?

Allergy = Atopy
Atopy = IgE mediated allergy on

What is Atopy?

Urticaria (Hives)
What is Allergy?

Allergy = Atopy
Atopy = IgE mediated

What is Atopy?

Anaphylaxis
Allergy – Diagnostic Strategies

Investigation Options

- History
  - Atopy is a necessary condition for IgE mediated allergy
- Skin testing
- Serum testing
  - IgE mediated allergy only
- Provocation testing

History is the most important component

- Should not be ignored
  - Don’t accept discordant test results without careful reconsideration
Mechanism of Atopic Response
Mechanism of Atopic Response

FcE-R1
- IgE receptors on the Mast cell
- Upregulate when IgE increases
- Binding of allergen
  - brings FcE-R1 into proximity
  - Activates mast cell
    - Cytokine production
    - Arachidonic acid production
    - Degranulation
- IgG crosslinking can cause the same effect
  - a cause of chronic Idiopathic Urticaria
Skin tests

- Prick test relative to intradermal
  - Less sensitive
  - More specific
  - Food allergens
    - Intradermal has poor correlation for foods
    - Prick test is better for foods but non-specific
      - Serum testing can help here
      - Food challenge

- Less chance of anaphylactic response
  - A few case reports with skin prick
  - Deaths only observed with intradermal
  - Rare so relative risk not clear
Serum Allergy Testing

- **Allergen**
- **Substrate**
- **Allergen-specific IgE**
- **Labelled Anti-IgE**

Diagram showing the interaction between IgE, Allergen, Substrate, Label, and Labelled Anti-IgE.
Serum Allergy testing

- Avoids risk of anaphylactic response to skin test
  - Peanut
  - Hymenoptera
- More specific with hyper-responsive patients >90%
- Less sensitivity compared to prick test ~90%
- May give falsely negative results due to IgG competition for assay binding sites
  - Methodology related

- Useful when patient has poor quality skin eg dermatitis
- Patient has dermatographism
Serum Allergy testing (cont’d)

• Drug Inhibition of Allergic response?
  • Antihistamines/benzodiazepines/tricyclic antidepressants/corticosteroids do not interfere

• Very young or very old patients
What does a Negative Test result mean?

• 80 – 90% sensitivity sounds good but…
  • for an allergen in which there is a likelihood of anaphylactic response this may not be good enough
  • Serum allergy testing is less sensitive for food allergy than skin prick testing
Non specific allergic response

- Skin prick test shows reaction to everything
- History confused by potential reactivity to many allergens
- Confounders
  - poor correlation of skin prick response and clinical response
  - Cross Reactivity
- Serum testing (usually) is not affected by non-specific reactivity
What does a Positive Test result mean?

An Allergen is a mixture of substances
(sometimes hundreds of compounds)

• Any one( or more) of which may be allergenic

• Allergen chemists work to isolate the individual components
  • Allergenicity (validity) determined by clinical correlation

• The “Allergen” is then a mix of the top candidate compounds
  • Some “Allergens” are only enriched with the specific allergenic compounds
  • Some “Allergens” are not manipulated at all.
Allergen Components

• Different manufacturers may choose
  • Different compounds
  • In different relative amounts

• This contributes to the lack of correlation between
  • History
  • Skin tests
  • Serum tests
  • Different manufacturers of Serum tests
Pediatric Food Allergy

- Egg, milk, peanut ➔ 85% of cases
  - Serum testing
    - Sensitivity 70 – 90%
    - Specificity >95%

- Scenario for the potential use of Serum specific IgE
  - History
    - suggestive of allergy to food “w,x,y,z”
    - Severity +/-
  - Skin prick test (for food is not specific)
    - Skin Prick test positive for food “x”

- To food challenge or Not to food challenge?

Sampson, HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. J. Allergy Clin Immunology May, 107(5):891-6
Pediatric Food Allergy

-Serum allergy testing is specific (>95%)
- But not very sensitive (70 – 90 %)

Use serum allergy testing to identify
- Obvious **positives**
  - No food challenge necessary
- Presumed **negatives**
  - Food can be reintroduced at home with observation
- **Intermediate** cases
  - Physician supervised food challenge
- **Caveats**
  - Solid history should override “Presumed negatives”
  - Only for high prevalence allergens
    - Egg, milk, peanut - 85% of cases
  - Based on quantitative food-specific cutoffs

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Sampson, HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. J. Allergy Clin Immunology May, 107(5):891-6
Cross reactivity

Still developing knowledge about cross reactivities and their basis/mechanisms

- Skin testing and serum testing Cross Reactivity correlates well
  - Serum testing is less likely to show cross reactivity

- Clinical vs testing concordance is poor.
  - Test cross reactivity doesn’t imply clinical cross reactivity
  - Lack of test cross reactivity doesn’t preclude clinical cross reactivity

Rodriguez, Julia; Crespo, Jesus F. Current Opinion in Allergy & Clinical Immunology. 2(3):233-238, June 2002.
Cross reactivity

Can be a good thing if the question is…
- Is my patient allergic to dust mites?
- Lack of cross reactivity means more species need to be tested
  - D. farinae,
  - D. pteronyssinus
    - Has some unique allergens

Can be a bad thing if the question is one of
- Shrimp vs cockroaches

IF YOU LIKE SHRIMP

Tree Pollen Cross-Reactivities

<table>
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<th>Genus/family</th>
<th>Maples / Box elder</th>
<th>Cedar / Juniper</th>
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<tr>
<td></td>
<td>• Acer</td>
<td>• Juniperus</td>
</tr>
<tr>
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<td>Juglandaceae</td>
<td>Walnut / Hickory / Pecan</td>
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<td></td>
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<tr>
<td>Oleaceae</td>
<td>Olive / Ash / Privet / Lilac</td>
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</tr>
<tr>
<td></td>
<td>• Oleaceae</td>
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</tbody>
</table>
Pollens and foods share homologous allergens

- Sensitizations to Pollens
  - Birch, mugwort, hazelnut

- Lead to cross reactivities to Foods
  - Apple, celery, carrot

Patient may **not** be allergic to these foods if positive for any of these foods, then consider pollen allergy
Syndromes

- Latex-food
  - Banana/avocado/chestnut
Serum Allergy Panels and Screens

• Similar sensitivity to Individual Allergens
  
  • Allergen is diluted among others on the panel
  • Some allergen components may be omitted

• Reduced Specificity
  
  • Mild or non-specific responses from several allergens may add up to give a positive result.
The Future: Allergen Component Analysis

• Analysis of individual allergen component molecules
  • may improve the diagnostic accuracy of allergy testing

• ~ 80 % of patients with peanut allergy do not have peanut allergy
  • Serious impact on lifestyle

• How to sort out these cases?
  • Food challenge
    • In vitro allergy testing sensitivity ~ 60% using “Peanut Allergen”
  • Allergen component analysis
    • May provide guidance to the allergy specialist
The peanut allergen (f13)

Severity of cross reactions will depend on allergenic molecules with structural similarities often related to botanical relationship.

IgE to components Ara h 1, 2, 3 and 9 and in particular if combinations in between. Severe reactions may occur especially if high levels.

IgE to Ara h 8: mild or even no reactions.
Ara h 2: 2S albumin  
Pis v 1, Jug r 1, Brazil nut, almond, sesame

Ara h 1: vicilin  
Cor a 11 – Ana o 1 – Pis v 3 – Jug r 2

Ara h 3: 11S glycin  
Cor a 9 - Ana o 2 - Pis v 2
Peanut allergy – use of component analysis

- High risk of systemic reactions
- Probably tolerant of an oral challenge
- If any – oral allergy symptoms
- Peanut NOT the primary sensitiser

**IgE (kU/l)**

- **Peanut**: Present
- **Ara h 2**: Present
- **Ara h 1**: Present
- **Ara h 3**: Present

Scores:
- **Peanut**: 7
- **Ara h 2**: 1
- **Ara h 1**: 1
- **Ara h 3**: 1

**Notes**:
- Probably tolerant of an oral challenge
- If any – oral allergy symptoms
- Peanut NOT the primary sensitiser
Food Allergen Patterns - BC

- Halibut
- Pine Nut
- Tuna
- Cod
- Sesame
- Salmon
- Brazil Nut
- Pecan Nut
- Lobster
- Soybean
- Crab
- Seafood Mix
- Egg
- Yolk
- Food Mix
- Cashew Nut
- Nut Mix
- Walnut
- Hazelnut
- Wheat
- Almond
- Shrimp
- Egg White
- Cow's Milk
- Peanut

Positive
Negative
Pediatric Food Allergen Patterns - BC

Positive
Negative
Inhaled Allergen Pattern - BC

![Bar chart showing the distribution of inhaled allergens in BC. The x-axis represents different allergens, including Common Ragweed, Cottonwood, Alternaria tenuis, Cedar, House Dust, Yeast, A. fumigatus, Feather Mix, Alder, Birch, D. pteronysinus, D. farinae, Latex, Dog hair dander, Mould Mix, Cat hair dander, Grass Mix, and Mite Mix. The y-axis represents the count of positive and negative responses. The chart uses bars to compare the number of positive and negative responses for each allergen.](chart_url)
Serum Allergy Testing

IgE mediated allergy only
- Useful adjunct to skin testing
  - Especially for foods
- Useful alternative to skin testing
  - When skin testing is inappropriate
    - Skin condition or hyperreactivity
    - Medications which suppress skin response
    - Risk of anaphylactic response
    - Very young or old patients

- History is the most important component
- Atopy is a necessary condition for IgE mediated allergy
- Don’t accept discordant test results without careful reconsideration