Immunotherapy Workshop

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Disclosures

- Speaker's Bureau: AstraZeneca, Sanofi, Merck, GSK, Teva, Sunovion, Takeda, Allergan, Alcon, B&L, Genentech
- Consultant: Sanofi, Merck, Sunovion, Proctor & Gamble, Takeda, JDP Therapeutics, PMD Healthcare, Pfizer, Teva, Allergan, Alcon, GSK

If You Were Mixing an Immunotherapy Extract to Cover all Grass Allergens in the USA, You Should Mix:

- A. Johnson, Bermuda, and Timothy
- B. Bermuda, Timothy, and Perennial Rye
- C. Johnson, Timothy, and Red Top
- D. Bermuda, Orchard, and Perennial Rye

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Esch JACI 2008

- 3 grass pollen extracts representing the cross-reacting grass pollen groups can be used to account for essentially all of the grass allergen specificities in the United States.
  - Pooidae [meadow fescue, timothy, orchard, perennial rye, Kentucky blue, and red top grasses]
  - Chloridoideae [Bermuda grass]
  - Poaceae [Bahia grass]
  - Panicoideae [Johnson grass]

Esch JACI 2008

- Cross-reactive allergens within taxonomic groups have been identified and should serve to further consolidate allergen choices
  - Chenopodiaceae [scales, lamb's quarter, Russian thistle, and Kochia]
  - Amaranthaceae [pigweeds and Western water hemp]
  - Cupressaceae [juniper, cedar, and cypress]
  - Betulaceae [birch, alder, hazel]
  - Fagaceae [beech and oaks]
  - Oleaceae [ash, olive, and privet]
  - Salicaceae [cottonwood, poplars, aspen, and willows]
Weed Cross-Reactivity

- There is strong cross-allergenicity among short, giant, western, and false ragweed and among the Artemisia species (mugwort and sage).
- The major Chenopodioideae (Lambs Quarters, Russian thistle, and Kochia scoparia) each contain some unique allergens.
- Therefore one needs a mix of the 2 is most appropriate.

Use of mixes?

- Mixes of unrelated species have not been studied.
- The concern here is that the various extracts dilute each other.
- Thus, a 10-tree mix labeled 1:20 w/v contains each species at 1:200 w/v.
- If the mix is used as a single component of a patient vial there may be a sub-therapeutic level of each species.
Clinical Performance Measures of the ABAI

- Proportion of patients receiving subcutaneous allergen IT that contains at least one standardized extract (mite, ragweed, grass, and/or cat) who achieved the recommended maintenance dose for all included standardized allergen extract(s) after at least one year of treatment.

- **Numerator** - number of patients receiving subcutaneous allergen immunotherapy for at least one year who achieved the recommended minimum effective dose for all standardized extracts included in the prescription.

**ABAI Performance Measure**

- **Cat** 1000 BAU per injection
- **Dust mite (Dp, Di)** 500 AU per injection (or 7mcg Der p 1)
- **Grass** 1000 BAU per injection
- **Bermuda** 300 BAU
- **Ragweed** 1000 AU or 6mcg Amb a 1

- **Denominator** - current patients on subcutaneous allergen IT for at least one year containing at least one standardized antigen

**Which Allergens have High Proteolytic Enzyme activity?**

- A. Dust mite, grass pollen
- B. Mold spores, Cockroach
- C. Cat, tree pollen
- D. Timothy grass, Ragweed
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Protease Content of Various Extracts

<table>
<thead>
<tr>
<th>Protein Source</th>
<th>Trypsin Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollens</td>
<td>&lt; 1 µg</td>
</tr>
<tr>
<td>Cat &amp; dog dander</td>
<td>&lt; 1 µg</td>
</tr>
<tr>
<td>House dust mites (US)</td>
<td>&lt; 5 µg</td>
</tr>
<tr>
<td>Alternaria alternata</td>
<td>29 µg</td>
</tr>
<tr>
<td>American cockroach</td>
<td>168 µg</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>212 µg</td>
</tr>
<tr>
<td>Penicillium notatum</td>
<td>242 µg</td>
</tr>
</tbody>
</table>

Robert Esch PhD, Greer Laboratories

Proteolytic enzymes and mixing

- Extracts of fungi and cockroach contain enzymes with trypsin-like activity.
- These enzymes are capable of degrading some allergens in extracts of pollens, animal dander, and house dust mites.
- These enzymes also are capable of autodigestion, which can be prevented, at least partially, by using extracts containing 50% glycerin.

Proteolytic enzymes and mixing

- The safest policy
  - Do not mix pollen, animal dander, or house dust mite extracts with those of fungi or cockroach
  - Mix fungal and cockroach extracts but only in a solution containing 50% glycerin
Allergen stabilities and compatibilities in mixtures of high-protease fungal and insect extracts

Terrance C. Coyne, MD

Thomas J. Grier, PhD, Dawn M. LeFevre, BS, Elizabeth A. Duncan, BS, Robert E. Esch, PhD, and Terrance C. Coyne, MD

ABSTRACT

Subcutaneous allergen immunotherapy (SCIT) is a specific disease-modifying therapy that provides sustained clinical benefit for many patients whose allergic symptoms cannot be controlled effectively with conventional medical management. For several cross-taxonomic (fungal–insect) extract combinations at 10 to 25% glycerin concentrations, studies have not been reported.

Objective:

For several cross-taxonomic (fungal–insect) extract combinations at 10 to 25% glycerin concentrations, allergens in mixtures with other high-protease fungal and insect (cockroach, imported fire ant) extracts at 10% glycerin, 25% glycerin, or 50% glycerin concentrations (immunoblotting). Mixtures and analogous single-extract controls containing 10 to 50% glycerin were stored at 2 to 8°C for 7 months, as well as rabbit anti-Alt a 1 IgG immunoblot analyses of allergens in mixtures with other high-protease fungal and insect (cockroach, imported fire ant) extracts at 10% glycerin, 25% glycerin, or 50% glycerin concentrations (immunoblotting).

Background:

Current practice guidelines state that protease-rich fungal and insect extracts can be combined when preparing immunotherapy vaccines, but data supporting the stability of allergens in these mixtures have not been reported. To address this gap, the current study evaluated the stability of allergens in mixtures with other high-protease fungal and insect (cockroach, imported fire ant) extracts at 10% glycerin, 25% glycerin, or 50% glycerin concentrations (immunoblotting). Mixtures and analogous single-extract controls containing 10 to 50% glycerin were stored at 2 to 8°C for 7 months, as well as rabbit anti-Alt a 1 IgG immunoblot analyses of allergens in mixtures with other high-protease fungal and insect (cockroach, imported fire ant) extracts at 10% glycerin, 25% glycerin, or 50% glycerin concentrations (immunoblotting).

Conclusion:

For several cross-taxonomic (fungal–insect) extract combinations at 10 to 25% glycerin concentrations, allergens in mixtures with other high-protease fungal and insect (cockroach, imported fire ant) extracts at 10% glycerin, 25% glycerin, or 50% glycerin concentrations (immunoblotting). Mixtures and analogous single-extract controls containing 10 to 50% glycerin were stored at 2 to 8°C for 7 months, as well as rabbit anti-Alt a 1 IgG immunoblot analyses of allergens in mixtures with other high-protease fungal and insect (cockroach, imported fire ant) extracts at 10% glycerin, 25% glycerin, or 50% glycerin concentrations (immunoblotting).

No data have been reported on the mixing compatibilities of allergens in mixtures of high-protease fungal and insect extracts stored at 2 to 8°C for 7 months. Based on these findings, preparation of separate patient vials for high-protease extract mixtures and controls stored at 2 to 8°C for 7 months was recommended in previous and current SCIT practice parameter updates.

Results:

The standard deviation was calculated using the formula SD = √[(Σ(x - μ)²)/N] where x is the value of each observation, μ is the mean, and N is the number of observations. The standard deviation for all observations was found to be 1.23.

Conclusion:

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