Immunotherapy Guide
Increases Dosing Accuracy

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Disclosures

None
Background

- Immunotherapy (IT) is a therapeutic tool used to treat allergic rhinitis and allergic asthma for decades.
- In 2011, practice parameters were published on the practice of IT.
  - Within these practice parameters are recommendations on IT doses for standardized and non-standardized antigens.
  - These recommendations are meant to optimize therapeutic results while minimizing the risk of adverse shot reactions.
Background

- In general, administration of higher doses increases the likelihood of clinical effectiveness.
- Low doses are less likely to be effective, and very low doses usually are ineffective.
Recommended Doses

- Multiple studies demonstrate that the efficacious dose for allergen immunotherapy is between 5-20 μg of the major allergen per injection
  - Based on clinical trials involving single antigens

- **Using recommended doses is shown to:**
  - Provide early improvement in symptoms
  - Along with the duration of treatment, improves long-term benefit
QI Project Background

- Many of the physicians in our clinic utilized a chart created to simplify the IT ordering process.
- Concentrations of each antigen were based on the number of different antigens included in each vial.
- While this chart was useful, it was created several years before the recent practice parameters were released.
  - As such, utilization of this chart had the potential to under or overdose IT prescriptions.
Project Aims

- To align the process of ordering IT with current practice parameter guidelines
- Simplify the IT ordering process
- Determine the effect of providing a new dosing guide that adheres to practice parameters on dosing accuracy
Measures

- Review of the last 10 new IT orders (excluding venom)
- 55 allergen data points
- Determined if prescribed dose fit within practice parameter guidelines
- Prescriptions were categorized as
  - **Very high**: $\geq 2x$ the highest recommended dose
  - **High**: $> \text{recommended maximum dose, } < 2x \text{ recommended maximum dose}$
  - **Appropriate**: within recommended dose range
  - **Low**: $< \text{recommended minimum dose, } > 1/2 \text{ recommended minimum dose}$
  - **Very Low**: $\leq 1/2 \text{ recommended minimum dose}$
  - **N/A**: not applicable, no recommendations on dose
Dosing Accuracy - All Antigens

- Appropriate: 25%
- High: 13%
- Very high: 9%
- N/A: 9%
- Very low: 35%
- Low: 9%

N = 55 antigen prescriptions
ON TARGET

N = 50 antigen prescriptions

All Antigens (excluding molds)

- Very low: 38%
- Low: 10%
- Appropriate: 28%
- High: 14%
- Very high: 10%
Standardized extracts include cat, dust mite, grass, and ragweed.

N = 24 antigen prescriptions

Dosing Accuracy - Standardized Antigens

- Appropriate: 46%
- Very high: 21%
- Very low: 8%
- High: 25%
Accuracy by Schedule

- **0.25 ML/SHOT**
- **0.5 ML/SHOT**
- **1 ML/SHOT**
- **ANIMAL (0.2 ML/SHOT)**

*Animal schedule 0% accurate*
Measures - Common Themes

- Prescriptions that were High and Very High were exclusively Grass and Ragweed
- Very few of the trees were dosed within the recommended range
  - Under-dosed
- All prescriptions in the "very low" group were either on a 0.25 ml/shot schedule or received a mix or both
- All of the Rx written for mixes (6 tree or common weed) were “very low” for the individual antigens contained in the mix
Mixes

- “The maintenance concentrate should be formulated to deliver a dose considered to be therapeutically effective for each of its constituent components”
- Eastern 6 tree mix - recommendations for pollens are within the range of 1:200 w/v - 1:100 w/v
  - Stock concentration = 20,000 PNU/ml = 1:46 w/v
  - Concentration for each of these unrelated allergens is only 1/6 of this = 3,333 PNU/ml = 1:276 w/v
- Therefore, even at our stock concentration on a 0.5 ml/shot schedule, a patient would receive 1,667 PNU per injection = 1:552 w/v/antigen = major underdose!
Intervention/Methods

- Created a new chart to be used as a guide for IT dosing based off of practice parameter recommendations
- New chart uses a **0.5 ml/shot schedule only**
  - Most IT Rx can achieve therapeutic dose with a 0.5 ml injection
  - 0.25 ml/injection difficult to provide sufficient dose in injection amount for most antigens
<table>
<thead>
<tr>
<th>Antigen</th>
<th>Target Dose</th>
<th>Starting Conc.</th>
<th>Prescription Dose</th>
<th>Approx. Vol. (ml/10 ml vial)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td>Ragweed Mix</td>
<td>6-12 AgE U</td>
<td>1:20 w/v</td>
<td>1:200 w/v</td>
<td>1:160 w/v</td>
</tr>
<tr>
<td>Pollen</td>
<td>1:200-1:100 w/v</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Common Weed Mix&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20,000 PNU/ml</td>
<td>15,500 PNU/ml</td>
<td>20,000 PNU/ml</td>
<td>20,000 PNU/ml</td>
</tr>
<tr>
<td>Eastern 6 Tree Mix&lt;sup&gt;b&lt;/sup&gt;</td>
<td>20,000 PNU/ml</td>
<td>20,000 PNU/ml</td>
<td>20,000 PNU/ml</td>
<td>20,000 PNU/ml</td>
</tr>
<tr>
<td>Eastern Oak Mix</td>
<td>20,000 PNU/ml</td>
<td>4,000 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>6,666 PNU/ml</td>
</tr>
<tr>
<td>Elm Mix</td>
<td>1:20 w/v</td>
<td>1:200 w/v</td>
<td>1:160 w/v</td>
<td>1:100 w/v</td>
</tr>
<tr>
<td>Birch Mix</td>
<td>20,000 PNU/ml</td>
<td>3,333 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>6,000 PNU/ml</td>
</tr>
<tr>
<td>Western Walnut Mix</td>
<td>20,000 PNU/ml</td>
<td>3,333 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>6,000 PNU/ml</td>
</tr>
<tr>
<td>Ash Mix</td>
<td>1:20 w/v</td>
<td>1:200 w/v</td>
<td>1:160 w/v</td>
<td>1:100 w/v</td>
</tr>
<tr>
<td>Maple/Box Elder Mix</td>
<td>1:20 w/v</td>
<td>1:200 w/v</td>
<td>1:160 w/v</td>
<td>1:100 w/v</td>
</tr>
<tr>
<td>Hickory Mix</td>
<td>20,000 PNU/ml</td>
<td>4,000 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>6,666 PNU/ml</td>
</tr>
<tr>
<td>Willow/Black Salix Nigra</td>
<td>1:20 w/v</td>
<td>1:200 w/v</td>
<td>1:160 w/v</td>
<td>1:100 w/v</td>
</tr>
<tr>
<td>7 grass mix&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1,000-4,000 BAU</td>
<td>100,000 BAU/ml</td>
<td>2,000 BAU/ml</td>
<td>5,000 BAU/ml</td>
</tr>
<tr>
<td>KORT</td>
<td>300-1500 BAU</td>
<td>10,000 BAU/ml</td>
<td>750 BAU/ml</td>
<td>1,500 BAU/ml</td>
</tr>
<tr>
<td>Dust mite mix, Dp, or Df</td>
<td>500-2,000 AU</td>
<td>10,000 AU/ml</td>
<td>1,000 AU/ml</td>
<td>2,500 AU/ml</td>
</tr>
<tr>
<td>Cat hair/Cat pelt&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1,000-4,000 BAU</td>
<td>10,000 BAU/ml</td>
<td>2,000 BAU/ml</td>
<td>5,000 BAU/ml</td>
</tr>
<tr>
<td>Dog</td>
<td>15 μg Can f 1</td>
<td>1:100 w/v</td>
<td>1:250 w/v</td>
<td>1:250 w/v</td>
</tr>
<tr>
<td>Fungi</td>
<td>Highest Tolerated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alternaria Tenuis</td>
<td>20,000 PNU/ml</td>
<td>2,500 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>10,000 PNU/ml</td>
</tr>
<tr>
<td>Cladosporium Herbarum</td>
<td>20,000 PNU/ml</td>
<td>2,500 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>10,000 PNU/ml</td>
</tr>
<tr>
<td>Penicillium Mix</td>
<td>20,000 PNU/ml</td>
<td>2,500 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>10,000 PNU/ml</td>
</tr>
<tr>
<td>Aspergillus Fumigatus</td>
<td>20,000 PNU/ml</td>
<td>2,500 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>10,000 PNU/ml</td>
</tr>
<tr>
<td>Hormodendrum Hordei</td>
<td>1:20 w/v</td>
<td>1:160 w/v</td>
<td>1:80 w/v</td>
<td>1:40 w/v</td>
</tr>
<tr>
<td>Bipolaris</td>
<td>20,000 PNU/ml</td>
<td>2,500 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>10,000 PNU/ml</td>
</tr>
<tr>
<td>Fusarium Molliniforme</td>
<td>20,000 PNU/ml</td>
<td>2,500 PNU/ml</td>
<td>5,000 PNU/ml</td>
<td>10,000 PNU/ml</td>
</tr>
<tr>
<td>Insects&lt;sup&gt;d&lt;/sup&gt;</td>
<td>HTD</td>
<td>Can mix dust mite and molds. Cannot mix pollens with molds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Honey Bee Venom</td>
<td>100 μg/ml</td>
<td>100 μg/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow Jacket Venom</td>
<td>100 μg/ml</td>
<td>100 μg/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow Hornet Venom</td>
<td>100 μg/ml</td>
<td>100 μg/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wasp Venom</td>
<td>100 μg/ml</td>
<td>100 μg/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed Vespid Venom</td>
<td>300 μg/ml</td>
<td>300 μg/ml</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Individual antigen concentration in mix is 1/5 of total PNUs

<sup>b</sup>Individual antigen concentration in mix is 1/6 of total PNUs

<sup>c</sup>Kentucky Blue/June, Meadow Fescue, Orchard, Perennial Ryegrass, Sweet vernal, Timothy

<sup>d</sup>Insects are on a REGULAR schedule (1 ml/injection)
Methods

- New dosing guides were used over the course of 4 months with occasional minor modifications
  - Unknown whether the ordering provider used the new dosing guide
- Education was provided in the form of 1:1 coaching, didactic training sessions and real time guidance
- At the end of 4 months the 10 most recent IT prescriptions were evaluated
  - 58 allergen data points
- Results compared to those obtained prior to initiation of the new guide
ON TARGET

Relative improvement = 128%
Absolute improvement = 32%

N = 58
Relative improvement = 143%
Absolute improvement = 40%
p = < 0.0001

N = 49
ON TARGET

Relative improvement = 74%
Absolute improvement = 34%
p = < 0.0001

N = 20
Conclusions

- Implementation of the new dosing guide significantly improves the accuracy of dosing IT.
- Using antigen mixes for SCIT rarely provides sufficient amounts of each individual antigen to dose within practice parameter guidelines.
- Most antigens can reach a sufficient dose using a 0.5 ml/shot schedule alone.
Future Directions

Look at shot reaction rates before and after implementation of the dosing guide.

Review charts from those with previous shot reactions to see if overdosed.
Special Thanks

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