Immunotherapy

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Immunotherapy

- Treats IgE-mediated allergy by the intentional exposure to regular, progressive doses of the same specific inhalant allergens that are responsible for producing symptoms.
- This results in down regulation of the immune response and the control of symptoms associated with usual levels of environmental exposure to that allergen.

History of Immunotherapy

- Pasteur, Von Behring, Kitasato – concept of passive transfer of antibodies against toxins.
- Curtis used whole weed extracts with some success.
- 1907 Besredka and Steinhardt conducted animal studies.
- 1911 Leonard Noon introduced concept of quantitation.
- 1915 Cooke introduces immunotherapy into the United States.

Classic Triad of Management

IT
Meds
Avoidance

Efficacy of Immunotherapy

- Since 1954, 22 out of 26 of the best DBPC studies have demonstrated the efficacy of immunotherapy for allergies and asthma.
- Effective for pollen, dust, cat, Alternaria.
- Most studies focused on allergies to single pollens.
- Effective in 90% of patients.
- Often misunderstood by patients.
- Still considered “voodoo medicine” by some practitioners.

Benefits of Immunotherapy

- Improvement in quality of life.
- Reduction in symptoms.
- Decrease in reliance on medications.
- Decrease in the risk of developing asthma.
- Preventing new sensitizations.
### Indications for Immunotherapy

- Demonstration of IgE-mediated disease that correlates to symptoms.
- Effective for AR, asthma, stinging insect allergy
- Insufficient response to avoidance and pharmacotherapy
- Significant side effects to medical therapy
- Unable to comply with medical therapy
- Moderate to severe symptoms lasting for a majority of the year or spanning across 2 or more seasons

### (Relative) Contraindications for Immunotherapy

- Concomitant therapy with a beta-blocker
- Contraindication to administering epinephrine
- Noncompliance by the patient
- Autoimmune disease
- Pregnancy (may continue IT, but do not start)
- Uncontrolled asthma
- HIV+ or other immunodeficiency

### Mechanisms of Immunotherapy

- A short period of increase in antigen specific IgE above pre-treatment levels over the first 2-3 months, followed by gradual decline over the next 2 years.
- Decline in IgE does not correlate to clinical improvement.
- As IgE levels decline, there is a rise in IgG1 followed by IgG4
- Increase in IgG4 correlates to symptom relief.

### Mechanisms of Immunotherapy

- Increase in antigen-specific suppressor T-cells
- Shift in TH1/TH2 balance (role of Tregs)
- Decline in the levels of pro-allergic cytokines
- Reduced basophil, mast cell and lymphocyte reactivity to antigens
- Blunting of the post-seasonal rise in specific IgE antibody
- Gradual decrease in symptoms with repeated exposures to same allergen levels

### Schedule of Immunotherapy

- Total treatment is 3-5 years
- Escalation phase – 6-9 months
  - Begins with safe, starting point
  - Ends with maintenance dose
  - Symptom relieving dose is achieved during this phase
  - Each vial is 5X stronger than the one before
- Maintenance phase – till the end
  - Once every 2 weeks in the second years
  - Once every 3-4 weeks for the remainder

### Pre-Immunotherapy Counseling and Consent

- Explain the concept of IT
- Explain the differences between environmental control, meds, and IT
- Explain the length of the treatment
- Explain that local reactions are expected
- Explain that systemic reactions are rare
- Explain that regular treatments are critical
- Explain that follow-up with MD is necessary
- Give a prescription and instruct the patient in the use of a self-administered epi kit
A Word to the Wise ...

- Immunotherapy is a potentially life-threatening treatment which should not be undertaken lightly or performed haphazardly.
- It should be administered only for IgE-mediated respiratory allergy in an exact and precise manner to sufficiently symptomatic patients inadequately responsive to avoidance strategies and pharmacotherapy.

Dose Calculation and Vial Preparation - General Rules

- Nurse should not be interrupted.
- All calculations should be double-checked.
- Create a 5cc vial which will last approximately 3 months.
- Label vials carefully with name, vial # and expiration date.
- Separate low sensitivity antigens and high sensitivity antigens.

Let’s Start Simple

- Start with the endpoint when basing IT on IDT.
- Start with one dilution weaker than the class designation when basing IT on in vitro testing and call this the endpoint.

Single Antigen Vial

- Sensitive to Cat, endpoints on #3.
- Start with a dose of .05cc from #3.
  - .02 cc from the endpoint.
  - .02 cc from the confirmatory (=0.1cc endpoint).
  - Total of 0.12cc has already been given.
- Escalate by .05cc each week until 0.5cc is reached (above 0.5 cc is painful).
- Give .05cc from a vial that is 5x stronger than the first one (#2).
- Continue until maintenance is reached.

<table>
<thead>
<tr>
<th>VIAL #1</th>
<th>VIAL #2</th>
<th>VIAL #3</th>
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</thead>
<tbody>
<tr>
<td>.05 cc</td>
<td>.05 cc</td>
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<td>0.15</td>
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Multiple Antigen Vial

- Each patient has their own vial.
- Minimize the number of injections.
- Keep the injection volume low.
- The vial must last about 3 months.
- Multidose vials contain 10 doses – 5 cc vial with an assumed dose of 0.5 cc each time.
- Problem – how do you fit all that antigen into one vial?
### Math Review
- 0.5 cc of #3 Antigen A (endpoint)
- 0.1 cc of #2 Antigen A
- 0.02 cc of #1 Antigen A
- For a 5 cc, 10 dose vial for Antigen A alone, take maximum dose (0.5 cc) from #3 x10 doses = 5 cc

### Multiple Antigen Vial

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<th>EP</th>
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<tr>
<td>Antigen A</td>
<td>6</td>
<td>5 cc #6</td>
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<td>3</td>
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<tr>
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<td>5</td>
<td>5 cc #5</td>
<td>0.2 cc #3</td>
</tr>
<tr>
<td>Antigen D</td>
<td>2</td>
<td>5 cc #2</td>
<td>0.2 cc C</td>
</tr>
<tr>
<td>Total vol. Ag</td>
<td>20 cc</td>
<td>Add glycerine</td>
<td>Add diluent</td>
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<tr>
<td></td>
<td></td>
<td></td>
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Add 0.8 cc glycerine
Add 3.4 cc diluent
Total volume
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**Safety Vial Test**

- A good idea to do all the time
- Always done when IT is based on in vitro testing
- Consider it highly when whealing patterns were unusual
- Raise a 4 mm intradermal wheal and read in 10-15 minutes
- If resulting wheal is > 13 mm, dilute vial 5x and give the first dose the following week, otherwise give the 1st dose on that day.

**References**