Expanding Allergy Treatment in Primary Care

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EPIDEMIOLOGY AND PREVALENCE
An allergic reaction is the body’s immune system reacting inappropriately to a foreign substance, such as pollen. The immune system perceives the benign substance as dangerous, thereby triggering a reaction.
An allergen can be almost anything which acts as an antigen (agents eliciting an antibody response) to stimulate an immune response.
Common Allergens

- Food
- Molds
- Grasses
- Trees

- Weeds
- Dust-Mites
- Animals
- Drugs
The Allergy & Asthma Crisis in America is well documented. While there may be debate on causation (i.e. the clean hypothesis, increased pollution) there is no debate to the facts of an ever increasing number of Americans suffering from allergic disease. At least 1 of every 5 patients in a primary care setting (>55 million nationwide) has allergic disease.
Putting Allergies in Perspective

The Allergy Aggravators

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinson's</td>
<td>3</td>
</tr>
<tr>
<td>Alzheimer's</td>
<td>5</td>
</tr>
<tr>
<td>Stroke</td>
<td>6</td>
</tr>
<tr>
<td>CHD</td>
<td>7</td>
</tr>
<tr>
<td>Cancer</td>
<td>10</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18</td>
</tr>
<tr>
<td>Allergy</td>
<td>60</td>
</tr>
</tbody>
</table>
Allergies account for 8.4 million office visits each year.

- About 30% of patients seen in a primary care setting present with “Allergy-Like” Symptoms
- Allergies are responsible for the loss of over 3.5 million workdays and 2 million school days per year
Patients with allergies cost the healthcare system over $20 billion annually

- $5 billion antihistamine market and growing
- Approximately 60% of patients on antihistamines do not have allergies
Need for Access

- **Physician Specialties**
  - ~ 80,000 Family Practice Physicians
  - ~ 14,000 Dermatologists
  - ~ 10,000 Pediatricians
  - ~ 5,000 ENT Physicians
  - ~180,000 APPs in primary care

  Total physicians in these groups: ~ 113,000

  Each Physician would have to see ~ 490 patients

- 55,000,000 patients with allergies
  - 4,000 Allergists in the US
  - Each Allergist would have to see ~ 14,000 patients!
The demand for allergists will increase 35% by 2020, while at the same time the number of medical students choosing the specialty tumbles. The ACAAI predicts “a shortfall of more than 2,100 allergists with no solution in sight.”

"By the year 2020, there will not be enough allergists to handle the increased amount of patients suffering from allergies." - American College of Allergy, Asthma & Immunology
Clinicians Commonly Treat Symptoms & Not The Cause

- History & Physical exam alone often leads to an incorrect diagnosis (Bad guessers).
- Negative results can be as informative as positive results, ruling out allergy as the cause of symptoms.
- With allergic diseases, clinicians frequently progress directly from signs and symptoms to pharmacotherapy, even when diagnostic evidence is readily available. Empiric management may result in unnecessary repeat office visits, inappropriate medication, greater costs, and unnecessary referrals.
As the number of medical students choosing the specialty of allergy continues to plummet it is obvious that “more allergists” will not be the solution. The solution will be other specialists (primary care) taking a more active role in allergy evaluation and management.
Allergy Services

- Percutaneous skin testing
- Pulmonary function testing
- Immunotherapy Rx
- Immunotherapy injections
- Sublingual immunotherapy
- Avoidance measures / education
- Evaluation & Management
ALLERGY TESTING
Who Should be Tested?

- All Patients complaining of allergy-like symptoms, red-itchy eyes, sneezing or upper respiratory infections
- Patients who chronically use allergy medications
- Pediatric patients especially those with a stubborn rash, chronic ear infections or GI symptoms
- Persistent asthmatics
Allergy Testing

**in vivo**
Skin-Prick Test

**in vitro**
Blood Testing

Antibodies (IgE)
In Vitro Allergy Testing Pros and Cons

- No risk of immediate side effects
- Cost is fairly high
- Anti-histamines do NOT need to be discontinued
- Quality-controlled quantitative results
- Minimally invasive to the patient
- One blood sample multiple determinations
- Must wait for lab results
- Follow up required
- Less clinically sensitive/specific
Finger Stick Testing

First lab-based quantitative Sp IgE test using a finger stick blood specimen

FDA Cleared
Demonstrated Proficiency (CAP)

Current Mini-Panel
Total IgE &
10 Common Allergens

Phase I: Allergy
# Finger Stick Testing

<table>
<thead>
<tr>
<th>Allergen</th>
<th>N</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mountain Cedar</td>
<td>90</td>
<td>88%</td>
<td>93%</td>
<td>90%</td>
</tr>
<tr>
<td>Timothy Grass</td>
<td>96</td>
<td>94%</td>
<td>97%</td>
<td>90%</td>
</tr>
<tr>
<td>Bermuda Grass</td>
<td>87</td>
<td>86%</td>
<td>97%</td>
<td>91%</td>
</tr>
<tr>
<td>Short Ragweed</td>
<td>90</td>
<td>90%</td>
<td>95%</td>
<td>92%</td>
</tr>
<tr>
<td>Housedust Mite (pt.)</td>
<td>93</td>
<td>96%</td>
<td>93%</td>
<td>95%</td>
</tr>
<tr>
<td>Cat Hair</td>
<td>90</td>
<td>96%</td>
<td>89%</td>
<td>93%</td>
</tr>
<tr>
<td>Wheat (food)</td>
<td>92</td>
<td>85%</td>
<td>93%</td>
<td>90%</td>
</tr>
<tr>
<td>Cows Milk</td>
<td>85</td>
<td>81%</td>
<td>92%</td>
<td>89%</td>
</tr>
<tr>
<td>Egg White</td>
<td>83</td>
<td>80%</td>
<td>94%</td>
<td>92%</td>
</tr>
<tr>
<td>Alternaria (Mold)</td>
<td>82</td>
<td>87%</td>
<td>94%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>System Average</strong></td>
<td>89</td>
<td>88%</td>
<td>94%</td>
<td>91%</td>
</tr>
</tbody>
</table>

Comparison to Phadia CAP System specific IgE FEIA
### Recommended Interpretation of Food Allergen-Specific IgE levels (kU/L)

<table>
<thead>
<tr>
<th></th>
<th>Egg</th>
<th>Milk</th>
<th>Peanut</th>
<th>Fish</th>
<th>Soy</th>
<th>Wheat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive if &gt;</td>
<td>7</td>
<td>15</td>
<td>14</td>
<td>20</td>
<td>65</td>
<td>80</td>
</tr>
<tr>
<td>Possibly reactive (physician challenge)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td>26</td>
</tr>
<tr>
<td>Unlikely reactive if &lt; (home challenge)</td>
<td>0.35</td>
<td>0.35</td>
<td>0.35</td>
<td>0.35</td>
<td>0.35</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Skin Prick Test (Scratch Tests)
Skin Testing Pros and Cons

- Risk of systemic reaction albeit low
- Anti-histamines must be discontinued (3-5 days)
- Minimally invasive
- Method is technique dependent
- Usually performed by trained staff
- Positive result means actual physical manifestation to allergen
- Highly sensitive and specific
- Cost effective
- Same day results
Skin Prick Testing Devices

Several devices available
Result in various degrees of trauma to the skin
Skin Testing Procedure

- Off Beta-Blockers
- Off anti-histamines
- What about other meds
- Anaphylaxis kit available (EpiPen minimum)
- Placing technique
- Wait time
- Interpretation
- Documentation
Environmental Management
## Causal Relationship of Triggers

- **Sufficient evidence of **Causal** Relationship**

<table>
<thead>
<tr>
<th>Cat</th>
<th>Cockroach</th>
<th>ETS (preschooler)</th>
<th>House dust mite</th>
</tr>
</thead>
</table>

- **Sufficient evidence of an **Association**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Molds</th>
<th>Rhinovirus</th>
<th>NO$_2$ &amp; NO$_x$</th>
</tr>
</thead>
</table>

- **Limited evidence of Association**

Formaldehyde, Fragrances, RSV, ETS (school-aged and older children)
Encase all pillows and mattresses of the beds the child sleeps on with allergen-impermeable encasings.
- Wash bedding weekly to remove allergen.
- Wash in HOT water (130° F) to kill mites.
- For non-encased bedding (e.g., blankets and quilts) choose items that can withstand frequent hot water washing.
- Remove or wash and dry stuffed toys weekly.
- Vacuum with a HEPA vacuum cleaner.
- Avoid humidifiers.
Dust Mites:
More expensive interventions (have skin-test-proven allergy to dust mites prior to implementation)

- Replace draperies with blinds
- Remove carpet from child’s bedroom
- Remove upholstered furniture
Animal Allergens: Interventions

- Find a new home for indoor pets
- Keep pet outside
- If these aren’t possible...
  - Similar interventions as with dust mites: Encasings, HEPA air cleaner, HEPA vacuum,
  - Keep pet out of bedroom
- Takes 24-30 weeks before allergen levels reach those of non-cat households
Bathing cats MAY be effective at reducing allergen (n = 8 cats)

- The reduction was not maintained by 1 week.
- Therefore it **had** been recommended to bathe the cat twice a week......

- However, a more recent study of 12 cats suggests the decrease in dander after bathing lasts about 1 day.
Cockroach Allergen

- Integrated pest management (IPM)
  - Least toxic methods first
- Clean up food/spills
- Food and trash storage in closed containers
- Fix water leaks

- Clean counter tops daily
- Boric acid
- Bait stations/ gels
- Don’t!!
  - Spray liquids in house, especially play and sleep space
  - Use industrial strength pesticide sprays that require dilution
Ways to control moisture and/or decrease humidity to < 50%:
- Dehumidifier or central air conditioner
- Do not use a humidifier
- Vent bathrooms/clothes dryers to outside
- Use exhaust fan in bathroom/ other damp areas
- Check faucets and pipes for leaks and repair

Complete mold abatement may be required using a licensed contractor
Items too moldy to clean should be discarded.
An area larger than 3 ft x 3 ft should be professionally cleaned.
Chlorine solution 1:10 with water is acceptable for smaller areas.
  - Don’t mix chlorine with cleaners containing ammonia!
  - Quaternary ammonium compounds are also good fungicides if bleach isn’t used.
  - Identify and stop sources of water intrusion.
Allergen Immunotherapy
Allergen Immunotherapy Definitions

- Immunotherapy
- Allergen Vaccine
- "Desensitization"
- "Hyposensitization"
- "Allergy shots"
Allergen Immunotherapy

- Exposing patients to a specific allergen in order to: promote tolerance to a specific allergen with the ultimate clinical goal of causing a sustained decrease in allergic symptoms.
- Allergen immunotherapy is distinct from available pharmacologic treatments. Its aim is sustained alteration in immune response beyond discontinuation of treatment.
How long has Allergen Immunotherapy been in practice?

- Almost 100 years
- Oldest continuously practiced form of medicine
Allergen Immunotherapy: Clinical Trials

- **Benefits:**
  - Reduced symptoms
  - Reduced medication use
  - Reduced treatment cost
  - Clinical remission (?)

- **Indications**
  - Allergic rhinitis
  - Asthma
  - Stinging insect hypersensitivity

- **Multiple allergens studied**
Long-Term Clinical Efficacy of Grass-Pollen Immunotherapy

Initial Placebo Trial vs Current Trial

**Pollen Count**
- Study group:
  - Immunotherapy
  - Placebo

**Symptom Score**
- Immunotherapy:
  - Maintenance
  - Discontinuation
  - None (control)

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Initial Placebo Trial</th>
<th>Current Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunotherapy</td>
<td>1989 May June July Aug</td>
<td>1993 May June July Aug</td>
</tr>
<tr>
<td>Placebo</td>
<td>1989 May June July Aug</td>
<td>1995 May June July Aug</td>
</tr>
</tbody>
</table>

**Seasonal Pollen Counts**
- Green line: Pollen (grains/m³)
- Study groups:
  - Immunotherapy
  - Placebo
Allergen Immunotherapy in the Pediatric Population

- May prevent sensitization to new allergens
- May prevent progression to asthma
### Immunotherapy Prevents the Development of New Allergen Sensitizations

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Patients</th>
<th>None</th>
<th>Cat</th>
<th>Dog</th>
<th>Alternaria</th>
<th>Grass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunotherapy</td>
<td>22</td>
<td>10</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Control group</td>
<td>22</td>
<td>0</td>
<td>12</td>
<td>8</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

## Estimated Costs of Treatment of Allergic Rhinitis

<table>
<thead>
<tr>
<th>Treatment Year</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total 5 Year Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(single injection)</td>
<td>$800</td>
<td>$290</td>
<td>$290</td>
<td>$290</td>
<td>$290</td>
<td>$1960</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(oral &amp; topical)</td>
<td>$1200</td>
<td>$1200</td>
<td>$1200</td>
<td>$1200</td>
<td>$1200</td>
<td>$6000</td>
</tr>
</tbody>
</table>
When writing a prescription, consider:
(1) cross-reactivity of allergens
(2) Optimization of the dose of each allergen
(3) Enzymatic degradation of allergens
Involves administration of increasing quantities of allergen vaccine subcutaneously

Types of schedules

1. Conventional / routine
2. Daily
3. Cluster
4. Rush / modified rush
Immunotherapy: Treatment Schedules

Conventional schedules

- Most commonly used
- Injections given 1-2 times a week
- Approximately 18-27 doses increments until maintenance dose is achieved
- Average build-up phase from 3-6 months
- Patients with higher degree of allergen sensitivity may require longer build-up phase
Sublingual immunotherapy (SLIT):

- Drops, sprays, or dissolving tablets placed beneath the tongue have studied and used in European countries.
- Dosing of sublingual therapy likely requires several times the concentrations used for subcutaneous immunotherapy.
- Data from European studies suggest efficacy with a favorable safety profile.
- Most studies of SLIT have been with single allergens and translation of these studies to treatment with multiple allergens needs to be further studied.
- Currently no FDA approved formulations in the US (studies to obtain such approval are underway).
Summary

- Allergen Immunotherapy is effective for:
  - Allergic asthma
  - Allergic rhinitis and conjunctivitis
  - Stinging insect allergy
- May help prevent further allergen sensitization and asthma in children
- Cost-effective
Questions?
During immunotherapy, two primary changes in T cells have been observed:

- Immune deviation of allergen-specific cell responses from a Th2 pattern to a Th1 pattern
- The induction of regulatory cells resulting in tolerance of energy of antigen-specific effector T cells
References


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