

## Allergen Immunotherapy: A Practice Parameter

*This practice parameter was developed by the Joint Task Force on Practice Parameters of the American Academy of Allergy, Asthma and Immunology (AAAAI); the American College of Allergy, Asthma and Immunology (ACAAI); and the Joint Council of Allergy, Asthma, and Immunology (JCAAI). The parameter provides a framework for the use of allergen immunotherapy in the treatment of patients with allergic rhinitis, allergic asthma and Hymenoptera sensitivity. It is not intended to replace clinical judgment or establish a protocol for all patients. This and previous practice parameters are available online at <http://www.jcaai.org>.*

### Allergen immunotherapy is appropriate in patients who:

- have symptoms of allergic rhinitis or allergic asthma with natural exposure to allergens and who demonstrate specific IgE antibodies (by skin tests or in vitro tests) to relevant antigens, and symptoms not controlled adequately by pharmacotherapy and avoidance measures, or a need to avoid adverse effects of pharmacotherapy or a wish to reduce long-term use of pharmacotherapy.
- have a history of systemic reaction to Hymenoptera venom and specific IgE antibodies (by skin tests or in vitro tests) to venom.

### Efficacy of Immunotherapy

Randomized, double-blind, placebo-controlled studies show that immunotherapy is effective for the treatment of allergic rhinitis, allergic asthma, and stinging insect hypersensitivity. In patients with these disorders, immunotherapy should be considered.

### Safety of Immunotherapy

Allergen immunotherapy should be administered in a setting where procedures that can reduce the risk of anaphylaxis are in place and where the prompt recognition and treatment of anaphylaxis is assured. Patients should remain in the physician's office at least 20-30 minutes after an injection.

### Patient Selection

Allergen immunotherapy should be considered for patients who have specific IgE antibodies to clinically relevant allergens. The decision to begin allergen immunotherapy depends on the degree to which symptoms can be reduced by avoidance and medication, the amount and type of medication required to control symptoms, and the adverse effects of medications. Patients who wish to avoid or reduce the long-term use of medications are good candidates for immunotherapy.

Venom immunotherapy should be strongly considered in patients with a history of a systemic reaction to a Hymenoptera sting (especially if the reaction was associated with respiratory or cardiovascular symptoms) and specific IgE antibodies.

### Allergen Selection and Handling

Immunotherapy vaccines should contain only clinically relevant allergens.

Immunotherapy is effective for pollen, fungi (molds), cat dander, dust mite, cockroach, and Hymenoptera sensitivity.

In mixing allergen vaccines, the following factors must be considered: 1) the cross-reactivity of the allergens, 2) the optimal dose of each constituent, and 3) possible enzymatic degradation of the allergens.

The efficacy of immunotherapy depends on achieving an optimal therapeutic dose of each of the clinically relevant constituents in the vaccine. Separation of extracts (vaccines) with high proteolytic enzyme activities (e.g., fungi, dust mites, cockroach, and insect venoms) from other extracts (vaccines) (e.g., pollen) is recommended.

### Immunotherapy Schedules and Doses

The highest concentration of a vaccine projected as the therapeutically effective dose is called the maintenance concentrate. The maintenance concentrate should be selected to deliver a dose considered to be therapeutically effective for each of its constituent components.

The maintenance concentrate and serial dilutions, whether a single vaccine or a mixture of vaccines, should be prepared and labeled for each patient. Use of a consistent, uniform labeling system for dilutions from the maintenance concentrate may reduce errors in administration.

The vaccine contents, informed consent for immunotherapy, and administration of vaccines should be carefully documented.

### Special Considerations in Immunotherapy

Allergen immunotherapy may prevent the development of asthma in children with allergic rhinitis.

Allergen immunotherapy may be continued in the pregnant patient, but allergen immunotherapy is usually not initiated during pregnancy.

### Clinical Indications for Allergen Immunotherapy

#### In patients with allergic rhinitis

Symptoms of allergic rhinitis after natural exposure to aeroallergens, demonstrable evidence of clinically relevant specific immunoglobulin (Ig)E antibodies, and one of the following:

- Poor response to pharmacotherapy or allergen avoidance
- Unacceptable adverse effects of medications
- Desire to avoid long-term pharmacotherapy and reduce the cost of medication
- Coexisting allergic rhinitis and asthma
- Possible prevention of asthma in children

#### In patients with allergic asthma

Symptoms of asthma after natural exposure to aeroallergens, demonstrable evidence of clinically relevant specific IgE antibodies, and one of the following:

- Poor response to pharmacotherapy or allergen avoidance
- Unacceptable adverse effects of medication
- Desire to avoid long-term pharmacotherapy and reduce the cost of medication
- Coexisting allergic rhinitis and allergic asthma

#### In patients with reactions to Hymenoptera stings

- History of a systemic reaction to a Hymenoptera sting (especially if the reaction was associated with respiratory or cardiovascular symptoms) and demonstrable evidence of clinically relevant specific IgE antibodies\*
- Age greater than 16 years, history of a systemic reaction limited to the skin, and demonstrable evidence of clinically relevant specific IgE antibodies
- History of a systemic reaction to imported fire ant and demonstrable evidence of clinically relevant specific IgE antibodies

\* Patients younger than 16 years who present with a history of only cutaneous symptoms to Hymenoptera stings may not require immunotherapy.

## Allergen Immunotherapy: A Practice Parameter *continued*

### Guidelines for Mixing Vaccines

#### Allergens with high protease activity (may be mixed together)

- Arthropods (dust mites)
- Fungi (mold spores)
- Insects (cockroach)

#### Allergens with low protease activity (may be mixed together)

- Grass pollens
- Tree pollens
- Weed pollens (other than ragweed)
- Animals (cat and dog allergens)

#### Other allergens

- Ragweed (may be mixed with either group above)
- Insect venoms (require a separate vial and a separate injection)

### Immunotherapy Content Form

The purpose of this form is to define the contents of the vaccine in enough detail that it could be duplicated if necessary.

This form should include the following:

- Appropriate patient identifiers, including patient name, medical record number, and birth date
- Vaccine contents, including common name or genus and species of individual allergens and detailed description of all mixtures

- Extract (vaccine) manufacturer and catalogue number or lot number of each component
- Volume of individual components of manufacturer's vaccine and final concentration of each
- Type of diluent used (if any)
- Vaccine expiration date

### Labels for Vaccine Vials

Each vial of vaccine should be labeled in a way that permits easy identification. Each label should include the following information:

- Appropriate patient identifiers, including patient name, medical record number, and birth date
- General description of the vaccine contents. The detail with which the contents can be identified depends on the size of the label and the number of allergens in the vial. Due to space limitations, it may be necessary to abbreviate the antigens. Possible abbreviations are as follows: tree, T; grass, G; bermuda, B; weeds, W; ragweed, R; mold, M; *Alternaria*, Alt; *Cladosporium*, Cla; *Penicillium*, Pcn; cat, C; dog, D; cockroach, Cr; dust mite, DM; *D farinae*, Df; *D pteronyssinus*, Dp; mixture, Mx. A full and detailed description of vial contents should be recorded on the prescription/content form.
- The dilution from the maintenance concentrate in volume per volume. If colors, numbers, or letters are used to identify the dilution, they also should be included.
- Vaccine expiration date

### Recommended Maintenance Doses of Allergen Immunotherapy

| Allergen                              | Dose, standardized units | Dose, major allergen | Maintenance concentrate, wt/vol* |
|---------------------------------------|--------------------------|----------------------|----------------------------------|
| <i>Dermatophagoides pteronyssinus</i> | 600 AU                   | 7-12 µg Der p1       | NA                               |
| <i>Dermatophagoides farinae</i>       | 2,000 AU                 | 10 µg Der f1         | NA                               |
| Cat                                   | 2,000-3,000 BAU          | 11-17 µg Fel d1      | NA                               |
| Grass (e.g., timothy)                 | 4,000 BAU                | 7 µg Phl p5          | NA                               |
| Short ragweed (standardized)          | NA                       | 6-24 µg Amb a1       | 1:100-1:30                       |
| Other pollen (nonstandardized)        | NA                       | ND                   | 1:100-1:30                       |
| Fungi/mold (nonstandardized)          | NA                       | ND                   | 1:100-1:50                       |

AU, allergy unit; BAU, bioequivalent allergy unit; NA, not applicable; ND, not determined.

\*Based on a maintenance injection of 0.5 mL.

### Suggested Methods for Labeling Dilutions from the Maintenance Dose Vaccine

| Dilution from maintenance concentrate | Label    |        |        |
|---------------------------------------|----------|--------|--------|
|                                       | Vol/vol  | Number | Color  |
| Undiluted                             | 1:1      | 1      | Red    |
| 10-fold                               | 1:10     | 2      | Yellow |
| 100-fold                              | 1:100    | 3      | Blue   |
| 1,000-fold                            | 1:1,000  | 4      | Green  |
| 10,000-fold                           | 1:10,000 | 5      | Silver |

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