

2006 American Academy of Allergy, Asthma & Immunology member immunotherapy practice patterns and concerns

To the Editor:

A 25-item Zoomerang questionnaire on immunotherapy practice patterns and concerns was posted for 6 weeks in May-June 2006 and publicized to the 6100 American Academy of Allergy, Asthma & Immunology (AAAAI) members by 2 e-mail messages with links to the online questionnaire. AAAAI records list 3113 allergists in part-time or full-time clinical practice in the United States and Canada, 161 international member physicians in part-time or full-time clinical practice, and 161 advance practice allied health professionals (nurse practitioners and physician assistants) licensed to independently examine patients and prescribe treatments among the 6100 e-mail recipients. The number of clinician Academy members to whom a questionnaire about immunotherapy practice patterns and concerns might apply is thus 3435. The web page had 768 visits, and 554 questionnaires were completed. Questionnaires were completed at 72% of web page visits and by 16.1% of clinician Academy members if we can assume that all completed questionnaires were by clinician Academy members and that no individual completed the questionnaire more than once.

The 2004 and 2006 questionnaire responses are posted in [Table E1](#) in this article's Online Repository at www.jacionline.org.

As regards oral β -blockers: 67% of respondents perform skin tests on such patients, and 33% do not. A total of 48% never place patients on oral β -blockers on immunotherapy, 21% do so only for venom immunotherapy, 24% do so "occasionally" for inhalant aeroallergens, and 7% do not see oral β -blockers as a contraindication to skin testing or immunotherapy.

As regards β -blockers eye drops: 33% of respondents never place such patients on immunotherapy, 13% do so only for venom immunotherapy, 29% do so "occasionally" for inhalant aeroallergens, and 21% do not see β -blockers eye drops as a contraindication.

As regards angiotensin-converting enzyme (ACE) inhibitors: 37% of respondents are concerned about the safety of immunotherapy in patients taking these drugs.

As regards HIV: 74% of respondents skin test patients known to have HIV, 40% start them on immunotherapy as they would other patients, and 9% start immunotherapy for insect venoms only. A total of 60% continue all immunotherapy on learning that a patient is HIV-positive, and 6% do so only for venoms.

Medicare's unique billing and administrative requirements were not viewed as an obstacle to offering skin testing and immunotherapy to Medicare patients.

As regards staffing: Physician always present, 83%; nurse practitioner or physician's assistant, 8%; registered nurse, 7%; medical assistant, 2%.

Regarding the wait period after immunotherapy: None, 1%; 20 minutes, 54%; 30 minutes, 45%; >30 minutes, 1%. Overall, 66% of respondents increase the wait period for patients who continue on immunotherapy after systemic reactions, 60% to 30-45 minutes, 31% to 45-60 minutes, and 9% to greater than 60 minutes.

As regards medications to have immediately available for 4-6 hours after each allergy shot: Epinephrine, 37%; H-1 blockers, 40%; H-2 blockers, 5%; LTC receptor blockers, 2%; other medications, 7%; none, 45%.

A total of 69% of respondents ask patients to avoid strenuous physical exercise after immunotherapy, 51% for up to 2 hours, and 18% for 3-4 hours.

Overall, 16% of respondents allow some home immunotherapy, 2% as an option during build-up and maintenance, 1% as an option at maintenance, and 13% occasionally or rarely for patients in particular circumstances.

Although only 88 respondents stated that they allow some home immunotherapy, 145 answered the question, "If you allow home immunotherapy, do you provide emergency medications to use in case of reactions and instruct patients in their use?" Of these, 108 (74%) said "yes."

A total of 96% of respondents use a preimmunotherapy injection health survey, 49% by informal verbal questionnaire, 31% recording results on a written checklist, and 16% providing a written preinjection questionnaire for patients or their parents.

Overall, 88% of respondents perform some preimmunotherapy peak expiratory flow rate screening, 5% for all patients, 37% for all patients with asthma, and 46% for selected high-risk patients with asthma.

A total of 52% of respondents ascertain and document antihistamine use before each allergy shot, 20% for all immunotherapy patients and 32% for selected known high-risk immunotherapy patients. Overall, 81% recommend premedication to reduce the risk of immunotherapy reactions, 15% for all immunotherapy patients, and 66% for selected high-risk patients only.

Overall, 78% of questionnaire respondents give H-1 antihistamines alone or with other drugs to prevent or mitigate immunotherapy reactions, 10% give H-2 antihistamines, 14% give leukotriene receptor blockers, and 4% give other drugs.

As regards skin tests: 7% record the longest diameter of wheal, 31% record longest the diameter of wheal and erythema, and 14% record the longest diameter of wheal and erythema + the longest orthogonal diameter of each. A total of 27% record as a numeric score with the scoring criteria included when records are transferred, 12% as a numeric score without attaching scoring criteria, and 10% as a measurement of wheal and/or erythema + a numeric score.

Either the skin test record form or accompanying documentation when records are transferred list the type of skin test device for 49% of respondents, concentration of testing material for 58%, extract manufacturer for 38%,

anatomic location where skin tests placed for 36%, name of testing technician for 71%, and patient date of birth for 73%.

Immunotherapy prescription forms or accompanying documentation when records are transferred include the name of extract manufacturer for 59% of respondents, concentration of extract used for 92%, volumes of extract and diluent used for 85%, lot number of each extract present in each vial for 32%, expiration date of each extract present in each vial for 37%, and a vial expiration date not to exceed the expiration date of any individual ingredient for 71%.

Responses to the questionnaire indicate 4 areas in which data collection from interested Academy members who give immunotherapy under these circumstances may give us otherwise unavailable quantitative risk estimates. Three involve immunotherapy under conditions already identified by our Practice Parameters Task Force as probably associated with increased risk, although data are currently lacking to quantify that risk. These conditions are immunotherapy in patients receiving β -blockers, patients receiving ACE inhibitors, and patients receiving immunotherapy at home. The wide scatter in use of prophylactic medications before immunotherapy identifies this as another area worthy of study.

With regard to ACE inhibitors, case reports exist of anaphylaxis after both insect stings and venom immunotherapy,^{1,2} with 1 report suggesting that 24-hour interruption of ACE inhibitor dosing reduces the risk. However, no quantitative risk data exist. If enough AAAAI members are electing to offer immunotherapy to significant numbers of these patients and wish to share their safety experience, we may be able to estimate risk by tracking these patients prospectively.

It may be possible study the prophylactic value of H-1 and LTC receptor blockers, singly and in combination, in a similar prospective manner. The findings of Akdis et al³ that H-2 receptor activation is important for tolerance and successful immunotherapy is a reason not to include H-2 antihistamines in prophylactic regimens, at least initially.

Collection of safety data from members who have given immunotherapy to patients receiving β -blockers or at home and wish to share their data may permit quantitative estimation of the fatality risk of immunotherapy under those conditions.

No consistent difference was found in responses to questions asked in both 2004 and 2006.

In summary, variability continues to occur in the immunotherapy and allergy skin test practices of AAAAI member allergists. Unanswered questions include the safety of immunotherapy in certain medical conditions (eg, HIV, autoimmune disease), of immunotherapy administered without medical supervision, of immunotherapy with certain medications (eg, β -blockers, ACE inhibitors), and the role of prophylactic medications. Prospective studies may answer some of these questions, and retrospective data analysis may answer others.

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Vaccination with genetically modified birch pollen allergens: Immune and clinical effects on oral allergy syndrome

To the Editor:

Birch pollen-associated oral allergy syndrome (OAS) is mainly caused by IgE antibodies that cross-react with the major birch pollen allergen, Bet v 1, and with the major allergens from apple (Mal d 1), celery (Api g 1), and carrot (Dau c 1), as well as other plant-food allergens.¹⁻³ Preclinical data had indicated that vaccination with genetically engineered hypoallergenic derivatives of Bet v 1 (Bet v 1 fragments, Bet v 1 trimer) induced IgG antibodies that cross-react with Bet v 1-related plant-food allergens.^{4,5}

We have recently performed a preseasonal immunotherapy trial with the genetically engineered hypoallergenic derivatives of Bet v 1.⁶ Vaccination induced high levels of IgG antibodies that inhibited IgE recognition of Bet v 1, Bet v 1-induced release of inflammatory mediators, and Bet v 1-induced boosts of IgE production.⁶ In this substudy, we analyzed the effects of vaccination with genetically modified Bet v 1 derivatives on immune responses to food allergens in patients with birch pollen-associated OAS.

The subcutaneous injection immunotherapy study was conducted as a multicenter, placebo-controlled, double-blind randomized trial over a period of 12 months.⁶ Patients received 1 preseasonal treatment course with an equimolar mixture of Bet v 1 fragments,⁴ a hypoallergenic Bet v 1-trimer,⁵ or aluminium hydroxide alone (placebo). The study was approved by the local ethical committees, and written informed consent was obtained from each patient.

We analyzed 44 patients from 1 study center (Vienna; placebo: n = 19, fragments: n = 12, trimer: n = 13) who had allergic symptoms upon ingestion of birch pollen-associated plant food (apples: n = 42, hazelnuts: n = 36, carrot or celery: n = 21, other plant-derived foods: n = 16) and who had eaten the offending foods during the study