

RUSH IMMUNOTHERAPY

Harold S. Nelson, MD

Allergen-desensitization immunotherapy is the only potentially curative treatment for allergic asthma and rhinitis. Some physicians may view this form of immunotherapy as the last therapeutic resort for atopic disease, an option taken only when all other alternatives have failed. However, because of immunotherapy's unique ability to change the natural history of allergic respiratory diseases it is inappropriate to view it as only suitable for desperate cases. Immunotherapy is a reasonable option that can provide safe and cost-effective management for a substantial number of patients.

A form of immunotherapy often used at National Jewish is "rush immunotherapy", a name and approach that dates back 65 years, to an article written by the British physician John Freeman. The term "rush" derived from the relative speed at which the initial desensitization injections were administered. Our protocols today are less intense than the eight injections per day schedule first used by Freeman.

In a typical rush regimen at National Jewish an adult patient receives four injections daily, at hourly intervals, for five consecutive days; pediatric patients usually receive three injections daily at two-hour intervals. By the end of the fifth

day, the patient has usually been advanced to a maintenance allergen dose. In contrast, a patient who undergoes desensitization by a schedule of weekly injections would take six months to reach the same maintenance dose. Once maintenance

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is achieved, subsequent injections are given weekly, followed by a gradual progression to biweekly, and then monthly injections.

A graduated-dose desensitization program is necessary because the maintenance dose of antigen must be relatively large in order to be effective. The maintenance dose would cause a severe reaction in most patients who had not progressed through a series of desensitizing injections.

Immunotherapy candidates

Immunotherapy is an option for any patient with allergic rhinitis or asthma, although several other factors must also be considered when deciding whether to use immunotherapy. Two key criteria are the duration of the allergy symptoms each year, and the efficacy of other treatments in controlling symptoms.

Some allergies, such as those to animal dander, house dust mite, and mold, can occur year round. Other reactions, such as those to certain

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grass pollens, are limited to a few weeks each year. In general, patients with perennial or prolonged allergy seasons are better candidates for immunotherapy.

The increased number of available medications in recent years has provided

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patients with several therapeutic options that are often quite effective. These include cromolyn sodium inhalers, topical corticosteroids, and non-sedating antihistamines. The first two classes of drugs have become the main-

stays of asthma prophylactic therapy. It is not usually cost-effective to use immunotherapy in patients whose symptoms are well controlled by one of these treatments.

However, patients who require multiple medications to control their symptoms, or those who obtain limited symptom relief from these treatments are stronger candidates for immunotherapy. A general rule is that the more money it costs to control a patient's disease by symptomatic treatment, the more reasonable it is to consider immunotherapy as an alternative.

Age and the patient's health are two additional factors when deciding whether to use immunotherapy. The younger a patient is, the more apt we are to use immunotherapy. However, immunotherapy may still be a reasonable choice for a 60 year old who requires several drugs to control a perennial allergy. Once patients reach age 70, immunotherapy would rarely be a cost-effective option.

An additional factor is the cause of the patient's allergy, which relates to the quality of allergen extracts that are available for preparing the injection formulation. Some allergens, such as cat dander or pollens, make excellent extracts, while extracts from

dog dander and molds are rather poor. Immunotherapy is not as viable an option for patients with an allergy to dog, mold, or certain other allergens that lack good extracts.

Although rare, some patients can respond to a desensitizing injection with symptoms of anaphylaxis, including urticaria, angioedema, and hypotension. Asthmatic patients are prone to developing airway narrowing after allergy shots. Patients must be healthy enough to tolerate epinephrine, which is used when a patient has a severe reaction to a desensitizing injection. This criteria would preclude patients with arrhythmia or other significant heart disease.

Identifying the allergens

Once a patient is identified as a candidate for immunotherapy, the next step is to identify the allergens that cause symptoms in the patient and should be included in the injections. This is the facet of immunotherapy that requires the most insight and experience in treating allergies.

Skin testing is the basic way to identify a patient's allergies. The prick test panel used at National Jewish includes 24 different antigens when the patient has seasonal symptoms. We will use any one of 12 different panels, depending on the region of the United States where the patient lives. For example, we have antigen panels that apply to the Rocky Mountain region (Colorado, Idaho, Montana, Nevada, Utah, and Wyoming), the desert Southwest (New Mexico and Arizona), and the Pacific Northwest (Oregon and Washington). If the patient's symptoms are not seasonal, which suggests that pollens are not involved, then an eight-antigen panel is used.

The skin test results are tempered with the understanding that not all allergies may be relevant to a patient's symptoms. Two additional elements are critical comple-

ments to the skin test results: assessments of the patient's exposure, and of the patient's pattern of symptoms. These are identified by obtaining a careful, directed history that elicits the relevant information.

For example, skin testing may reveal that a patient is allergic to grass pollen. But if the patient's asthma occurs throughout the year and does not worsen in June, pollen is likely not a clinically relevant antigen, and immunotherapy for grass pollen is probably unnecessary.

Allergists or commercial laboratories

The importance of the patient's history and the ability to critically relate the information to the patient's allergic sensitivities means that it is less than ideal practice to start immunotherapy based on an in vitro IgE diagnosis alone. This is a service that has increasingly become available from commercial laboratories. They will accept a serum specimen from a patient, perform tests to determine the patient's prominent IgE reactivities, and formulate an immunotherapy mix of allergen extracts

based entirely on this information.

The efficacy of this approach was tested by me and my associates a few years ago. We arranged for 14 board-certified allergists to each

enroll 30 consecutive patients who were seen for the evaluation of rhinitis or bronchial asthma. Sera from 10 of each 30 patients were sent by us to a laboratory that routinely offered allergy diagnosis and recommendations for immunotherapy. The commercial laboratory used radioallergosorbent tests (RAST) to identify patient allergies. The laboratory's diagnoses and recommendations for allergy immunotherapy were compared to those made by the 14 participating allergists based on each

patient's history and skin tests results.

Overall, a diagnosis of allergy was made for 74 of 118 patients (63%) by the allergists and 59 of 118 patients (50%) by the laboratory. The higher number of allergic diagnoses by the allergists reflected the superior sensitivity of skin testing to RAST.

The laboratory recommended at least consideration of immunotherapy for all 59 patients found to have an allergy. In contrast, the allergists recommended immunotherapy for only 35 of the 74 patients they identified as having an allergy.

My associates and I also identified the "critical" antigens for immunotherapy of each allergic patient, based on the patient's skin-test results and history. Our determinations were considered the standard against which we compared the critical antigens identified by the allergists and the commercial laboratory. The allergists included all of the critical antigens for 80% of the 35 patients for whom they recommended immunotherapy. The commercial laboratory included all of the critical antigens for 49% of the 59 patients they said should consider immunotherapy.

Our results suggest that the appropriate diagnosis and treatment of allergic disease is best done by trained allergists. Although a commercial laboratory can provide a reasonably good identification of allergen-specific IgE, this information, even when accompanied by a written history supplied by the patient, is inadequate for deciding on therapeutic recommendations.

Administering immunotherapy

After a clinical diagnosis of allergy is made and it is determined that immunotherapy is appropriate, the panel of allergens is selected and an allergen extract is

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formulated using commercially-prepared extracts. Once we decide to proceed with immunotherapy we are liberal about including extracts in the formulation; any suggestion that an allergen is involved in a clinical response is sufficient cause for inclusion. The average patient receives a formulation that includes about 5-7 extracts.

I have already described the rush regimen we often use to bring a patient to maintenance dosing with immunotherapy, but of course some patients are less tolerant of the injections and proceed more slowly. We refrain from injecting asthmatic patients who have compromised pulmonary function just before the injection. The most common severe adverse effect from immunotherapy injections in an asthmatic patient is an asthmatic episode, which is often an exacerbation of preexisting chest tightness. Asthmatic patients routinely have their peak forced expiratory volume measured just before and 30 minutes after an injection to monitor their response. Patients without asthma are monitored by observation.

Compromised pulmonary function may be an important indication for immunotherapy in asthmatic patients. However, the need to withhold injections from asthmatic patients when they have impaired lung function may preclude ever achieving a maintenance dose. An advantage of rush immunotherapy is that it provides an opportunity to administer the entire course of allergen desensitization during a brief period that is outside of the patient's allergy season. In patients with year-round symptoms, a brief course of intensive asthma treatment may be given prior to and during the course of rush immunotherapy. This allows a physician to administer the immunotherapy regimen at a time when the patient's pulmonary function is optimal.

The definition of maintenance therapy for each patient is inexact. There is no reli-

able way to measure, on an individual basis, the impact of immunotherapy. Instead, we rely on data from controlled studies that established average allergen extract doses that improve allergy symptoms. These average doses are what we try to use for maintenance treatment.

For patients referred to National Jewish, the rush portion of their treatment is done at our center. When patients reach the maintenance phase they return home, and maintenance injections are administered by the referring allergist or primary care physician.

Expected Efficacy

After the first year of immunotherapy, responsive patients can expect a 50%-90% reduction in symptoms. However, these numbers are based on our experience with patients who remain on immunotherapy. A sizeable fraction of patients who start immunotherapy drop out, and we suspect that these dropouts include many who have a poorer response to treatment.

In general, patients will continue on immunotherapy for 3-5 years, and then stop for reevaluation. Gradually, a fraction of patients will relapse; in one prospective study, 5-10% relapsed during the first year off immunotherapy, 15% by the second year, and 30% by the end of the third year.

Patients who have a significant exacerbation of their allergies may be candidates for a second course of immunotherapy. In patients for whom the allergen extract mix is identical to their first course of treatment, an accelerated rush schedule can be safely used.

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Our new "DAY PROGRAM", offers a comprehensive approach to the diagnosis and management of respiratory diseases for pediatric patients. The new program was created in response to the nationwide ambulatory care trend and the need to decrease medical costs. Patients are evaluated and treated during the day on the children's and adolescent units at National Jewish, and they return to a hotel at night with their parents. Patients spend 10 hours a day, six days a week, at the Center for treatment and evaluation.

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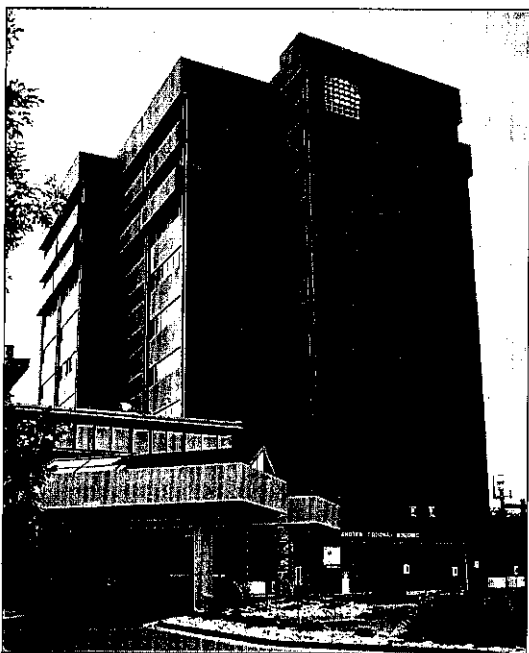


Photo by Lynda Miller

The entrance to the new Galter Pediatric Clinic is pictured above. Responding to national trends in health care delivery, National Jewish has completed a 15,000 sq. ft. addition to our outpatient clinic.

Commencing in October of this year, this facility will also house some University

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