

Immunotherapy in young children

To the Editor:

In a Rostrum article (J ALLERGY CLIN IMMUNOL 1994;94:662-5) Ownby and Adinoff discuss skin testing and allergy immunotherapy in young children (defined as younger than 5 years of age). It is stated that "Current evidence suggests that young children are at increased risk for systemic reactions from immunotherapy." This observation is contrary to our personal experience in that during conventional immunotherapy, systemic reactions occur much less frequently in children of all ages than they do in older patients.

The statement by Ownby and Adinoff is apparently based on a study by Hejjaoui et al.¹ published in the JOURNAL in February 1990. This study involved the administration of *Dermatophagoides pteronyssinus* in four different immunotherapy protocols. One subgroup of 290 patients aged 3 to 64 years received a 3-day rush program of immunotherapy to this antigen while hospitalized. The incidence of systemic reactions was slightly higher in the young children of this group. The other three subgroups were not analyzed by age because of inadequate numbers of systemic reactions. The data in this study are insufficient to make the generalization that young children are at increased risk for systemic reactions from immunotherapy, especially if a conventional protocol is being followed.

We fully agree with the implication that the need for immunotherapy in young children should be carefully substantiated and that it is probably relatively less commonly indicated than in other age groups with allergic illness. Less use of immunotherapy in this age group is because of the effectiveness of symptomatic treatment measures and relatively easier steps for environmental control, not because of an increased incidence of systemic reactions.

S. Scott Nicholas, MD
Clinical Associate Professor
University of Minnesota
Department of Internal Medicine
Eisenstadt Associates in Allergy and Asthma
221 Medical Arts Building
825 Nicollet Mall
Minneapolis, MN 55402

REFERENCE

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Reply

To the Editor:

In his letter Dr. Nicholas states that in his opinion, systemic reactions to immunotherapy occur less frequently in children of all ages than in older individuals. This is consistent with the data presented in Fig. 4 of the study by Hejjaoui et al.,¹ which showed a trend of

increasing rates of systemic reactions for age groups from 6 to 9 years to 31 to 40 years. However, the rate of systemic reactions was still higher in the 3- to 5-year age group than in the 31- to 40-year group and close to twice the rate of the 6- to 9-year and 10- to 15-year age groups.¹ The article by Hejjaoui et al.¹ is a study of rush immunotherapy in which the reaction rates were substantially higher than those we have observed with slower rates of immunotherapy advancement.² We recognize that reaction rates for different age groups during rush immunotherapy may not be directly comparable to reaction rates with immunotherapy administered in clinical practice, but this was the only study we found that provided comparison data.

The point we wished to make from the article of Hejjaoui et al.¹ is that allergists who care for children should not necessarily assume that those of younger than 5 years of age will react to immunotherapy in the same way that older children do. In light of the caution suggested by the data of Hejjaoui et al.,¹ we believe that those who advocate immunotherapy in young children should find or produce more than anecdotal data about the safety of immunotherapy in this age group.

Dennis R. Ownby, MD
Division of Allergy and Clinical Immunology
Henry Ford Health System
2799 West Grand Blvd.
Detroit, MI 48230

Allen D. Adinoff, MD
Colorado Allergy and Asthma Clinic
1450 S. Havana St.
Suite 500
Aurora, CO 80012

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Splenomegaly in idiopathic hypereosinophilic syndrome

To the Editor:

The insightful article by Butterfield and Gleick (J ALLERGY CLIN IMMUNOL 1994;94:1318-26) on treatment of idiopathic hypereosinophilic syndrome (IHS) with interferon- α was read with interest. I question whether all of their patients had IHS. Four of the six patients they reported on had splenomegaly, but chromosomal studies were done on only one patient. Splenomegaly (46%) and lymph node enlargement (14%) occur in IHS; however, patients usually have chromosomal analysis to exclude underlying disorders.¹ I would like to use the following case to exemplify the need to perform chromosomal

studies to exclude lymphoma in cases of "IHS" with adenopathy or splenomegaly.

The patient is a 28-year-old man who was first thought to have an atypical presentation of eosinophilia myalgia syndrome (EMS). His symptoms developed while he was taking a bodybuilding vitamin supplement. On presentation he had weight loss, myalgias, fever, night sweats, and fatigue. Results of an extensive workup, including bone marrow and lymph node biopsies, were negative except for an elevated aldolase level and erythrocyte sedimentation rate and diffuse lymphadenopathy with splenomegaly. Biopsy specimens revealed "benign reactive hyperplasia with eosinophil infiltrate." The patient continued to have an atypical presentation of EMS and required high-dose steroids to control his symptoms and hypereosinophilia. The diagnosis of IHS was considered after the analysis of the vitamin supplement was negative for L-tryptophan. The patient met the diagnostic criteria for IHS.¹ Repeat workup was initiated, which again included bone marrow and lymph node biopsies. Results of the workup were consistent with IHS until immunofluorescence studies were done. An increased number of CD4 lymphocytes in lymph node tissue was found. Cytogenetic studies were positive for a monoclonal lymphocyte proliferation of a T-cell line with an aberrant T-cell receptor beta chain. This is consistent with a T-cell lymphoma. Measurement of serum cytokines revealed an elevation of IL-5 before administration of steroids and a normal IL-4 level. Serum IL-5 was suppressed by steroids. The lymph node findings and the hypereosinophilia suggested Lennert's lymphoma.² The patient was treated with cyclophosphamide, prednisone, vincristine, and doxorubicin and is now in remission. This case emphasizes that IHS is an idiopathic syndrome and that other diagnoses, including lymphoma, need to be excluded. This is especially true of patients with IHS who are first seen with lymphadenopathy or splenomegaly. Although infrequent, lymphoma limited to the spleen does occur. Most cases of lymphoma confined to the spleen are diagnosed by splenectomy.³ Fine needle biopsy of the spleen may be an alternative.⁴ A lymphoma may require chromosomal studies to be excluded. Translocations involving the B- or T-cell receptor are found in about 70% of cases of non-Hodgkin's lymphoma.⁵ Undertreatment of hypereosinophilia, especially if the primary disease is a lymphoma, may limit the prognosis.

Timothy J. Craig
Jane K. Moeckli
University of Iowa
200 Hawkins Dr.
Iowa City, IA 52242
Steven D. Mawhorter
National Institutes of Health
Bethesda, MD

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Reply

To the Editor:

Dr. Craig reports a patient with marked peripheral blood eosinophilia in whom T-cell lymphoma was discovered by immunofluorescent staining of lymph node tissue and by molecular genetic studies. These tests identified a monoclonal lymphocyte proliferation of T cells with an aberrant T-cell receptor beta chain. Close monitoring of all patients with prolonged blood eosinophilia is indicated because chronic myelocytic leukemia, lymphoma, or lymphoblastic leukemia may eventually occur.

In our experience, routine cytogenetic studies to identify chromosomal abnormalities on bone marrow aspirates of patients with idiopathic hypereosinophilic syndrome (IHES) have not been fruitful. We reported cytogenetic results on one of our six patients; however, cytogenetic studies were actually performed on four patients (including studies on splenic tissue from one patient), and all were negative for chromosomal abnormalities.

As Dr. Craig points out, immunofluorescent and molecular genetics studies of lymph node tissue, when adenopathy is found, are indicated in patients with IHES; and the presence of lymphadenopathy should alert the physician to the possibility of an underlying disorder. Routine splenectomy in patients with IHES, though, is probably not indicated; and in the one patient in whom cytogenetic studies were done on splenectomy tissue, no chromosomal abnormalities were found. We have witnessed suboptimal or little response to interferon- α therapy in two patients initially diagnosed with IHES: in one acute lymphoblastic leukemia subsequently developed, and in the other a T-cell lymphoproliferative disorder was found.

J. H. Butterfield, MD
G. J. Gleich, MD
Mayo Clinic
200 First St., SW
Rochester, MN 55905
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