

Correspondence

Better drug trials: Reply

To the Editor:

Dr. Kelso¹ has written concerning what he perceives as a flaw in our study of fluticasone (Chervinsky P, Van As A, Bronsky EA, et al. Fluticasone propionate aerosol for the treatment of adults with mild to moderate asthma. *J ALLERGY CLIN IMMUNOL* 1994;94:676-83). We believe that our trial design was an improvement over previous similar trials and will lend itself to a better comparison of new and old drugs. In addition, the use of predetermined patient stability criteria can guard against severe deterioration and may be applicable in clinical management. However, Dr. Kelso believes, and justifiably so, that the most important factor is whether the drug is better than those currently available. Before this judgment about a new product can be made, however, it is necessary to assess the dose of the new preparation to be used and to establish efficacy. Only after these studies are done is it appropriate to do comparative studies. I am sure that Dr. Kelso can look forward to the publication of these studies now that the basic work has been completed. I am unaware of any drug development program that has not been conducted in this fashion. The most important question that the drug companies and the clinical investigator must answer is whether the new product is better than currently available products. If it is not, why would a drug company want to market the product?

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REFERENCE

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1/8/67049

Bronchial asthma caused by onion

To the Editor:

I read with great interest the article "Bronchial asthma, rhinoconjunctivitis, and contact dermatitis caused by onion" by Valdivieso et al. (*J ALLERGY CLIN IMMUNOL* 1994;94:928-30). They demonstrated IgE-specific antibodies against the onion with both skin and in vitro tests. But they did not comment on other possibilities of hypersensitivity caused by onions. Some studies have shown that platelet aggregation is inhibited by both onion (*Allium cepa*) and garlic (*Allium sativum*). Makheja et al.¹ reported that chemically similar compounds contained in both of these *Allium* species inhibit platelet aggregation by blocking thromboxane synthesis. Recently, Kawakishi and Morimitsu² found a new inhibitor

of platelet aggregation in onion oil. Bayer et al.³ isolated inhibitors of cyclooxygenase and lipoxygenase in onions and named these compounds *cepaenes*.

Is there any possibility that bronchial asthma and rhinitis caused by onion was induced by a mechanism similar to that in aspirin-sensitive asthma?

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1/8/64825

Reply

To the Editor:

Our article "Bronchial asthma, rhinoconjunctivitis, and contact dermatitis caused by onion" (*J ALLERGY CLIN IMMUNOL* 1994;94:928-30) was published as a "Brief communication." Eventually, we would like to expand our work regarding onion hypersensitivity and other interesting properties of *Allium* family.

We found in our patients that IgE and cell-mediated mechanisms were active, but we do not discount the possibility that in other patients the mechanisms mentioned by Dr. Hiroshi Kawane may be present, although this must be investigated.

We thank Dr. Kawane for his interest and comments about our research.

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1/8/64824

Allergen immunotherapy in young children

To the Editor:

I am writing to comment on the article entitled "Rostrum: The appropriate use of skin testing in allergen immunotherapy in young children" by Dr. Dennis Ownby and Dr. Allen Adinoff (*J ALLERGY CLIN IMMUNOL* 1994;94:662-5). Several situations have not been considered in this report, and I believe these situations are important and might modify the authors' conclusion that immunotherapy is relatively contraindicated in young children. Many children are allergic to cats. It has

been my experience that cat owners are a breed unto themselves and are often reluctant, if not completely unwilling, to remove the cat from the house. In this situation, exclusion of the cat from the bedroom, perhaps associated with regular washing of the cat (if possible), should be tried. In those situations in which this is unsuccessful, many of the children have chronic, recurrent asthma. If there is no alternative to removal of the cat and these children do not respond to symptomatic treatment, immunotherapy has been extremely helpful.^{1,2}

The authors concentrate on the psychologic factor of allergy injections. There is no comment on the psychologic factor of chronic asthma. Many children with chronic asthma require repeated bursts of oral prednisone. This is usually given in a liquid form, which has a very unpleasant taste. Although this medication is usually effective, there are unpleasant side effects that range from hyperactivity to depression with steroid therapy. No mention is made of the emotional impact of these medications or of the effect of recurrent wheezing. Immunotherapy is certainly, in my opinion, indicated when children require 3 to 4 bursts of prednisone in 1 year and are otherwise receiving optimal therapy. At present, no nebulized form of corticosteroids is available in this country. Administration of corticosteroids through a metered-dose inhaler with a spacer device is not always satisfactory in young children. When other medications are not effective, according to the guidelines of the National Heart, Lung, and Blood Institute Consensus Report,³ immunotherapy may decrease the need for repeated doses of steroids. Immunotherapy would not appear to be contraindicated in these situations.

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2. Counsell CM, Greenstein JL, Garman RD, Ohman JL. Cat immunotherapy decreases T cell reactivity and skin test reactivity to *Fel d* I, the major allergen of cat allergy [Abstract]. *J ALLERGY CLIN IMMUNOL* 1994;93:231.
3. National Heart, Lung, and Blood Institute. Guidelines for the diagnosis and management of asthma. Washington, DC: US Dept of Health and Human Services; 1991. US Dept of Health and Human Services publication no. 91-3042.

1/8/65914

Reply

To the Editor:

Dr. Wolf raises two important points in favor of immunotherapy in young children. The first point is the

potential use of immunotherapy to treat cat allergy in children living with cats in their homes. The second point is the relative risks, psychologic and otherwise, of immunotherapy versus recurrent asthma or medication side effects.

We agree with Dr. Wolf that it is difficult and frequently impossible to convince cat-loving parents to remove cats from the home for the sake of their child's health. On the basis of our work concerning the dispersal of cat allergen on clothing and the failure of washing to reduce cat allergen shedding, we do not believe that keeping the cat out of the child's bedroom and washing the cat are clinically effective in most cases.^{1,2} A very difficult part of this problem is the question of how forceful allergists should be in their efforts to remove cats from the homes of children allergic to cats. If we say, "Get rid of the cat!" but then offer immunotherapy as an alternative, it is unlikely that many cats will become homeless. We should ask ourselves whether it is ethical to give a child any therapy with potential significant side effects, either immunotherapy or oral prednisone, just so parents can keep their cats.

A critical question is the effectiveness of cat allergen immunotherapy for asthma in children. Several blinded, controlled studies including those by Taylor et al.,³ Ohman et al.,⁴ Van Metre et al.,⁵ and Alvarez-Cuesta et al.⁶ have evaluated cat immunotherapy. These blinded studies, in teenagers and adults, have shown that immunotherapy can modestly increase the dose of allergen required to produce positive skin test results and cause a 20% fall in forced expiratory volume in 1 second, but there is no evidence that this degree of change is sufficient to reduce the medication requirements of patients with cat-sensitive asthma who are living with cats.

Dr. Wolf's second point concerns the psychologic risks of immunotherapy versus pharmacotherapy. Contrary to Dr. Wolf's statement, in the *Rostrum* article we did state that "The possible risks of psychologic trauma from immunotherapy or any other treatment must be balanced against the known risks of poor control of chronic allergic disease, especially asthma." Among the known risks of poor control of asthma are psychologic problems.^{7,8} Unfortunately, the double-blind study presented by Adkinson et al. at this year's Academy meeting failed to show any effect of immunotherapy on the course of asthma in children.⁹ Children receiving immunotherapy required as many days of glucocorticoid therapy as children receiving placebo therapy.⁹

On the basis of available information, we still believe that the potential risks of immunotherapy are justified only if immunotherapy can be shown to be safe and effective in children younger than 5 years of age. We believe that the available evidence supports the benefit of cat immunotherapy in asthmatic patients allergic to cats who have episodic cat exposure, but that this benefit

been my experience that cat owners are a breed unto themselves and are often reluctant, if not completely unwilling, to remove the cat from the house. In this situation, exclusion of the cat from the bedroom, perhaps associated with regular washing of the cat (if possible), should be tried. In those situations in which this is unsuccessful, many of the children have chronic, recurrent asthma. If there is no alternative to removal of the cat and these children do not respond to symptomatic treatment, immunotherapy has been extremely helpful.^{1,2}

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is unlikely to be clinically apparent in patients who continue to live with cats. No studies of cat immunotherapy in young children have been done, and current evidence does not demonstrate a steroid-sparing effect of polyallergen immunotherapy in asthmatic children.⁹ If allergists are to remain credible, we must base our practice of medicine on available scientific evidence and not on our personal beliefs or anecdotal experience.

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