

additives (such as epinephrine) or preservatives in the injectable local anesthetics implicated in the original, initial adverse reactions. For example, Novocaine, brand of procaine, contains Na bisulfite. Likewise, Xylocaine, brand of lidocaine (possibly the most commonly used injectable local anesthetic), contains methylparaben in certain vials without epinephrine and Na metabisulfite (with or without methylparabens) in certain vials with epinephrine.

Furthermore, certain vials of Carbocaine, brand of mepivacaine, contain methylparaben, and Carbocaine with neocobefrin, contains Na bisulfite, but 3% Carbocaine injectable in 1.8 ml dental cartridges contains no preservatives, whereas Marcaine, brand of bupivacaine, contains methylparaben. Those with epinephrine contain Na bisulfite. *Facts and Comparisons*, published by J. B. Lippincott Co., lists a wide variety of other brands and preparations of injectable local anesthetics that do or do not contain preservatives. Such variety makes it difficult indeed to obtain accurate past histories.

Although the article by Chandler et al. indicates that challenges were made with local anesthetics free of epinephrine or other vasoconstrictors, no mention is made of preservatives in the test and challenge solutions. If the test solutions were preservative free, consideration must be given to the possibility that failure to react on rechallenge may be explained by the fact that some of the original adverse reactions were due to preservatives. Demonstration of sensitivities to preservatives, especially sulfites, in injectable local anesthetics is an important subject for investigation and may prove to be a crucial factor in the selection of that type of drug for use in the future.

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Reply

To the Editor:

The letter of Dr. Ostrov outlines the complexity of dealing with potential problems of pharmacologic products that must be administered for the best interests of a patient.

The provocative test dosing protocol is conducted with the local anesthetic product that will actually be used by the referring physician, surgeon, or dentist. Thus, although the test dosing is primarily done for the local anesthetic, the protocol also is a test dose for additives or preservatives. At the conclusion of a successful test dose, the patient and referring professional are informed that the patient has received that dose of the preparation without reaction and is at no greater risk than the general population.

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Allergenic cross-reactivity among legume foods

To the Editor:

We would like to offer the following comments to the readers of *THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY* with respect to the article by Barnett et al.,¹ concerning allergenic cross-reactivity among legume foods that appeared in the March 1987 issue of the *JOURNAL*. In our opinion, this study makes some very useful in vitro observations about cross-reactivity among legumes, but it draws unsupported clinical conclusions based on these in vitro measurements. In the Introduction, there appears the statement that "Multiple allergies to a number of the legumes are frequently observed." No reference is offered as a basis for this statement. In the Discussion, the statement is made that "... the results of this article suggest that exclusion from the diet of the whole legume group is indicated where strongly positive diagnosis indicates hypersensitivity to one of the highly cross-reactive legumes." This statement appears to be based on the in vitro studies performed by these authors. The major weakness of this article is that no challenge studies were performed to test the hypothesis that the in vitro studies of cross-reactivity have clinical relevance.

In studies from our groups, we have rarely found clinical significance to the theory of frequent cross-reactivity between members of botanic food groups, including the legumes. Examination of the results from all of the double-blind, food-challenge studies in the literature reveals that an adverse reaction to a single food is by far the rule and that, when multiple food reactions are reproduced, it is most often caused by foods that are botanically unrelated, such as peanut and egg or milk and soy.²⁻⁶ It might even be speculated that botanical relationships are rather irrelevant compared to antigenic relationships that have yet to be discovered.

Recommendations based on botanical relationships, whether or not they have in vitro correlates, cannot be made, even to patients who have double-blind, placebo-controlled food challenge-confirmed hypersensitivity to a legume. For some time we have been trying to persuade our colleagues to examine each food for which there is a history of an adverse reaction and a positive puncture skin test by double-blind, placebo-controlled food challenge. Skin tests, RASTs, and other in vitro tests cannot substitute for proper clinical observations if we are to be of maximum service to our patients at this time. We take exception to the first sentence in the Discussion that states that "... multiple food allergy among the legumes is likely to be common." Much clinical work, including hundreds of blind-food chal-

lenges, refute this statement. If the authors have data to support their claim, it should have been included. The authors also suggest that their data may have relevance to immunotherapy, an approach with no scientific validation at this time.

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Reply

To the Editor:

Before replying to the criticisms of our article, as presented in the letter by Professors Bock, Atkins, and Sampson, we would like to make it clear that we agree that skin prick tests, RAST, and other in vitro tests cannot substitute for proper clinical evaluation, including, where it is appropriate, double-blind food challenges.

Our article was directed to “examine the possible occurrence and extent of allergenic cross-reaction between commonly eaten legumes,” as stated in the final paragraph of the introduction. In vitro techniques are most appropriate for this purpose, since any multiple allergies indicated by in vivo tests could be due to separate sensitization. Challenges were not therefore carried out and, indeed, were avoided in this study because of the possibility of severe reaction to such challenges (detailed in Table I). This is in sharp contrast to the work referred to in the clinical studies

of Bock et al. (see letter this issue) in which most of the patients were reported as suffering comparatively mild symptoms. Three of the articles referred to in the letter concern mainly cutaneous reactions to food, and those patients with anaphylactic reactions were wisely excluded.

Our replies to some of the specific criticisms are as follows:

1. *Multiple allergies to a number of legumes are frequently observed.* This comment was based partly on our experience with the sera of more than 200 peanut-sensitive patients, for which RAST tests with allergen disks (many of which are not commercially available) indicated that almost all the sera contained measurable IgE antibody not only to peanut but also to another legume or legumes. Our clinical colleagues have informed us of many cases in their experience of multiple legume allergies with clinical manifestation. Fries^{1,2} studied two groups of 30 patients, one group, sensitive to peanut, and the other group, to soybean. Of these, 18 and 27 patients, respectively, were also positive by skin prick tests to other legumes. Fries reported three such cases in detail in which severe symptoms were produced on exposure to peanut, peas, and lentils or peanut, soybean, and pea. Speer³ specifically mentions, in his article on multiple food allergy, the close allergenic relationship of peanut to pea and beans.
2. *Botanical relationships are irrelevant.* There are numerous references in the literature that appear to refute this statement. To quote from Fries¹ again, “Usually patients reactive to one member of a large family food group, such as the legume family, are reactive to other members of that botanical family.” A similar point was made in the study of cereal allergies by Sutton et al.⁴ in which the apparent allergenic cross-reactivity of wheat, rye, and barley was explored. Perlman⁵ gave a balanced summing up by pointing out that clinical experience is the final basis for the determination of food allergy and also emphasizing that foods of a single family may possess some common allergens. This latter statement is also supported by the results of our IgE-binding study of lectins from different legumes.⁶
3. Finally, there is the sentence dismissing as invalid the practice of immunotherapy as a treatment for allergies. We have only suggested that clinicians take our in vitro results into account if immunotherapy is contemplated. Such treatment is rarely carried out for food allergies,⁷ although it has been used with success for some inhalant allergies.⁸ Since it is true that the precise mechanisms operating in immunotherapy are not clear, the relevance of in vitro results needs to be considered.

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