

IgE-mediated reaction to a banana-flavored drug additive

To the Editor:

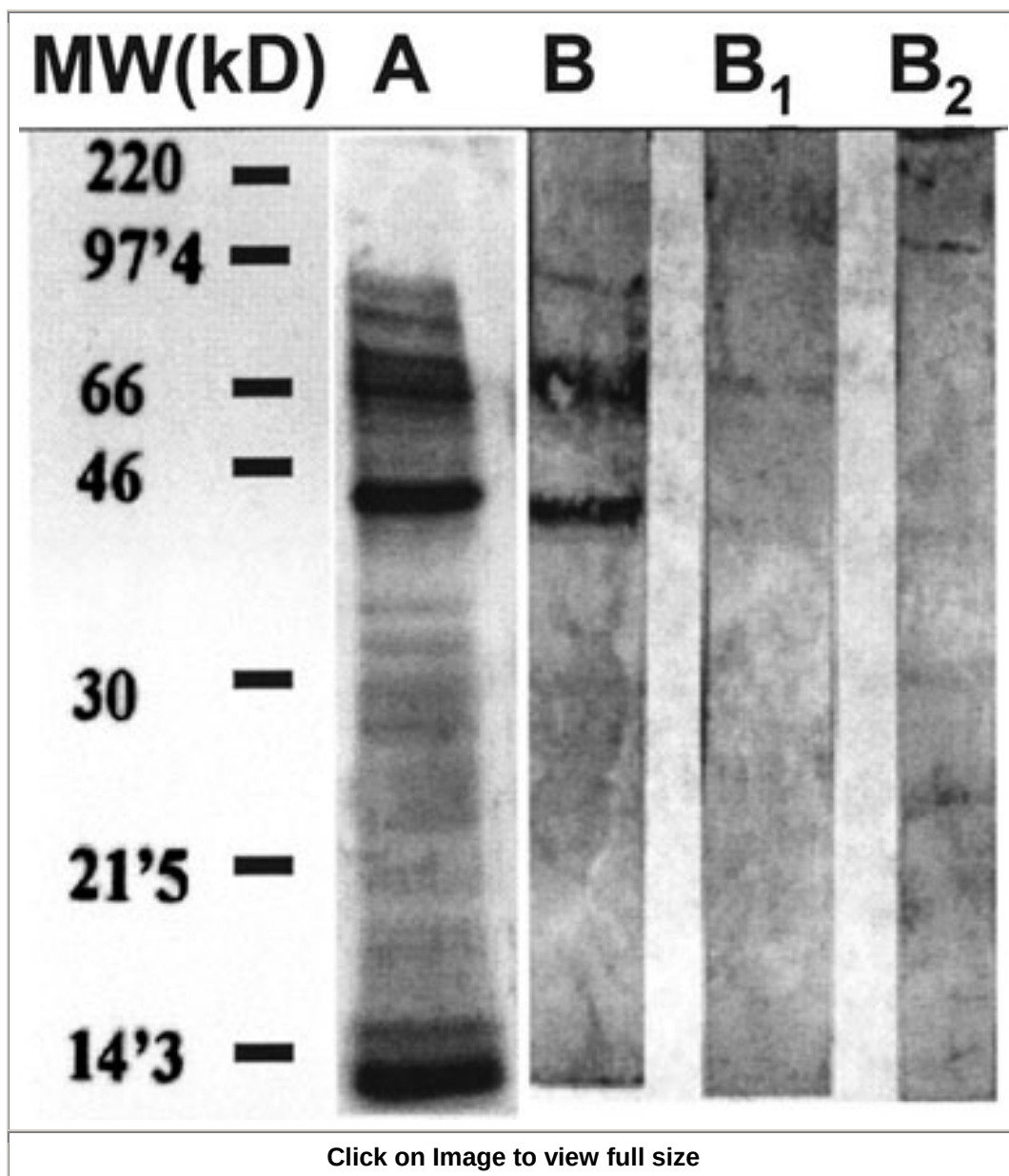
Potential drug allergens in IgE-mediated penicillin-adverse reactions include polymers, hapten-protein conjugates, impurities, and additives. However, true hypersensitivity to additives such as dyes, preservatives, and antiseptics has rarely been proved.

We describe an 8-year-old girl in whom oral itching with wheals developed over her face and trunk and angioedema developed on both eyelids within 1 hour of receiving her first oral dose of 250 mg of Penilevel (Laboratorios ERN SA, Barcelona, Spain) containing phenoxy-methyl-penicillin and banana essence as a flavoring additive. Symptoms resolved within 24 hours after treatment with antihistamines. She had tolerated 2 previous doses of intramuscular injections of Penilevel containing only the active ingredient. She had previously been found to have hay fever and oral allergy syndrome to several vegetables (celery and carrot) and fruits (banana, peach, melon, and watermelon).

After a washout period, prick and intradermal skin tests with benzylpenicilloyl polylysine, minor determinant mixture, penicillin G, and phenoxy-methyl-penicillin yielded negative results. A commercial skin prick test with banana yielded negative results, but a prick-prick test with fresh fruit elicited a positive wheal reaction (11 × 7 mm). The total IgE level was 71.7 kU/L. The specific IgE response to penicillin G, penicillin V, and amoxicillin was negative and to banana was 1.25 kU/L (class II, CAP system; Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden). After parental informed consent was obtained, oral open challenge with active principle, phenoxy-methyl-penicillin, in increasing amounts to therapeutic dose, was well tolerated.

Pure banana essence and banana extract were purified by a gel-filtration and desalting column with a polyacrylamide column (BioGel P-6DG columns; BioRad Laboratories, Hercules, Calif). Total protein concentrations of 0.2 mg/mL of each were used for SDS-PAGE and immunoblotting with serum of the patient. Results are presented in Fig 1.

Fig. 1. Immunoblotting experiment. *Lane A*, Immunoblot with processed banana extract demonstrating serum-specific IgE against proteins ranging from 14 to 97 kd. *Lane B*, Immunoblotting with processed banana essence showing IgE-binding proteins ranging 30 to 66 kd. *Lane B₁*, Banana essence inhibited by banana fruit showing that antigenic components were homologous in both extracts. *Lane B₂*, Banana essence inhibited by banana essence. *MW*, Molecular weight.



We present a case of urticaria and angioedema by sensitization to a flavoring excipient contained in a pediatric drug. A type I hypersensitivity to essence was strongly suggested by the results of SDS-PAGE immunoblotting. Allergic reactions to hidden allergens, although infrequent, are increasingly being reported. Some studies reveal that as much as the 30% of the anaphylactic shock episodes are due to a hidden or inadvertently consumed allergen. In addition, 10.2% of anaphylactic shocks are considered idiopathic, raising the hypothesis of allergy to masked food allergens.¹ It is also known that some proteins usually contained in vaccines of live attenuated virus, which have been cultured in chicken embryo fibroblasts, potentially may be dangerous, and caution must be exercised in children allergic to egg protein.² More recently, several cases of IgE-mediated reactions to gelatin as hidden allergen in vaccines³ or foods,⁴ as well as hyaluronidase in pediatric oncologic drugs,⁵ have been reported.

Natural and artificial fruit essences such as strawberry, banana, or peach are commonly used as flavoring agents in drugs in the pediatric pharmacopoeia, like some antibiotics, nonsteroidal anti-inflammatory drugs, anticonvulsants, or antihistamines. Natural fruit components may be also present in essences or syrups.

In vitro studies with fruits and some other extracts that contain high amounts of carbohydrates are difficult. For that reason we processed our extracts through a desalting gel-filtration column to improve the resolution of the studies, and we were able to disclose the allergenic proteins present in the banana essence. We could demonstrate that those proteins were also present in the banana fruit to which the patient was allergic. Besides coincidental reactions, the possibility of an iatrogenic adverse effect caused by excipient sensitization should be considered in atopic patients with food allergy. The inclusion of the excipients in the allergologic study could exclude the responsibility of the β -lactamic component in the reaction of this patient. We believe that the study of food additives in drug allergy should always be considered.

1/8/111239

doi:10.1067/mai.2000.111239

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