

and bedding encasements⁷ was not sufficient to produce a sustained beneficial reduction in mite allergen levels. This could be related to the persistence of reservoirs such as mattress bases, because mites can disperse from one location to another within a short period. To rationalize allergen avoidance, advice should be given concerning mattress bases. Box springs, the usual mattress bases in the United States, can be encased. If encasing does not seem feasible, slatted bases are an alternative.

We thank Dr. Guy Hedelin for skillful assistance with the statistical analysis and Mrs. Béatrice Oesterlé for preparing the manuscript.

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IgE-mediated systemic reactions to gelatin included in the varicella vaccine

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Anaphylactic reactions to measles, mumps, rubella, and the combined measles-mumps-rubella (MMR) vaccines have been frequently reported and have been suggested to be caused by allergy to the egg proteins contained in the vaccines.¹ However, the anaphylactic reactions have been reported to occur after administration of the MMR vaccine in children who tolerated eggs.¹ Recently, Kelso et al.² reported that a patient who experienced anaphylaxis in response to the MMR vaccine had IgE antibodies to gelatin detected by an immunoblotting method. Previously, we found that 10 of the 11 children who experienced anaphylactic reactions to measles or mumps vaccine had anti-gelatin IgE

Abbreviation used

MMR: Measles-mumps-rubella

antibodies, and we assumed that most of the reactions were caused by the gelatin contained in the vaccine.³

In Japan the varicella vaccine that contains gelatin has been licensed for administration to normal and high-risk children since 1986.⁴ This vaccine has protected children against varicella infection. Its safety has been confirmed in clinical trials,⁴ and anaphylactic reactions to this vaccine have not been reported previously.

In this study we report four children who had IgE-mediated systemic reactions to the varicella vaccine. To clarify the relationship between the gelatin in the vaccines and the reactions, we measured the anti-gelatin IgE antibody.

METHODS

Physicians and vaccine manufacturers sent serum samples from four children with anaphylactic reactions to varicella vaccination together with clinical reports to the Japan National Institute of Health. As a negative control, serum samples from 50 children (1 to 4 years old; mean age $\pm$ SD, 2 years 4

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J Allergy Clin Immunol 1997;99:263-4.

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0091-6749/97 \$5.00 + 0 1/54/77911

TABLE I. Clinical and laboratory findings for children with IgE-mediated systemic reactions to the varicella vaccine*

Patient no.	Age	Sex	Allergic reaction	Specific IgE to gelatin (Ua/ml)
1	4 yr 0 m	M	Urticaria, vomiting, airway obstructions with wheezing	11.5
2	1 yr 4 mo	M	Urticaria, angioedema, airway obstruction with wheezing	1.4
3	1 yr 10 mo	M	Urticaria, wheezing, cough	5.6
4	4 yr 8 mo	M	Urticaria	11.0

*Fifty children who had no reaction to the vaccine and no anti-gelatin IgE served as a negative control group.

months $\pm$ 1 year 1 month) who had no allergic reaction to the varicella vaccine were kindly supplied by Dr. Takao Ozaki of Showa Hospital, Konan, Japan. The live varicella vaccine is derived from infected human embryo lung cells. The vaccine contains both bovine gelatin (1 mg/shot) and hydrolyzed gelatin (12.5 mg/shot) as a stabilizer. IgE antibody to bovine gelatin (Wako Junyaku, Tokyo, Japan) was measured by Pharmacia CAP system (Pharmacia, Uppsala, Sweden), which is a solid-phase immunoassay and a standard assay method for the specific IgE antibody.³

CASE REPORTS

Clinical and IgE data for the four children are shown in Table I. In patient 1, the anaphylactic reactions (generalized urticaria and pruritus, vomiting, and airway obstruction with wheezing) were observed within 40 minutes after administration of the varicella vaccination. The patient immediately received the necessary treatment, and the symptoms disappeared several hours later. By the next morning, his condition was normal.

In patient 2, anaphylactic reactions (generalized urticaria and pruritus, angioedema around the eyes, and airway obstruction with wheezing) began 20 minutes after administration of the vaccination. He received the necessary treatment, and the main allergic symptoms disappeared 30 minutes later. During observation for several days, he had no significant allergic reactions.

Patient 3 experienced generalized urticaria, wheezing, and coughing 1 hour after the vaccination. He immediately received the necessary treatment, and the reactions disappeared the next day.

Patient 4 experienced only generalized urticaria, beginning 20 minutes after the vaccination. He immediately received the necessary treatment, and the reaction disappeared 6 hours later. In the prick test, 1% gelatin solution caused wheal (23 $\times$ 13 mm) and erythema (40 $\times$ 38 mm). Interestingly, he had experienced systemic urticaria four times after eating gelatin-containing food before the vaccination. We suspected that he had a food allergy to gelatin (a double-blind controlled study has not been done).

DISCUSSION

We found that one patient had experienced the allergic reaction to food containing gelatin. Previously, we

reported that some children who had IgE-mediated systemic reactions to measles and mumps vaccines also had allergic reactions to foods containing gelatin before or after vaccination.⁵

The four children in this study had anti-gelatin IgE values ranging from 1.4 to 11.5 Ua/ml (Table I). All of the 50 children who had no reaction to the vaccine (negative control group) had no anti-gelatin IgE antibody. No etiologic relationship exists between egg proteins and anaphylactic reactions to the varicella vaccine, because this vaccine is derived from human embryo cells. These findings suggest that such reactions in children are caused by the gelatin contained in the vaccine.

The varicella vaccine is produced by only one vaccine manufacturer in Japan. A large amount of gelatin and hydrolyzed gelatin (13.5 mg/shot) is needed to maintain virus infectivity in the vaccine. The varicella vaccine containing gelatin must be used with the same caution as the MMR vaccine.

We thank the vaccine manufacturer for assistance with the serum sampling.

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