

IgE antibody to gelatin in children with immediate-type reactions to measles and mumps vaccines

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Many cases of anaphylactic reactions, to measles, mumps, and rubella (MMR) vaccines have been reported.¹ Anaphylaxis to the vaccines has been suggested to be caused by the allergy to egg proteins in the vaccines.¹ However, this immediate allergic reaction after MMR vaccines has also been described in children who tolerated eggs.² This reaction might be due not only to egg proteins but also to some other vaccine constituents. Recently, Kelso et al.³ reported that a child who had anaphylaxis to MMR vaccine had IgE antibody to gelatin detected by an immunoblotting method, and they concluded that this anaphylaxis was caused by the gelatin included in the vaccine.

In this study to elucidate the relationship between the gelatin in the vaccines and the immediate-type reactions, including anaphylaxis, we measured anti-gelatin IgE antibody by the CAP system (Pharmacia, Uppsala, Sweden) in the sera of 11 vaccine recipients with immediate-type reactions and in the sera of 24 vaccine recipients with nonimmediate-type reactions associated with measles and mumps vaccines.

METHODS

Sera

Physicians and some vaccine manufacturers sent sera from 35 children along with clinical reports to Japan National Institute of Health in 1994. Table I shows the clinical characteristics of 11 children (mean age $\pm$ SD, 29 ± 10.0 months) with systemic immediate-type reactions that occurred within 30 minutes after vaccine injection. Seven of children (nos. 3 to 7, 9, and 10) showed apparent anaphylaxis. Four children (nos. 1, 2, 8, and 11)

Abbreviation used

MMR: Measles, mumps, and rubella

had immediate-type reactions (e.g., systemic urticaria) without severe anaphylactic symptoms. The remaining 24 children (mean age $\pm$ SD, 20.0 ± 5.3 months) had nonimmediate-type allergic reactions 3 to 24 hours after the vaccination. These children had erythema and swelling at the injection site, and some had mild systemic cutaneous reactions; none of them had any respiratory or cardiovascular symptoms.

Vaccines

The vaccines used were three measles vaccines (produced by Kitasato Institute, Tokyo; Takeda Chemical Industries, Osaka; Research Foundation for Microbial Diseases of Osaka University, Kagawa, Japan) and a mumps vaccine (by Kitasato Institute), all of which were derived from chick embryo cells. These vaccines included gelatin or polygelin (polymer of bovine gelatin bridged by hexamethylene diisocyanate; Behringwerke, Frankfurt, Germany), the amount of which ranged from 1.5 to 10 mg per shot. Nine of 11 children with the systemic immediate-type reactions received measles vaccines, and two received mumps vaccines (Table I). Twenty of the 24 children with nonimmediate reactions received measles vaccines, and the other four received mumps vaccines.

Measurement of gelatin-specific IgE antibody

IgE antibody to bovine gelatin (Wako Junyaku, Tokyo, Japan) and ovalbumin was measured by the CAP system. We ordered Pharmacia for preparation of the gelatin-specific CAP system for this study.

RESULTS AND DISCUSSION

We measured the anti-gelatin IgE by the CAP method in the sera of children who had adverse reactions after measles and mumps vaccinations. We found a strong relationship between the immediate-type reactions after vaccination and the pres-

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TABLE I. Clinical and laboratory data on children with immediate-type reactions to measles and mumps vaccine

Patient No.	Age (mo)	Sex	Vaccine	Amount of Gelatin (mg/shot)	Reaction to vaccine	Specific IgE (Ua/ml) to	
						Gelatin*	Ovalbumin*
1	29	F	Measles	1.5	Urticaria, laryngeal edema	8.0 (3)	<0.35
2	38	F	Measles	10†	Urticaria, laryngeal edema	7.3 (3)	<0.35
3	36	F	Measles	10†	Urticaria, airway obstruction with laryngeal edema	14.0 (3)	<0.35
4	36	M	Mumps	10†	Urticaria, airway obstruction with laryngeal edema	22.0 (4)	<0.35
5	36	F	Mumps	10†	Urticaria, airway obstruction with laryngeal edema	46.0 (4)	<0.35
6	36	M	Measles	1.5	Anaphylactic shock, hypotension, vascular collapse	15.0 (3)	10.7 (3)
7	12	M	Measles	1.5	Urticaria, airway obstruction with wheezing	40.0 (4)	2.9 (3)
8	43	F	Measles	2.5	Urticaria	3.5 (3)	3.9 (3)
9	19	F	Measles	1.5	Urticaria, airway obstruction with wheezing	28.0 (4)	74.0 (5)
10	18	M	Measles	1.5	Urticaria, airway obstruction with wheezing	4.5 (3)	1.2 (2)
11	19	M	Measles	1.5	Urticaria, vomiting	<0.35	<0.35

*CAP scores given in parentheses.

†As polygelin.

ence of anti-gelatin IgE in the children's sera. Surprisingly, 10 of 11 children with the immediate-type reactions had anti-gelatin IgE levels ranging from 3.5 to 46 Ua/ml (Table I). According to clinical histories, two children (nos. 5 and 8) had systemic urticaria after eating gelatin-containing candies. For the other children, no information was available.

Five of 11 children also had specific IgE to ovalbumin. Fasano et al.,² using a competitive ELISA, found only 37 pg of ovalbumin-like material in MMR vaccines. Ogura et al.,⁴ using sandwich ELISA, found 50 to 260 pg of ovalbumin in five measles vaccines, 90 and 145 pg in two mumps vaccines, and from less than 50 to 120 pg in five MMR vaccines produced in Japan. We found that the level of ovalbumin content in all the vaccines used in this study was very low. This extremely low quantity of ovalbumin is very unlikely to provoke

anaphylaxis. Businco et al.⁵ reported that a total of 434 children with egg allergy received measles vaccines without allergic reactions, whereas 39 children without egg allergy had immediate reactions virtually unrelated to egg sensitivity.

Only one child (no. 11) who experienced mild systemic urticaria and vomiting in response to the vaccine had no specific IgE antibody to gelatin or ovalbumin. Allergens other than gelatin and ovalbumin might have caused the immediate-type reactions in this child.

None of the 24 children with nonimmediate-type reactions had any anti-gelatin IgE. Nine of them had anti-egg IgE. At present, the mechanism of nonimmediate allergic reactions in these children remains unknown.

The extremely large amount of gelatin (1.5 to 10 mg per shot) in the vaccines may have caused systemic allergic reactions on vaccination, if

vaccine recipients had IgE antibody to gelatin. Animal gelatin has long been used as a stabilizer in not only live virus vaccines but also inactivated vaccines; it was believed to have no antigenicity to human beings. To prevent gelatin anaphylaxis on vaccination, alternative stabilizers that have no antigenicity to human beings should be explored. For treatment of anaphylaxis, children should stay at the clinic for 30 minutes after vaccination. Prior questioning of vaccine recipients and their parents about allergic symptoms associated with ingestion of gelatin-containing foods may be help to prevent anaphylaxis in some children.

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Inhaled beclomethasone and bone metabolism in young asthmatic children: A six-month study

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Inhaled corticosteroids (ICs) are established as first-line treatment of chronic severe asthma. Because of their pharmacokinetics, ICs have a high local antiinflammatory potency with minimal systemic side effects. Numerous studies agree that moderate doses of ICs do not inhibit long-term linear growth. However, doubt remains about the effects of ICs on bone metabolism in children. Data are scarce for very young children. The aim

Abbreviations used

BDP:	Beclomethasone dipropionate
ICs:	Inhaled corticosteroids
25(OH)D:	25 Hydroxy vitamin D
1,25(OH) ₂ D:	1,25 Dihydroxy vitamin D
PTH:	Parathyroid hormone

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of this study was to assess the effects of ICs on bone turnover in very young asthmatic children.

METHODS

Eleven asthmatic infants (4 girls) with a mean age of 21.7 months (range, 9 to 53 months) were studied from November 1992 to February 1993. All the infants had had at least three episodes of wheezing dyspnea in the previous 12 months. Severity was assessed by at least one monthly episode during the previous 3 months or daily