

Development of IgE antibody to gelatin in children with systemic immediate-type reactions to vaccines

Masahiro Sakaguchi, PhD,^a Takami Yoshida, MD,^b Takahiro Asahi, MD,^c
Tomonobu Aoki, MD,^c Yukimasa Miyatani, MD,^d and Sakae Inouye, MD^a
Tokyo, Shizuoka, Fukuoka, and Chiryu, Japan

Many cases of anaphylactic reaction to measles-mumps-rubella (MMR) vaccines have been reported.¹ Such reactions have been suggested to be caused by allergy to the egg proteins in these vaccines,¹ but the reactions after receiving MMR vaccines have also been described in children who can tolerate eggs.²

Recently, Kelso et al.³ found that a patient who had anaphylaxis in response to MMR vaccine had IgE antibody to gelatin, detected by an immunoblotting method. In a previous study, we found that 10 of 11 children who showed systemic immediate-type reactions, including anaphylactic reactions to vaccines, had anti-gelatin IgE.⁴ Furthermore, some of children who had anaphylactic reactions also had systemic allergic reactions when they ate gelatin-containing foods.³⁻⁵

To clarify the development of IgE antibody to gelatin, we examined the time courses of serum antibody levels in three children who had systemic immediate-type reactions to vaccines.

CASE REPORT

Case 1

A girl, 1 year and 5 months old (child no. 1 in Table I), showed systemic immediate-type reactions (systemic urticaria, angioedema around eyes) to measles vaccine, which contained 1.5 mg of gelatin per injection. Serum samples were collected three times: the day after vaccination, 10 days after, and about 3 months later. She had received oral polio and diphtheria-tetanus-acellular pertussis (DTaP) vaccines (3 times) before but had no allergic reaction to these vaccines. The DTaP vaccine contained 35 µg of gelatin per injection.

Case 2

A girl, 2 years and 1 month old (child no. 2, Table I), showed mild anaphylactic reactions (systemic urticaria, angioedema around the eyes, and cough) to measles vaccine, which contained 1.5 mg of gelatin. Serum samples were collected four times: the day after vaccination, 8 days after, and 3 and 6 months later. She had received bacille Calmette-Guérin, oral

Abbreviations used

DTaP: Diphtheria-tetanus-acellular pertussis
MMR: Measles-mumps-rubella
Ua: Unit allergen

polio, and gelatin-containing DTaP vaccines before but had no allergic reaction to them.

Case 3

A boy, 3 years and 5 months old (child no. 3, Table I), showed mild anaphylactic reactions (systemic urticaria and wheezing) to mumps vaccine, which contained 1.0 mg of gelatin. Serum samples had been collected three times before the allergic episode, and another sample was collected 8 days afterward. He had had allergies to some allergens. The physician had periodically measured specific IgE to allergens and stored the remaining sera at -70° C. The patient's vaccination histories were oral polio, DTaP (3 times), bacille Calmette-Guérin, rubella, and measles vaccines given before the mumps vaccine. He had not shown any allergic reactions to these vaccines. The measles vaccine contained 1.5 mg of gelatin per injection, but gelatin was not included in the rubella and bacille Calmette-Guérin vaccines. We have no information about the presence of gelatin in the DTaP vaccines that he received (the manufacturer's name was ambiguous to us).

RESULTS AND DISCUSSION

We assayed serum IgE antibody to gelatin and egg white by the CAP method (Pharmacia, Uppsala, Sweden). Children nos. 1 and 2 had anti-gelatin IgE (14 and 11 Unit allergen (Ua)/ml, respectively) immediately after showing reactions to vaccine. After about 1 week, the antibody levels had markedly increased (Table I), but after several months, they decreased. To determine whether this rapid rise in antibody level was an anamnestic response or whether the low level at the time of allergy was due to absorption of the antibody by the gelatin antigen in the injected vaccine, we did an in vitro absorption experiment. On the assumption that all the gelatin (1.5 mg) injected enters the blood, the estimated concentration of gelatin in the serum would be approximately 3 µg/ml. We therefore added gelatin at this concentration to the serum samples collected 10 and 8 days (children nos. 1 and 2, respectively) after the allergic reaction and then assayed the antibody level. We found that the respective IgE antibody levels in the sera

From ^athe Department of Epidemiology, National Institute of Health, Tokyo; ^bShizuoka Children's Hospital; ^cFukuoka Children's Hospital and Medical Center for Infectious Diseases; and ^dMiyatani Clinics, Chiryu.

Reprint requests: Masahiro Sakaguchi, PhD, Department of Epidemiology, National Institute of Health, Toyama 1-23-1, Shinjuku-ku, Tokyo 162, Japan.

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TABLE I. Development of IgE antibody to gelatin in children with allergic reactions to vaccine

Child No. 1						
Age	↓ 1 yr, 5 mo					
Time after allergy	0 day		1 day		10 days	
IgE to gelatin (Ua/ml)	NT	→	14	→	540	→
IgE to egg white (Ua/ml)	NT		<0.35		<0.35	
Child No. 2						
Age	↓ 2 yr, 1 mo					
Time after allergy	0 day		1 day		8 days	
IgE to gelatin (Ua/ml)	NT	→	11	→	120	→
IgE to egg white (Ua/ml)	NT		1.8		2.2	
					3.3	→
						50
						2.1
Child No. 3						
Age	1 yr, 5 mo		1 yr, 8 mo		1 yr, 11 mo	
Date	3/19/93		6/18/93		9/6/93	
Time after allergy	-2 yr		-1 yr, 9 mo		-1 yr, 6 mo	
IgE to gelatin (Ua/ml)	<0.35	→	<0.35	→	1.7	→
IgE to egg white (Ua/ml)	95		67		61	
					NT	→
						54
						79

Arrows indicate the time of systemic allergic reactions. NT, Not tested.

were decreased only by 28% and 34%. Therefore we think that both children showed an anamnestic IgE response.

Child no. 3 had no anti-gelatin IgE on June 18, 1993, but had a low level (1.7 Ua/ml) on September 6, 1993. On November 23, 1993, he received gelatin-containing measles vaccine without any adverse reaction. On March 20, 1995, he had anaphylactic reactions to gelatin-containing mumps vaccine. Serum samples at the time of the allergic reaction to the vaccine were not available, but serum obtained 8 days later showed a high level of anti-gelatin IgE.

As for IgE antibody to egg white, child no. 1 had none. Children nos. 2 and 3 had the antibody, but the levels showed little change during the observation period.

In Japan, acellular pertussis vaccines combined with diphtheria and tetanus toxoids (DTaP vaccine) are being produced by six manufacturers, replacing the whole cell preparations. Four of six DTaP vaccines contain gelatin (about 30 to 100 µg/injection). Furthermore, all the DTaP vaccines contain alum adjuvant and purified pertussis toxoid, both of which enhance IgE production.^{6,7} The gelatin-containing DTaP vaccines may play a role in the development of anti-gelatin IgE, thereby producing sensitivity to gelatin.

In our study we found that children with systemic immediate-type reactions to vaccines showed a

booster response of IgE antibody to gelatin. These children were probably sensitized to gelatin present in previous vaccine injections and/or foods. The vaccination histories of many other children who have had adverse reactions to vaccines are now being examined in detail.

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