

Allergic Reactions to MMR Vaccines in Egg- and Non-Egg-Sensitive Children: A Continuing Controversy

ARNALDO CANTANI, M.D., Ph.D., ANNA SERRA, M.D.,
GIOVANNA ARCESE, M.D., and PATRIZIA LUCENTI, M.D.

ABSTRACT

Measles vaccines prepared in chick embryo fibroblast culture have been used since 1963. Since then, dramatic reductions of the incidence of measles have been observed where the vaccination was extensively applied in the pediatric population, with the best results observed in the initial phase when the target population was that producing over 90% of cases in the prevaccinal era. Since the virus vaccine is grown in cultures of chicken fibroblast cell, although egg proteins could not be found in vaccines, a possible limiting factor to the diffusion of measles vaccination is represented by the assumption that allergy to egg proteins contraindicates the vaccination. It is known that there is a controversy in the literature about the safety of measles vaccine and measles, mumps, and rubella vaccine (MMR) in egg-allergic children. Recent data suggest that reactions to MMR vaccine can be mediated by gelatin and/or neomycin. In this paper, current knowledge on the safety of measles immunization in children with and without egg allergy is discussed. In addition, we propose that all children to be immunized with MMR vaccine and their families should be questioned about neomycin and related antibiotic allergy.

INTRODUCTION

THE ADMINISTRATION OF MEASLES, mumps, and rubella vaccine (MMR) in egg-sensitive children is still a controversial issue; however, a recent report shows that prevalence of potential allergic reactions to MMR is confined to between 0.18% and 0.0007%.⁽¹⁾ Several studies have questioned the utility of the guidelines set forth by the American Academy of Pediatrics (AAP). The procedure currently recommended by the AAP specifically states that persons with a history of anaphylactic reactions (urticaria, swelling of the mouth and throat, wheezing, laryngospasm, hypotension, or shock) following egg ingestion should not be vaccinated until they have been skin tested; this in turn has led to the recommendation that an appropriate series of skin tests be performed prior to the vaccine administration.⁽²⁾ According to the Red Book, children with immediate hypersensitivity reactions following egg ingestion should undergo a series of 5 skin tests (prick test with 1:10 dilution in saline of the vaccine followed by intradermal 1:100, and 1:10 dilutions if the result of the prick test is negative and, in addition, 1 positive control with histamine and 1 negative control with saline solution) before immunization. If the tests are positive, the vaccine should be ad-

Allergy and Clinical Immunology Division, Department of Pediatrics, University of Rome "La Sapienza," Rome, Italy.

ministered as previously described by Herman.⁽³⁾ Briefly, 0.05 ml of MMR vaccine are diluted, first, 1:100 then 1:10, and the neat vaccine is given every 20 minutes until the full dose of 0.5 ml is achieved. The Centers for Disease Control guidelines recommend that MMR vaccination not be given to children with IgE-mediated egg allergy or with an allergic reaction after eating eggs serious enough to require medical assistance.⁽⁴⁾ These suggestions come largely from previous reports,^(3,5,6) especially one by Herman et al.,⁽³⁾ of anaphylactoid reactions following MMR vaccine in 2 children with egg allergy. The authors' conclusion was that a cross-reactivity could be operating between chick embryo fibroblasts, on which the virus is grown, and egg proteins.

ANALYSIS OF CHILDREN GIVEN MMR VACCINE

Children with documented egg allergy

Kamin et al.^(7,8) first reported 22 children with documented IgE-mediated egg allergy who experienced no anaphylactoid reactions following measles immunization (MI); however, still quoted is the subsequent study by Herman et al.,⁽³⁾ in which only 2 children with unconvincing histories of egg sensitivity developed an immediate, generalized reaction after the administration of the measles vaccine. We emphasize that the allergic reactions to egg were not scientifically documented in the children, since only skin tests to egg were performed, without a confirmation by RAST or a challenge test.⁽³⁾ Therefore, we cannot exclude the possibility that the anaphylactoid reactions reported by Herman et al. were unrelated to egg sensitivity. We summarize briefly recent work by several authors who failed to confirm any allergic reaction due to MMR vaccine in 1466 children with egg allergy (Table 1). We understand that a meta-analysis of the studies we discuss is rather difficult, since the methods to detect and diagnose egg allergy varied in the different studies, as did the methods of performing and evaluating the skin testing. However, we will attempt, in the following list, to provide a useful compilation of information as a basis for sound discussion.

TABLE 1. NUMBER OF EGG SENSITIVE CHILDREN SAFELY VACCINATED WITH MMR VACCINE AND NUMBER OF THE ANAPHYLACTIC REACTIONS

<i>Authors (Ref.)</i>	<i>No. of vaccinated with no reaction</i>	<i>Anaphylactic reactions (no. of cases)</i>
Aickin et al. (19a)	410	4 ^a
Bruno et al. (15, 16)	125	
Fasano et al. (13)	140	
Freigang et al. (19b)	500	
Greenberg & Birx (14)	15	
Hermann et al. (3)	8	2 ^b
Kamin (7)	11	
Kamin (8)	11	
Kemp et al. (10)	35	
Lavi et al. (11)	111	3 ^b
Panayiotopoulou et al. (15)	63 ^c	
Puvvada (24)	8	
Tounian et al. (17)	17	
Trotter et al. (18)	12	2 ^a
Total	1466	11

^aThe reactions observed by the authors have not required the administration of adrenaline or other medications, and the children completed the normal vaccination.

^bThe children presented with urticaria, which spontaneously disappeared, and were subsequently vaccinated according to the desensitization protocol of Herman.

^cThe children were regularly vaccinated following the above protocol.

ALLERGIC REACTIONS TO MMR VACCINES

1. The above-cited 22 children reported by Kamin et al.^(7,8)
2. Juntunen-Backman et al. described 134 children affected by atopic diseases (asthma, atopic dermatitis, and food allergy, including egg allergy) safely immunized with MMR vaccine.⁽⁹⁾
3. Kemp et al.⁽¹⁰⁾ reported 32 children with immediate reactions to egg ingestion who received MI without any side effects. Three highly allergic children developed strong positive prick tests to egg, although they had never been exposed to egg; even these children were safely immunized, and Kemp et al. stated that measles vaccine can be given safely without performing vaccine skin tests, despite a history of immediate hypersensitivity reactions to egg proteins.⁽¹⁰⁾ An accompanying editorial⁽⁵⁾ contested their conclusions and commented: "Such IgE-mediated reactions are admittedly unusual; this rarity explains why Kemp et al. could immunize 32 consecutive children without a reaction if such reactions occur in 1 in 100 chances or less."
4. In the study by Lavi et al.⁽¹¹⁾ 24 of 114 (21%) egg-allergic children had a positive response to skin tests with MMR vaccine. There was a relationship between the severity of the reaction reportedly following egg ingestion and the probability of a positive reaction to the skin test with MMR vaccine. Three out of 24 patients who had positive skin tests to the vaccine and who were immunized with a graded desensitization regimen developed generalized urticaria between the second and fourth dose of the neat MMR vaccine. However, the "generalized urticaria" disappeared gradually and spontaneously without any emergency treatment. Accordingly, these 3 patients could receive the subsequent doses of MMR vaccine according to the desensitization protocol with no systemic reactions.⁽¹¹⁾ This suggests that the urticaria was not triggered by an anaphylactic reaction to the vaccine, and that an IgE-mediated allergic reaction to egg protein was not likely in the 3 children. In order to prevent potential systemic reactions it would have been necessary to treat the patients with antiallergic drugs. Since 90 of 114 (78.9%) egg-allergic children with negative skin tests to the vaccine were immunized safely. Lavi et al. concluded that their data confirmed the reliability of negative reactions to skin tests with a diluted MMR vaccine in predicting the safe administration of the vaccine in such children.⁽¹¹⁾
5. Subsequently, Beck et al. observed 28 egg-allergic children who had negative tests to MMR vaccine and were all vaccinated without complications.⁽¹²⁾
6. Similarly, Fasano et al.⁽¹³⁾ reported that 140 children with various degrees of egg allergy received MMR vaccine without reactions. Skin-prick tests to the vaccine were positive in 2 of 71 children (2.8%), and intradermal skin tests were positive in 3 of 6 tested children and in 3 of 6 nonallergic adult controls. Regardless of the results, all 71 children received the vaccine with no reaction; only in 1 highly allergic child, four small hives developed 15–25 minutes after MMR administration.⁽¹³⁾
7. Greenberg and Birx⁽¹⁴⁾ vaccinated without adverse reactions 15 children aged 15–36 months with positive tests to egg and negative skin tests to MMR vaccine.
8. Recently, 63 infants with a mean age of 22.65 months,⁽¹⁵⁾ all with a positive history of anaphylactic reactions to egg, received the MMR vaccine according to the protocol of Herman et al.⁽³⁾ It should be noted that in all infants intradermal testing was done, and results were positive in 11 of 63 (45.8%); however, the MMR vaccine was administered regardless of the results. There were no systemic reactions; only mild local reactions were noted, and these faded spontaneously by the end of the desensitization protocol.
9. To ascertain whether MI actually induces adverse reactions in egg-allergic children, we have studied 125 children (78 males, 47 females), aged 16 months to 6 years (median age, 2 years, 5 months) with documented egg allergy. The diagnosis of egg allergy was made on clinical grounds and confirmed by positive prick tests, as well as by specific IgE and challenge tests to egg. The children were given an attenuated measles vaccine (Morbilvax, Sclavo). No allergic reactions after MI were observed; only the common late reactions, including fever and rashes were recorded in sporadic cases.⁽¹⁶⁾
10. Tounian et al.⁽¹⁷⁾ reported 17 children vaccinated with no reactions. Two had positive intradermal tests with the vaccine and received divided doses following the protocol set forth by Herman et al.⁽³⁾
11. Trotter et al.⁽¹⁸⁾ recently published a study of 12 egg-allergic children aged 12 months to 5 years, 2 of whom presented systemic hypersensitivity reactions while undergoing desensitization to the MMR, which was done with injections of the undiluted vaccine. The authors' report is inconclusive, since 1 child experienced only vomiting, and the other, urticaria associated with a drop in his saturation to 80% as measured by pulse oximetry. Remarkably, both children promptly recovered following intramuscular diphenhy-

dramine; the second also required intravenous fluids and supplemental oxygen. On the basis of our experience and the experience of others, we believe that only epinephrine is successful in treating systemic anaphylaxis in children. It is of note that the first child above had negative responses to both the skin-prick test to egg and the MMR 1:10 diluted vaccine, whereas she experienced urticaria following the MMR 1:100 (more diluted vaccine). Both children were subsequently regularly vaccinated.

12. Aickin et al. vaccinated 410 children with a median age of 26.2 months with clinical reactions to egg and/or positive skin tests to egg. Reactions were observed in 4 children who did not require any medication and the reactions resolved by two hours. One of the 4 children was comprised in a subgroup of 96 babies subjected to intradermal testing with vaccine. She was a 13-month-old girl with a 3-mm wheal on intradermal testing who developed perioral urticaria at 1 hour. ^(19a)

13. Freigang et al. vaccinated 500 children with proven allergy to egg, but only 5 children showed minor rashes. ^(19b)

Children virtually without egg allergy presenting with immediate and anaphylactic type reactions to measles or MMR vaccine

As previously mentioned, severe immediate reactions following the MMR immunization were noted in 47 children that were virtually unrelated to egg allergy^(1,3,9,13,19c-22) (Table 2). A discussion can be generated from the studies discussed below.

1. Juntunen-Blackman et al. reported that 7% of their children had a positive skin-prick tests to measles/mumps vaccine. However, 4 children who had skin-prick tests negative to the vaccine experienced immediate reactions following MI, whereas 2 children received the vaccine with no side effects, despite the positive skin test response.⁽⁹⁾

2. Pollok and Morris^(19c) have reported that immediate reactions following MI occurred in 9 of 170,000 children with no egg allergy (0.00005%).

3. Thurston et al.⁽²⁰⁾ vaccinated 2 healthy infants who exhibited immediate, generalized urticaria and shock after MI. In both studies^(19c,20) the children were classified as not egg-allergic, although no allergy tests were performed.

4. Van Asperen et al.⁽²¹⁾ reported anaphylactic reactions to MI in 3 of 6 children.

5. McEwen et al.⁽²²⁾ documented early-onset adverse reactions (30 minutes) occurring in 15 children given MI.

6. Aukrust recorded an additional 6 children with skin tests negative to the vaccine who had immediate reactions to MMR vaccine.⁽²³⁾

7. Fasano et al.⁽¹³⁾ reported 2 non-egg-allergic children who reacted systemically to the vaccine.

TABLE 2. NUMBER OF IMMEDIATE AND ANAPHYLACTIC-TYPE REACTIONS TO MEASLES OR MMR VACCINE NOT RELATED TO EGG ALLERGY

<i>Authors (Ref.)</i>	<i>Immediate reactions (no. of cases)</i>	<i>Egg-allergic (no. of cases)</i>
Aukrust et al. (22)	6	0/6
Fasano et al. (13)	2	0/2
Juntunen-Backman et al. (9)	4	0/4
Kalet et al. (1)	5	0/5
Kelso et al. (24)	1	1/1
McEwen (22)	15	0/15
Pollock & Morris (19)	9	0/9
Thurston (20)	2	0/2
Van Asperen et al. (21)	3	0/3
Total	47	1/47

ALLERGIC REACTIONS TO MMR VACCINES

8. Recently, 5 patients without a history of egg allergy experienced immediate reactions to the MMR vaccine, requiring emergency treatment with antihistamines and epinephrine.⁽¹⁾

9. Puvvada et al. regularly vaccinated 8 children with history of egg allergy, and reported that 2 11 to 22-month-old children allergic to egg (as determined by prick tests and RAST) could not be vaccinated because they had systemic reactions after MMR intradermal skin testing, which cast doubt on the safety of MMR vaccine.⁽²⁴⁾ A close reading of their report reveals that one boy had a 5-mm wheal after the skin prick test to egg and an uneventful test to MMR 1:10 diluted vaccine, whereas he experienced generalized urticaria and pruritus following the MMR 1:100 (more diluted vaccine), similar to the girl reported by Trotter et al.⁽¹⁸⁾ In the second case, no egg skin test was done; however the MMR 1:100 (more diluted vaccine) resulted in local swelling greater than 5 mm as well severe dyspnea and wheezing, requiring emergency department care. Her parents refused to further proceed with MMR desensitization.⁽²⁴⁾

Alarming, recent reports have documented that anaphylactoid reactions can be due to the gelatin contained in some MMR vaccines as a stabilizer⁽²⁵⁾ or to the neomycin also contained in the vaccine.⁽²⁶⁾

QUESTIONS TO BE ANSWERED

Reliability of skin testing

These data stress that the clinical accuracy of skin tests to MMR vaccine is rather poor, thus supporting previous data showing that skin tests to egg proteins are questionable.^(27,28) The sensitivity of skin test to egg is 1.00, the specificity is 0.28, and the positive predictive value is 0.23, while the negative predictive value and of 1.00 is remarkable.⁽²⁸⁾ Consequently, the utility of skin testing egg-allergic children to predict untoward reactions to MMR vaccine appears to be doubtful. In addition, only in a few cases were the prick test results confirmed by a challenge test with egg, and we all know that this test is the golden standard in allergy diagnosis.⁽²⁷⁾ Further, several children manifested with systemic reactions to MMR vaccine, although they had negative skin tests to it. Fasano et al.⁽¹³⁾ performed the skin-prick tests with full-strength MMR vaccine, judging that this would increase the test sensitivity in comparison with the 1:10 dilution. Recent data, however, have revealed that the first step in the Red Book recommended procedure, that is, the MMR 1:10 diluted skin-prick test, can be negative while the more diluted intradermal testing 1:100 is positive.^(18,24) Therefore, the utility of skin testing egg-allergic children to predict allergic reactions to MMR vaccine seems to be questionable.

Suggested pathogenetic mechanisms

Herman et al. suggested that a cross-reactivity between chick embryo fibroblasts and egg proteins could be operating.⁽³⁾ During the processing, the egg-derived vaccines contain ng (nanogram) (10^{-9} g) of proteins, which may be antigenically similar or cross-reactive with egg protein. However, Fasano et al.,⁽¹³⁾ using a competitive ELISA assay, revealed 37 pg (1 pg = 10^{-12} g) of ovalbumin per 0.5 ml of standard MMR dose; this remarkably low quantity of ovalbumin seems unlikely to provoke allergic reactions. Accordingly, the anaphylactoid reactions might be due to other constituents of the vaccine, such as hydrolyzed gelatin⁽²⁵⁾ or neomycin.⁽²⁶⁾ The collagen base of gelatin is derived from pork; allergy to this meat, although rare, could conceivably be the cause of some systemic reactions to the vaccine.⁽²⁵⁾ The prevalence of reactions to gelatin is between 0.07 and 0.25%; however, among the risk factors we find the dietary intolerance to gelatin with a prevalence of 30%.⁽²⁹⁾ The injection dose of MMR vaccine contains 25 µg of neomycin. Allergy to neomycin is higher than 2% of treatments, however, anaphylactic shock is uncommon⁽²⁹⁾; more frequent (5%–6%) are the cutaneous manifestations,⁽³⁰⁾ thus explaining the very high prevalence of urticarial reactions in MMR-vaccinated children. In a child possibly reacting to the neomycin aliquot of the vaccine (a skin-prick test to neomycin was not feasible), immediate reactions were seen after the first dose of the desensitization protocol, consistent with type I hypersensitivity.⁽²⁶⁾ In addition, neomycin allergy can be a delayed type (cell-mediated immune) response; while these two hypersensitivity reactions are usually distinct entities, they are not mutually exclusive. However, we know that another child with a contact sensitivity to the antibiotic received the MMR vaccine safely.⁽³¹⁾

This data on the vaccine components might explain why non-egg-allergic children are at risk of adverse

reactions to MMR vaccine; however, we know that the prevalence in this group is as low as 0.00005%,^(19c) hence quite negligible.

Finally, we comment on two recent studies related to the risks of aseptic meningitis⁽³²⁾ and acute thrombocytopenic purpura following the MMR vaccine.⁽³³⁾ The first⁽³²⁾ clarifies that after the MMR vaccination the prevalence of meningitis appears to be 4 times lower than that occurring after natural mumps infection. We were informed in September 1992 that the MMR vaccine had been immediately withdrawn all over the world because the producers ascertained that after the MMR vaccination an uneventful meningitis complication developed in 1 vaccinated out of 11,000 (0.00009%), instead of 1 of every 300,000 to 500,000 (0.000033%–0.000002%), as predicted. As regards the severe thrombocytopenic purpura,⁽³³⁾ it occurs after MMR vaccination in 0.000033% of cases, a prevalence much lower than that following natural rubella or measles infection (0.0033%).

DISCUSSION

Probably Puvvada et al.⁽²⁴⁾ thought that their 2 patients were too young to attempt the MMR vaccination (11–22 months). They concluded that if severe reactions occur in 1 of 100 chances or less there is a high probability of missing them when the study population is less than 100. However, our analysis shows that among the 556 children we studied (Table 1) there were more than 100 with egg-induced severe reactions who received the measles vaccine without adverse reactions, while 46/47 non-egg-allergic children exhibited immediate reactions virtually unrelated to egg sensitivity (Table 2). We have commented on the 2 cases with systemic reactions to diluted MMR vaccine reported by Puvvada et al.,⁽²⁴⁾ the cases of so called anaphylactic reactions,^(3,18) and those attributed to regularly vaccinated children (Table 1). The systemic reactions occurred in 0.1% of MMR vaccinations ($p = 0.0001$). This is much lower than the 2.5% forecast by Fasano et al.⁽¹³⁾—as we understand from their paper, since the authors said that with the 140 patients studied we could be 95% confident that at least 97.5% of egg-allergic children would not react to the MMR. Therefore, the MMR vaccine is safe in children with IgE-mediated egg allergy, and the reported immediate reactions in non-egg-allergic children following the vaccine are probably unrelated to egg proteins. We suggest that all patients and their families be questioned about neomycin and related antibiotic allergy before the administration of MMR vaccine.

In conclusion, we do not advocate strictly following the AAP guidelines, which would not only be useless for preventing such reactions, but would complicate the vaccination procedure, thus depriving a large population of children of the vaccination. However, since the potential exists that any child with or without egg allergy may experience immediate reactions following MMR administration, even with the currently recommended Red Book procedure,⁽¹¹⁾ in children with documented egg allergy the immunization should be done in a supervised setting by a physician expert in the treatment of such reactions, with epinephrine in the same tray as the vaccine, and with appropriate emergency equipment at hand for prompt management of anaphylaxis. However, extending these recommendations to all children subjected to MMR vaccine⁽³⁴⁾ appears to be impractical, as that would eliminate all programs in which vaccination is performed by nurses without doctors in attendance, as occurs in most Third World countries and in almost all public health clinics in the industrialized nations. We believe that these recommendations should be reserved for those children with documented egg allergy, not all children.

REFERENCES

1. Kalet A, Berger DK, Bateman WB, et al. Allergic reactions to the MMR vaccine. *Pediatrics* 1992;89:168–169.
2. American Academy of Pediatrics. Report of the Committee on Infectious Disease (Red Book). Evanston, IL: American Academy of Pediatrics Publications, 1991;22–30.
3. Herman JJ, Radin R, Schneidemann R. Allergic reactions to measles (rubeola) vaccine in patients hypersensitive to egg protein. *J Pediatr* 1983;102:196–199.

ALLERGIC REACTIONS TO MMR VACCINES

4. United States Department of Health and Human Services. Measles, mumps, and rubella: What you need to know. Atlanta, GA: Public Health Service, Centers for Disease Control 1992;6.
5. Katz SL. Safety of measles vaccine in egg sensitive individuals. *J Pediatr* 1978;92:859.
6. Stiehm ER. Skin testing prior to measles vaccination for egg-sensitive patients. *Am J Dis Child* 1990;144:32.
7. Kamin PB, Fein BT, Britton HA. Live, attenuated measles vaccine: Its administration to children allergic to egg protein. *JAMA* 1963;185:647–650.
8. Kamin PB, Fein BT, Britton HA. Use of live, attenuated measles virus vaccine in children allergic to egg protein. *JAMA* 1965;193:1125–1162.
9. Juntunen-Backman K, Peltola H, Bachman A, Salo OP. Safe immunization of allergic children against measles, mumps and rubella. *Am J Dis Child* 1987;141:1103–1105.
10. Kemp A, Van Asperen P, Mukhi A. Measles immunization in children with clinical reactions to egg protein. *Am J Dis Child* 1990;144:33–35.
11. Lavi S, Zimmerman B, Koren G, Gold R. Measles, mumps and rubella vaccine. *JAMA* 1990;263:269–271.
12. Beck SA, Williams LW, Burks AW, Shirrell MA. Egg hypersensitivity in measles-mumps-rubella vaccine administration. *Pediatrics* 1991;88:913–917.
13. Fasano MB, Wood RA, Cooke SK, Sampson HA. Egg hypersensitivity and adverse reactions to measles, mumps, and rubella vaccine. *J Pediatr* 1992;120:878–881.
14. Greenberg MA, Bix DL. Safe administration of mumps-measles-rubella vaccine in egg-allergic children. *J Pediatr* 1988;113:504–506.
15. Panayiotopoulou K, Manoussakis M, Tapratzi P, et al. Administration of mumps, measles, and rubella virus vaccine (MMR) to egg-allergic children: Safety and correlation with the skin tests to the vaccine (abstract). *Allergy* 1993;48:13.
16. Bruno G, Lucenti P, Vazzoler C, et al. Egg hypersensitivity and safety of measles immunization (abstract). *Monatsschr Kinderheilkd* 1993;141:364.
17. Tounian P, Delacourt C, de Blic J, et al. Vaccinations des enfants allergiques à l'oeuf par un vaccin préparé sur oeuf. *Arch Fr Pediatr* 1993;50:191–195.
18. Trotter AC, Stone BD, Laszlo DJ, Georgitis JW. Measles, mumps, rubella vaccine administration in egg-sensitive children: Systemic reactions during vaccine desensitization. *Ann Allergy* 1994;72:25–28.
- 19a. Aickin R, Hill D, Kemp A. Measles immunization in children with allergy to egg. *BMJ* 1994;309:223–225.
- 19b. Freigang B, Jadavji TP, Freigang DW. Lack of adverse reactions to measles, mumps and rubella vaccine in egg-allergic children. *Ann Allergy* 1994;73:486–488.
- 19c. Pollok TM, Morris J. A 7-year survey of disorders attributed to vaccination in North West Thames region. *Lancet* 1983;1:753–757.
20. Thurston A. Anaphylactic shock reaction to measles vaccine. *JR Coll Gen Pract [Occas Pap]* 1987;37:41.
21. Van Asperen PP, McEniery J, Kemp AS. Immediate reactions following live attenuated measles vaccine. *Med J Aust* 1981;2:330–331.
22. McEwen J. Early onset reactions following measles vaccination, further Australian reports. *Med J Aust* 1983;2:503–505.
23. Aukrust L, Almeland TL, Refsum D, Aas K. Severe hypersensitivity or intolerance reactions to measles vaccine in six children. *Allergy* 1980;35:581–587.
24. Puvvada L, Silverman B, Bassett C, Chiaramonte LT. Systemic reactions to measles-mumps-rubella vaccine skin testing. *Pediatrics* 1993;91:835–836.
25. Kelso JM, Jones RT, Yunginger JW. Anaphylaxis to mumps, measles, and rubella vaccine mediated by IgE to gelatin. *J Allergy Clin Immunol* 1993;91:867–872.
26. Kwittken PL, Rosen S, Sweinberg SK. MMR vaccine and neomycin allergy. *Am J Dis Child* 1993;142:128–129.
27. Sampson HA, McCaskill RN. Food hypersensitivity and atopic dermatitis: Evaluation of 113 patients. *J Pediatr* 1985;107:669–675.

CANTANI ET AL.

28. Cantani A, Arcese G, Serra A, Lucenti P. Results of skin test, RAST, and food challenges in children with atopic dermatitis associated with food allergy. *Pediatr Padol* 1995.
29. Vervloet D, Pradal M. *Drug Allergy*. Uppsala, Sweden: Kabi Pharmacia, 1992.
30. Rietschel RL. Neomycin sensitivity and the MMR vaccine (letter). *JAMA* 1981;245:571.
31. Elliman D, Dhanray B. Safe MMR vaccine despite neomycin allergy (letter). *Lancet* 1991;337:365.
32. Miller E, Goldacre M, Pugh S, et al. Risk of aseptic meningitis after mumps, measles, and rubella vaccine in UK children. *Lancet* 1993;341:979-982.
33. Nieminen U, Peltola H, Syrjälä MT, et al. Acute thrombocytopenic purpura following mumps, measles, and rubella vaccination. A report on 23 patients. *Acta Paediatr* 1993;82:267-270.
34. Businco L, Granodolfo M, Bruno G. Safety of measles immunization in egg-allergic children. *Pediatr Allergy Immunol* 1991;2:195-198.

Address reprint requests to:
Arnaldo Cantani, M.D., Ph.D.
Via Baglivi 7
I 00161 Roma
Italy

This article has been cited by:

1. Khakoo, Lack. 2000. Guidelines for measles vaccination in egg-allergic children. *Clinical & Experimental Allergy* **30**:2, 288-293. [[CrossRef](#)]