

Double-Blind, Placebo-Controlled Food Challenges (DBPCFC) Demonstrating Acute IgE-Mediated Allergic Reactions to Good Start, Ultrafiltered Good Start, Alfaré, Nutramigen, and Alimentum in a Seven-Year-Old

MARK S. AMONETTE, M.D., ROBERT H. SCHWARTZ, M.D.,
LEISA MATTSON, R.N., M.S., LINDA B. PEERS, R.N.,
and DONALD M. ELDREDGE, M.D.

ABSTRACT

A 7-year-old girl with IgE-mediated cows' milk allergy (immediate reactor) underwent double-blind, placebo-controlled food challenge (DBPCFC) with three whey hydrolysate formulas (Good Start, Ultrafiltered Good Start, Alfaré) and two casein hydrolysates (Nutramigen, Alimentum), using a soy protein formula (Isomil) as a control. She developed acute reactions to Good Start (3 ml; gastrointestinal, respiratory), Ultra Good Start (8 ml; respiratory, cutaneous), Alfaré (158 ml; respiratory), Nutramigen (3 ml; respiratory, cutaneous), and Alimentum (4 ml; respiratory, cutaneous, gastrointestinal) and tolerated the Isomil control (318 ml) on three separate challenges under similar conditions. The generalized urticarial reactions to Nutramigen and Alimentum began 90 minutes after receiving less than 1 teaspoonful (3 ml and 4 ml, respectively) of formula. These observations indicate that all current commercially available cows' milk protein hydrolysate formulas can cause serious allergic reactions in the highly sensitized cows' milk-allergic child. To our knowledge, this is the first report of an acute allergic reaction to Alimentum, which is currently marketed as hypoallergenic. Although many less sensitive cows' milk-allergic children can tolerate these formulas, the authors believe that the term "hypoallergenic" can create a false sense of security.

INTRODUCTION

COWS' MILK (CM) ALLERGY is a common problem in infancy and childhood. The baby food and formula industry has tried to solve this problem by manufacturing formulas with reduced allergenicity by hydrolyzing cows' milk casein or whey proteins to less antigenic, lower molecular weight peptides and amino

Allergy, Asthma, Immunology of Rochester, P.C., Rochester, New York, and Division of Immunology, Allergy, Rheumatology and Nephrology, Department of Pediatrics, University of Rochester Medical Center, Rochester, New York.

acids. Unfortunately, promotion of these formulas as hypoallergenic has created a false sense of security among physicians and laypeople dealing with CM-allergic infants and children, since the term "hypoallergenic" often has been interpreted to mean nonallergenic. Although many CM-allergic children can tolerate one or more of these hydrolysate formulas, there have been reports of acute IgE-mediated reactions to several of these, including Alfaré (whey hydrolysate, Nestlé),⁽¹⁾ Good Start (whey hydrolysate, Carnation),⁽²⁾ Nutramigen (casein hydrolysate, Mead Johnson),^(3,4) and Pregestimil (casein hydrolysate, Mead Johnson).⁽⁵⁾

This report reviews the case of a 7-year-old girl who is part of a larger study of children with IgE-mediated CM allergy undergoing double-blind, placebo-controlled food challenge (DBPCFC) to CM protein hydrolysate formulas. These children are immediate reactors (within 45 minutes) to CM and, therefore, correspond to Hill's group I patients.⁽⁶⁾ Based on previous studies by one of the authors (RHS), these patients were further subclassified (Table 1) as group 1A, 1B, or 1C according to their profile of skin prick test positivity to CM, a whey hydrolysate, and a casein hydrolysate.^(7,8) The mean serum-specific IgE levels to CM also are significantly different between each group. Those in group 1A are mild "topical reactors" and those in groups 1B and 1C are more severe "systemic reactors."⁽⁸⁾ This patient fell into group 1C and is, therefore, markedly sensitive to CM. On DBPCFC, she had acute IgE-mediated reactions to five different hydrolysate formulas and negative challenges on three separate occasions to Isomil (soy formula, Ross), which was used as a negative control. This case emphasizes that none of these hydrolysate formulas is nonallergenic, and any one of them could cause acute allergic reactions in children very sensitive to CM. To our knowledge, this is the first report of an acute allergic reaction to Alimentum (Ross).

CASE REPORT

The patient (A.R.) is a 7-year-old girl who was brought to Robert H. Schwartz, M.D., at Allergy, Asthma, Immunology of Rochester, P.C., in July 1985 at age 17 months for evaluation of milk and egg allergy. She was the product of a normal pregnancy and delivery, and her mother reported that she had been breastfed from birth. Review of her nursery records, however, revealed that she received supplemental cows' milk formula on the first day of life (without incident). At 5 months of age, she was given a small amount of 2% cows' milk on the first attempt at weaning and, as described in her office chart, "rapidly developed generalized urticaria, itchy eyes, a constricted throat with some difficulty breathing and drowsiness." She also had developed generalized urticaria, itchy eyes, and a constricted throat after eating scrambled eggs. In addition, she had mild atopic dermatitis and a history of several episodes of raspy breathing that was diagnosed as asthma. Family history was significant for her father, who had childhood asthma as well as hay fever, and her mother, with hay fever and an intolerance to scallops, which caused vomiting.

Initial laboratory findings showed a serum IgG level of 332 mg/dl, which was at the lower limits of normal for age, with normal IgA (48 mg/dl) and IgM (71 mg/dl) levels. Serum IgE was elevated at 366 IU/ml. The borderline IgG level was thought to reflect transient hypogammaglobulinemia of infancy. RAST testing (Phadebas RAST, Pharmacia Diagnostics, Piscataway, NJ) was positive to whole cows' milk, α -lactalbumin, β -lactoglobulin, and casein, with all falling in a RAST class 4 category (class 0—none, class 1/0—equivocal,

TABLE 1. SUBCLASSIFICATION OF IMMEDIATE REACTORS TO COWS' MILK BASED ON SKIN PRICK TEST POSITIVITY TO COWS' MILK AND HYDROLYSATE FORMULAS^(7,8)

<i>Group</i>	<i>Prick skin test positivity^a</i>	<i>Serum IgE to CM (IU/ml)^b</i>
Group 1A (<i>n</i> = 20)	CM only	1.02 $\pm$ 0.87
Group 1B (<i>n</i> = 17)	CM and whey hydrolysate	10.6 $\pm$ 12.1
Group 1C (<i>n</i> = 13)	CM, whey hydrolysate, and casein hydrolysate	29.3 $\pm$ 12.6

^aCM (Similac), whey hydrolysate (Good Start), and casein hydrolysate (Nutramigen) were prepared according to the manufacturers' instructions on the can, frozen in aliquots, and used for skin prick testing on the patient's back.

^bANOVA reveals significant differences between the three groups ($p = 0.0004$).

ALLERGIC REACTIONS TO HYDROLYSATE FORMULAS

class 1—very low levels, class 2—low levels, class 3—moderate levels, class 4—high levels, class 5—very high levels). RAST to egg white was positive in the class 3 range. Scratch testing was 4⁺ to egg white and negative to the MMR vaccine, although intradermal testing to the MMR was positive at a 1:100 dilution. At that time, she was managed with a diet eliminating dairy products and egg, diphenhydramine for mild reactions due to inadvertent exposure, and withholding of the MMR vaccine. Her parents were instructed in the use of an epinephrine syringe. She had recurrent episodes of wheezing consistent with her diagnosis of asthma and also frequent clear rhinorrhea. The asthma was treated with a theophylline preparation and a β agonist. She continued to have intermittent bouts of cough and wheezing, requiring occasional courses of prednisone. Eventually, cromolyn sodium by nebulizer was added to her treatment. Most episodes of wheezing seemed to occur while she was at day care. Inadvertent CM exposure was considered but never documented. In fact, she never experienced wheezing alone with known inadvertent CM exposure but always experienced hives associated with respiratory and gastrointestinal symptoms.

Skin testing in March 1986 showed positive reactions to several inhalant allergens and persistent 4⁺ positive prick tests to CM and egg. In April 1987 at age 3 years, repeat levels of serum IgG, IgM, and IgA were all normal, and the serum IgE level was still markedly elevated at 1,342 IU/ml. RAST tests remained markedly positive to whole cows' milk, α -lactalbumin, β -lactoglobulin, casein, and egg white, with all falling in a RAST class 5 range.

The patient continued to demonstrate clinical sensitivity, having skin reactions on contact with dairy products and generalized urticarial reactions with rare accidental ingestion of foods containing CM protein. FAST testing (3M Diagnostic Systems, Inc., Santa Clara, CA) showed persistently high serum-specific IgE levels to CM (> 44 IU/ml), α -lactalbumin (> 44 IU/ml), β -lactoglobulin (> 44 IU/ml), and casein (> 44 IU/ml) in February 1990 and again in September 1990. These are equivalent to a class VI/VI by the modified RAST scoring system. Serum immunoglobulin levels were normal (IgG, 820 mg/dl; IgA, 126 mg/dl; IgM, 82 mg/dl). Serum IgE (4668 IU/ml) was markedly elevated. Prick skin testing was done with hydrolysate formulas prepared for feeding as directed by the manufacturers. On September 12, 1990, she showed large positive wheals to CM (23 $\times$ 12 mm), Good Start (35 $\times$ 14 mm), Alfaré (19 $\times$ 10 mm), and Nutramigen (15 $\times$ 11 mm). On December 6, 1990, she had a positive skin test to Alimentum (17 $\times$ 13 mm). The diluent and soy formula (Isomil) controls were negative, and the histamine controls were positive (4 $\times$ 4 mm and 4 $\times$ 3 mm). She also had a positive prick skin test to Ultrafiltered Good Start (26 $\times$ 13 mm), which is identical to the partial whey hydrolysate, Good Start, except that it is ultrafiltered to eliminate most of the larger peptides above 10,000 to 15,000 daltons.

DOUBLE-BLIND, PLACEBO-CONTROLLED FOOD CHALLENGE (DBPCFC) WITH HYDROLYSATE FORMULAS

After approval by the Research Subjects Review Board and signed informed consent from her parents, the patient agreed to a randomized series of DBPCFCs to Good Start, Ultrafiltered Good Start, Alfaré, and Nutramigen using Isomil as a negative control. The studies were conducted on the clinical research unit of Strong Memorial Hospital, University of Rochester Medical Center, with a physician (MSA) and a trained study nurse (LM or LBP) in constant attendance. The patient, parents, nurses, and all physicians were blinded to the formula identity. Differences in formula taste were masked with a special orange-vanilla flavoring. On separate days, the patient was given increasing amounts of one formula beginning with 1 ml, allowing 10 minutes between doses to observe for a reaction and to record objective and subjective cutaneous, upper respiratory, lower respiratory, and gastrointestinal signs and symptoms. Pulse, respiration, blood pressure, and peak expiratory flow rates also were monitored. Results, including the dates of each challenge, are shown in Table 2 (Part 1). Because of her marked sensitivity, she was not challenged to regular CM. Having shown positive reactions to all of these challenges (except Isomil), with institutional approval of a modified protocol and with informed consent, it was decided to perform DBPCFC to Alimentum (casein hydrolysate, Ross) as well, again using Isomil as a negative control. These results are also shown in Table 2 (Part 2).

TABLE 2. DBPCFC WITH CASEIN AND WHEY HYDROLYSATE FORMULAS IN A 7-YEAR-OLD GIRL (AR)

<i>Challenge^a</i>	<i>Formula</i>	<i>Total dose (ml)</i>	<i>Onset (minutes)</i>	<i>Reaction</i>
Part 1				
1. 9/21/90	Good Start (whey hydrolysate, Carnation)	3	20	GI discomfort, nausea, followed in another 10 min by agitation, nasal congestion and rhinorrhea, and mild cough. No change in vital signs
2. 10/8/90	Alfaré (whey hydrolysate, Nestlé)	158	70	Mild rhinorrhea and irritability
3. 11/12/90	Isomil (soy protein, Ross)	318		No reaction
4. 11/15/90	Ultrafiltered Good Start (whey hydrolysate, Carnation)	8	30	Mild hives and pruritis. Decreased activity, hoarseness and throat clearing without objective throat swelling. Hives resolved. At 40 min, mild rhinorrhea. At 70 min, more hives, which became generalized, and worsened rhinorrhea and cough. After 2 hr, 20 min, more hives and cough despite previous benadryl and epinephrine. No change in vital signs throughout
5. 11/23/90	Nutramigen (casein hydrolysate, Mead Johnson)	3	30	Mild pruritis without rash, occasional bouts of sneezing. Palatal itching, decreased activity. 90 min, generalized hives and severe itching. Moderate cough and wheezing. No change in vital signs
6. 11/28/90	Isomil (soy protein, Ross)	318		No reaction
Part 2				
1. 2/18/91	Isomil (soy protein, Ross)	318		No reaction
2. 2/20/91	Alimentum (casein hydrolysate, Ross)	4	5	Throat itching initially, irritability. 75 min, persistent throat itching, mild rhinorrhea. 85 min, pruritis, mild cough, basilar wheezes, decreased activity. 95 min, generalized hives, nasal congestion and rhinorrhea worse. Cough persisted. Tachycardia. Given benadryl and epinephrine. 150 min, repetitive vomiting and abdominal discomfort lasting 12 hr

^a Challenge procedure: First dose given at time 0. Time elapsed in minutes: ml given (Total ml) = 10:1(1), 20:2(3), 30:5(8), 40:10(18), 50:20(38), 60:40(78), 70:80(158), 80:160(318). Formulas were randomized. Part 2 formulas (2 Isomil and 1 Alimentum) were randomized. AR did not return for the last challenge (Isomil). Formulas were prepared by the clinical research center nutritionist using an orange-vanilla flavoring to mask differences in taste.

With all hydrolysate formulas, the patient had immediate subjective complaints of tongue and throat discomfort and later developed symptoms of decreased activity and irritability. She also had variable objective signs of nasal congestion, rhinorrhea, wheezing, and generalized urticaria, depending on the formula. Reactions were treated with subcutaneous epinephrine and oral diphenhydramine. Of note was that with Nutramigen she had initial mild symptoms but then, 1 hour after the last dose, developed generalized urticaria and cough. She also had a delayed response to Alimentum in developing rhinorrhea, cough, wheezing, and generalized urticaria between 55 and 75 minutes after the last dose. The reaction to Alimentum was protracted, with repetitive vomiting, abdominal discomfort, and lethargy lasting for 12 hours and requiring intravenous hydration in the emergency room.

DISCUSSION

The prevalence of adverse reactions to CM ranges from 0.3% to 7.5%.^(9,10,11) These figures reflect both IgE-mediated hypersensitivity reactions and non-IgE-mediated intolerance reactions. Over an 18-month period, one of the authors (RHS) saw 34 children out of 842 referrals (4%) with IgE-mediated CM allergy diagnosed by convincing history or positive oral challenges, positive skin prick tests, and the presence of serum-specific IgE antibodies to CM. CM allergy in adults is much less common, and onset in adult life is rare.⁽¹²⁾

IgE-mediated reactivity to CM usually is seen in the first year of life in breastfed infants of atopic parents at the time of weaning, when the infant is fed cows' milk for the first time. Prior sensitization may have occurred in utero, in the newborn nursery when fed small amounts of CM, via breast milk containing CM proteins ingested by the mother, or by inadvertent feedings of CM given by parents, siblings, grandparents, or baby sitters.⁽¹³⁾ The possible clinical manifestations of adverse reactions to CM are numerous. In a review of 100 infants and children with CM allergy, Hill et al.⁽¹⁴⁾ identified the following signs and symptoms: gastrointestinal (vomiting, diarrhea, colic, colitis, functional intestinal obstruction), anaphylaxis, dermatologic (generalized urticaria, angioedema, perioral lesions, morbilliform eruptions, eczema, and perianal eruptions), respiratory (stridor, rhinitis, cough, wheeze, tachypnea), and nervous system (irritability, syncope/collapse, convulsions). In compiling the data from challenges in five studies, Lebenthal⁽¹⁵⁾ found 88% with diarrhea, 44% with vomiting, 39% with abdominal pain or colic, 33% with atopic dermatitis, 31% with rhinitis, 31% with asthma, 13% with urticaria, and 12% with anaphylaxis. Cutaneous reactions may be seen in patients with either acute, recurrent, or chronic asthma or with atopic dermatitis. When reactions are IgE-mediated, vomiting or diarrhea usually is associated with cutaneous or respiratory symptoms. If they occur alone, they are more likely to represent non-IgE-mediated intolerance reactions.

Cows' milk consists of 80% casein and 20% whey. Although there are more than 25 CM proteins that may be antigenic to humans, the two most important allergens are β -lactoglobulin (a whey protein) and casein.^(14,16,17) α -Lactalbumin (another whey protein) and bovine serum albumin also are important allergens.⁽¹⁶⁾ It is through enzyme or heat hydrolysis of these proteins that formulas with reduced allergenicity have been prepared. Commercially available formulas include the casein hydrolysates (Nutramigen, Alimentum, Pregestimil) and the whey hydrolysates (Good Start, Alfaré). The casein hydrolysates in Nutramigen and Pregestimil are the same. Good Start is a whey hydrolyzed with trypsin, and Alfaré is a whey hydrolyzed with pancreozymes.

The term "hypoallergenic" was voluntarily removed from the Good Start can label by the manufacturer when it became apparent that some CM-allergic children experienced reactions to this formula. Soon after that, reports of reactions to Nutramigen appeared.^(3,4) The term "hypoallergenic" is still prominently displayed on the Alimentum label, the newest casein hydrolysate formula. We are aware of no peer-reviewed publications supporting its use in highly allergic patients. There has been a preliminary report on its efficacy in children with eczema and CM allergy.⁽¹⁸⁾ We believe that the term "hypoallergenic" can create a false sense of security among health professionals and laypeople dealing with CM-allergic children because it may be interpreted to mean nonallergenic.

With respect to IgE-mediated CM allergy, there is probably a rank order of allergenicity of various formulas, as suggested by the fact that our patient was able to tolerate 158 ml of Alfaré in contrast to only 3–8 ml of the other hydrolysate formulas before developing objective signs of a reaction. In our DBPCFC studies of 12 children with group 1B and 1C (systemic reactors) IgE-mediated cows' milk allergy, the rank order of positive reactions was Good Start (7/12) > Ultrafiltered Good Start (6/12) > Nutramigen (3/12) > Alfaré (1/12). Under the conditions of our study, Alfaré appears to be the least allergenic. However, AR did react to it, and Businco et al. reported anaphylactic reactions to this whey hydrolysate, which is sold in Europe.⁽¹⁾

The patient reported here had a convincing history, positive skin prick tests, and elevated serum-specific IgE levels to CM, supporting the diagnosis of IgE-mediated cows' milk sensitivity. DBPCFC, the gold standard for studying food allergy,⁽¹⁹⁾ confirmed the diagnosis of CM allergy in this patient. More importantly, it demonstrated, by a scientifically acceptable method, that acute allergic reactions to any of the current commercially available CM protein hydrolysate formulas can occur in the highly sensitized child. Therefore, they should not be recommended routinely for all CM-allergic children without further thought and

evaluation. Skin prick testing with the various hydrolysate formulas is useful in determining which ones are safe for a given individual. In our DBPCFC studies of 20 children with IgE-mediated CM allergy of varying degrees, a negative skin prick test to hydrolysate formulas has a negative predictive value of 100%. At this point, it should be stressed that skin testing is of no value if the adverse reaction to CM is a non-IgE-mediated intolerance reaction. In this instance, the clinician can only rely on challenge testing.

ACKNOWLEDGMENTS

The authors wish to thank AR and her parents for their participation in this study. Hopefully, some day she will be able to drink cows' milk. Perhaps this will be possible when the mechanisms of sensitization become better understood. Dr. Donald (Greg) M. Eldredge is her primary care physician. Mary Ashraf, research dietitian, helped with the formula randomization, preparation, and masking of taste differences. The case report is part of a larger study entitled, "Double-Blind, Placebo-Controlled Food Challenge with Cows' Milk Protein Hydrolysate Formulas in Children with Cows' Milk Allergy," sponsored by Carnation, Nutritional Products Division, Glendale, CA, and partially supported by 3M Diagnostics Systems, Inc., Santa Clara, CA. The authors wish to thank Steven A. Witherly, Ph.D., and Nick S. Harris, Ph.D., for their interest and support of this investigator-initiated research. The study was approved by the Research Subjects Review Board (RSRB 3885) of the University of Rochester and carried out at the Clinical Research Center (Protocol 353) of Strong Memorial Hospital.

REFERENCES

1. Businco L, Cantani A, Longhi A, Giampietro PG. Anaphylactic reactions to a cow's milk whey protein hydrolysate (Alfa-ré, Nestlé) in infants with cow's milk allergy. *Ann Allergy* 1989;62:333-335.
2. Ellis MH, Short JA, Heiner DC. Anaphylaxis after ingestion of a recently introduced hydrolyzed whey protein formula. *J Pediatr* 1991;118:74-77.
3. Bock SA. Probable allergic reaction to casein hydrolysate formula (correspondence). *J Allergy Clin Immunol* 1989;84:272.
4. Saylor JD, Bahna SL. Anaphylaxis to casein hydrolysate formula. *J Pediatr* 1991;118:71-74.
5. Lifschitz CH, Hawkins HK, Guerra C, Byrd N. Anaphylactic shock due to cow's milk protein hypersensitivity in a breast-fed infant. *J Pediatr Gastroenterol Nutr* 1988;7:141-144.
6. Hill DJ, Firer MA, Shelton MJ, Hosking CS. Manifestations of milk allergy in infancy: clinical and immunologic findings. *J Pediatr* 1986;109:270-276.
7. Schwartz RH, Keefe MW, Harris N, Witherly S. The spectrum of IgE-mediated acute allergic reactions to cow's milk in children as determined by skin testing with cow's milk protein hydrolysate formulas. *Pediatr Asthma Allergy Immunol* 1989;3:207-215.
8. Schwartz RH, Harris NS. Topical and systemic reactors to cow's milk (Abstract 526). *J Allergy Clin Immunol* 1991;87:271.
9. Gerrard JW, Mackenzie JWA, Goluboff N, Garson JZ, Maningas CS. Cows's milk allergy: prevalence and manifestations in unselected series of newborns. *Acta Paediatr Scand* 1973;234 (supplement): 1-21.
10. Bock SA. Prospective appraisal of complaints of adverse reactions in children during the first 3 years of life. *Pediatrics* 1987;79:683-688.
11. Jakobsson I, Lindberg T. A prospective study of cow's milk protein intolerance in Swedish infants. *Acta Paediatr Scand* 1979;68:853-859.
12. Olade S, Bensabat Z, Vives R, Fernandez L, Cabeza NC, Rodriguez J. Allergy to cow's milk with onset in adult life. *Ann Allergy* 1989;62:185a-185b.
13. Schwartz RH, Kubicka M, Dreyfuss EM, Nikaein A. Acute urticarial reactions to cow's milk in infants previously fed breast milk or soy milk. *Pediatr Asthma Allergy Immunol* 1987;1:81-93.

ALLERGIC REACTIONS TO HYDROLYSATE FORMULAS

14. Hill DJ, Firer MA, Ball G, Hosking CS. Recovery from milk allergy in early childhood: antibody studies. *J Pediatr* 1989;114:761-766.
15. Lebanthal E. Cow's milk protein allergy. *Pediatr Clin North Am* 1975;22:827-833.
16. Goldman SA, Anderson DW, Sellers WA, Saperstein S, Knicker WT, Halpern SR. Milk allergy. I. Oral challenge with milk and isolated milk proteins in allergic children. *Pediatrics* 1963;32:425-433.
17. Goldman AS, Sellers WA, Halpern SR, Anderson DW, Furlow TE, Johnson CH. Milk allergy, II. skin testing of allergic and normal children with purified milk proteins. *Pediatrics* 1963;32:572-579.
18. Sampson HA. Safety of a casein hydrolysate formula in children with cows' milk hypersensitivity (Abstract). *Pediatr Research* 1989;25:123A.
19. Bock SA, Sampson HA, Atkins FM, et al. Double-blind, placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. *J Allergy Clin Immunol* 1988;82:986-997.

Address reprint requests to:
Robert H. Schwartz, M.D.
Allergy, Asthma, Immunology
of Rochester, P.C.
919 Westfall Road
Rochester, NY 14618

This article has been cited by:

1. Christopher C. Copenhaver , Robert H. Schwartz , Jill S. Halterman , Kelly M. Conn . 2003. IgE-Mediated Cow's Milk Allergy: Skin Prick Test Subtypes and Clinical Phenotypes Using Cow's Milk Hydrolysate Infant FormulasIgE-Mediated Cow's Milk Allergy: Skin Prick Test Subtypes and Clinical Phenotypes Using Cow's Milk Hydrolysate Infant Formulas. *Pediatric Asthma, Allergy & Immunology* **16**:2, 67-76. [[Abstract](#)] [[PDF](#)] [[PDF Plus](#)]
2. C. T. Cordle, G. Duska-McEwen, L. M. Janas, W. T. Malone, M. A. Hirsch. 1994. Evaluation of the immunogenicity of protein hydrolysate formulas using laboratory animal hyperimmunization. *Pediatric Allergy and Immunology* **5**:1, 14-19. [[CrossRef](#)]
3. MARK S. AMONETTE, STEPHEN I. ROSENFELD, ROBERT H. SCHWARTZ. 1993. Serum IgE Antibodies to Cow's Milk Proteins in Children With Differing Degrees of IgE-Mediated Cow's Milk Allergy: Analysis by ImmunoblottingSerum IgE Antibodies to Cow's Milk Proteins in Children With Differing Degrees of IgE-Mediated Cow's Milk Allergy: Analysis by Immunoblotting. *Pediatric Asthma, Allergy & Immunology* **7**:2, 99-109. [[Abstract](#)] [[PDF](#)] [[PDF Plus](#)]
4. Robert H. Schwartz. 1993. RESPONSE TO DR. CANTANI'S LETTERRESPONSE TO DR. CANTANI'S LETTER. *Pediatric Asthma, Allergy & Immunology* **7**:1, 3-5. [[Citation](#)] [[PDF](#)] [[PDF Plus](#)]