

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

ROBERT H. SCHWARTZ, M.D.,¹ MARGARET W. KEEFE, R.D.¹
NICK HARRIS, Ph.D.,² and STEVEN WITHERLY, Ph.D.³

ABSTRACT

Children with adverse reactions to cow's milk (CM) often are given infant formulas containing CM proteins (casein or whey proteins) modified by hydrolysis to reduce their allergenicity. Recently, a few reports of acute allergic reactions to these CM hydrolysates have appeared in the medical literature. Therefore, between January 1, 1989, and August 31, 1989, we studied 26 children with a current history of recurrent acute respiratory (asthma, 19/26) or cutaneous (26/26, urticaria) reactions to CM. They were prick skin-tested with CM, two whey hydrolysates (Good Start HA and Alfaré), and two casein hydrolysates (Nutramigen and Alimentum). Serum-specific IgE (sIgE IU/ml) to CM was measured by the 3M Fast method.

Unexpectedly, high frequencies of positive prick tests were found to the whey (69%) and to the casein (38%) hydrolysate products. On the basis of skin test positivity, patients could be separated into three groups: group A ($n = 8$, positive only to CM), group B ($n = 8$, positive to CM and whey hydrolysate), and group C ($n = 10$, positive to CM, whey hydrolysate and casein hydrolysate). This skin test spectrum was reflected by significant differences (A vs B, $p < 0.05$; A vs C, $p < 0.001$; B vs C, $p < 0.001$) between the group means ($A = 1.0 \pm 0.28$; $B = 13.4 \pm 16.7$; $C = 33.8 \pm 8.8$ IU/ml) for sIgE to CM. Asthmatic reactions (100%) and acute generalized urticarial reactions (90%) occurred most frequently in group C patients. When 5 children ($A = 2$, $B = 1$, $C = 2$) were challenged with CM, group C patients had the most severe reactions (urticaria, angioedema, wheezing). Group A patients had milder reactions (contact urticaria).

¹Allergy, Asthma, Immunology of Rochester, P.C., Rochester, New York.

²3M Diagnostic Systems, Inc., Santa Clara, California.

³Carnation, Nutritional Products Division Los Angeles, California.

These observations indicate that allergenic determinants for humans are still present in commercially available CM whey and CM casein preparations after hydrolysis. They should be used cautiously. Also, there is a spectrum of immediate reactors (Hill's group I) to CM. We will classify them as IA, IB, and IC in future studies. Perhaps then, the physician caring for children will be able to predict which child with a history of IgE-mediated acute cutaneous and/or respiratory allergic reactions to CM will be able to tolerate "hypoallergenic" CM hydrolysate formulas and which will react adversely to them.

INTRODUCTION

RECENTLY, IT HAS BECOME apparent that cow's milk (CM) protein hydrolysate formulas, once considered to be "hypoallergenic," are capable of producing symptoms in some children with preexisting cow's milk allergy.⁽¹⁻³⁾ Acute severe allergic IgE-mediated reactions to CM whey and casein hydrolysate formulas have been reported, but the number of cases reported has been small.

We evaluated the immunogenicity of commercially available CM protein hydrolysate formulas by skin testing children who are clinically allergic and skin test positive to CM. We found that two thirds were also skin test positive to the casein and/or whey hydrolysate formulas.

We present our observations on a series of 26 children with a spectrum of acute IgE-mediated reactions to CM. We concluded that their skin test profile to the CM preparations and their serum specific IgE levels to CM reflect this spectrum.

There are three groups of patients—group A, group B, and group C—depending on whether or not they have positive skin tests to the casein and/or whey hydrolysates, in addition to positive skin tests to CM. Skin test reactivity increases with severity of disease. Clinically, group A is characterized by acute cutaneous (contact urticaria) reactions to CM, and group C by more severe acute cutaneous (generalized urticaria) and respiratory (asthma) reactions. Group B patients are intermediate. These children are being followed prospectively to see if the tests continue to predict the degree of reactions as occurred when 5 of them were challenged with CM.

Our observations indicate that antigenic determinants, which are allergenic for humans, are still present in commercially available casein and whey products after hydrolysis. Caution should be used when considering the use of hydrolyzed CM protein formulas in children who previously have had adverse reactions to CM. We suspect a subset will react unfavorably, and some will react dangerously.

PATIENTS AND METHODS

Study patients and subjects

Because of one author's (RHS) subspecialty, his interest in children with CM allergy, and his previous publications and presentations, Allergy, Asthma, Immunology of Rochester (AAIR), P.C., has children referred with CM allergy from the Rochester, NY (Monroe County) community.⁽⁴⁾ Since 1979, more than 60 children with a history of IgE-mediated immediate respiratory (asthma) and/or cutaneous (contact urticaria and/or generalized urticaria) reactions to CM have been seen for consultation and are followed periodically for management. This report is about 26

ALLERGIC REACTIONS TO COW'S MILK

consecutive new ($n = 8$) and follow-up patients ($n = 18$), seen between January 1, 1989, and August 31, 1989. After obtaining written informed consent from their parents, they had skin prick testing to CM and to commercially available CM protein hydrolysate formulas. Venous blood was drawn for determinations of specific IgE to CM.

Histories were obtained from parents and referring physicians. All of the children had a history of three or more acute wheezing or urticarial reactions immediately following intentional or inadvertent feeding of CM. At least one reaction had occurred within the 6 months before testing. All of the children had been breast-fed from birth and had their first reaction when given their first apparent CM feeding.

This study received approval by the Committee on Investigation of Human Subjects of the Genesee Valley Medical Center.

Skin testing

Skin testing was done by the prick method on the backs of all subjects. The wheals and flares were measured at their greatest diameter and at the midpoint perpendicular to that diameter and recorded in millimeters at 15 minutes. A ballpoint pen outline of the wheals and flares was transferred to a record using scotch tape. Thus, a semiquantitative description of the wheal size and a drawing of the presence or absence of pseudopods were recorded.

Subjects were tested with (1) diluent control (lot 4015M Hollister-Stier, Division of Miles Laboratories, Inc., Elkhart, IN), (2) histamine control (Histatrol lot 8C-14, histamine phosphate 2.75 mg/ml, Center Laboratories, Port Washington, NY), (3) whole cow's milk (CM) 1:20 wt/vol (Hollister-Stier), two whey hydrolysate formulas—(4) Good Start H.A. (Carnation) and (5) Alfaré (Nestlé), and two casein hydrolysate formulas—(6) Nutramigen (Mead Johnson) and (7) Alimentum (Ross). Nutramigen and Alimentum were purchased from a local grocery store. Good Start H.A. and Alfaré were supplied by Carnation Company, Nutritional Products Division. Formulas were prepared fresh according to the instructions on the can. They were frozen in aliquots and thawed before use. They were placed on the back as drops through which the skin was superficially abraided (plucked) with a straight pin. A new pin was used for each prick test in order to prevent carryover of antigen from one site to the next. The subjects and their skin test sites were constantly observed for 15 minutes. If a rapidly enlarging wheal was seen, the drops were quickly wiped off. Some very large immediate local reactions occurred in a few children. At 15 minutes, they were given an oral liquid antihistamine. Epinephrine (1:1,000), oxygen, and resuscitation equipment were readily available. No systemic reactions occurred.

Serologic studies

Specific IgE (IU/ml) to CM was determined by the 3M Fast-Plus method (3M Diagnostic Systems, Inc., Santa Clara, CA). Determinations were done in the research laboratory of AAIR, P.C., by one of the authors (MWK).

Oral provocative challenge studies

Five children had an open oral challenge with CM in our subspecialty office under the constant observation of a trained registered nurse while a physician (RHS) was physically present in the office. None had received antihistamines for at least 72 hours before testing. Vital signs and subjective and objective cutaneous, respiratory, and gastrointestinal signs and symptoms were taken and recorded after the patients received varying amounts of undiluted or diluted CM at 15–20 minute intervals. All five children had acute reactions ranging from contact urticaria and angioedema to acute generalized urticaria, angioedema, itchy watery eyes, rhinorrhea, cough, and wheezing. No hypotension occurred. As soon as the reactions became obviously progressive,

testing was immediately stopped, and treatment with an oral liquid antihistamine or subcutaneous epinephrine was given. In each case, the reaction was reversed. Double-blind, placebo-controlled food (milk) challenge (DBPCFC) was not done because (1) the approach was to confirm the degree of CM allergy and not to rule it out, and (2) each child had a history of multiple convincing episodes of acute reactions to CM.

RESULTS

Skin tests

Twenty-six of twenty-six children (100%) were prick test positive to CM (wheal size range 4×4 to 15×15 mm, median 12×8 mm). Eighteen of twenty-six (69%) were prick test positive to the whey hydrolysate, Good Start H.A. (wheal size range 4×4 to 50×15 mm, median 12×8 mm). Ten of twenty-six (38%) were prick test positive to the casein hydrolysate, Nutramigen (wheal size range 4×4 mm to 16×15 mm, median 12×5 mm). Those who were prick test positive to the casein hydrolysate were also positive to the whey hydrolysate. On the basis of skin test positivity, the patients were separated into three groups—group A ($n = 8$, positive only to CM), group B ($n = 8$, positive to CM and whey hydrolysate), and group C ($n = 10$, positive to CM, whey hydrolysate, and casein hydrolysate). All patients who were skin test positive to Good Start H.A. were also skin test positive to Alfaré. Eight of ten patients who were skin test positive to Nutramigen were also skin test positive to Alimentum. The largest reactions with pseudopods were found in the patients in group C. The whey hydrolysates produced the largest reactions. Four nonallergic controls had negative prick tests to CM and the CM protein hydrolysates.

Table 1 presents the skin test results in another way that shows the relative sizes of the wheals in the three groups.

Specific IgE (sIgE) Levels to CM

The mean, standard deviation, and range for each group are shown in Table 1. The one factor analysis of variance (ANOVA) on the sIgE (IU/ml) to CM demonstrated highly significant differences among the three groups of subjects (F ratio, 19.09; $p = 0.0001$). Table 1 contains the results of Fisher's least significant difference test (LSD) used in the multiple comparison of treatment means. All group means for sIgE to CM differed significantly from each other.

Clinical profiles by history

All patients had been breast-fed from birth and had their first reaction to CM at the time of their first feeding of CM. All had either contact or generalized urticarial reactions with or without acute respiratory asthmatic reactions occurring on at least three separate occasions. The CM reaction histories for groups A, B, and C are shown in Table 2.

Asthmatic reactions (100%) and acute generalized urticarial reactions (90%) occurred most frequently in group C patients. It should be noted that 31% of the total patients had a history of eczema (atopic dermatitis) and that these were evenly distributed among the three groups. Thus, the entire study group is not predominantly a group of milk-allergic atopic dermatitis patients.

Oral provocative challenges

Five patients had oral challenge with CM, as shown in Table 3. The two from group A developed contact urticarial lesions of the skin around the mouth but no respiratory symptoms or signs. One of these developed gastrointestinal symptoms. One patient from group B was

ALLERGIC REACTIONS TO COW'S MILK

TABLE 1. PRICK TESTS AND sIgE TO COW'S MILK IN 26 CHILDREN

<i>Skin test area of wheal^a</i>	<i>Group A^b (n = 8)</i>	<i>Group B^c (n = 8)</i>	<i>Group C^d (n = 10)</i>
Cow's milk (CM)			
Mean	87	57	155
SD	68	54	119
Range	30-225	10-150	36-486
Whey Hydrolysate			
Mean	Negative	41	191
SD	—	34	196
Range	—	4-112	42-750
Casein Hydrolysate			
Mean	Negative	Negative	62
SD	—	—	38
Range	—	—	9-135
Histamine			
Mean	14	16	16
SD	5	4	5
Range	9-25	9-25	9-25
sIgE to CM (IU/ml) ^e			
Mean	1.00	13.41	33.84
SD	0.28	16.70	8.80
Range	0.65-1.43	0.80-44	18-44
Age (years)			
Mean	2.7	3.5	5.3
SD	1.5	3.1	3.7
Range	1.3-5.9	1.3-11.4	1.6-13.8

^aSkin test area of wheal = A × B measured at 15 minutes. A = largest diameter or length of wheal in mm at 15 minutes B = width of wheal perpendicular to the midpoint of A.

^bGroup A = prick test (+) to CM.

^cGroup B = prick test (+) to CM and whey hydrolysate (Good Start H.A.).

^dGroup C = prick test (+) to CM, whey hydrolysate (Good Start H.A.), and casein hydrolysate (Nutramigen).

^esIgE to CM: Group A vs group B ($p < 0.05$).

Group A vs group C ($p < 0.001$).

Group B vs group C ($p < 0.001$).

One-way ANOVA used with Fisher's LSD for multiple comparisons.

tested. He developed contact urticarial lesions around the mouth and upper respiratory symptoms (sneezing, rhinorrhea, cough) but no obvious wheezing. The reaction was terminated with epinephrine. The two patients from group C developed rapid cutaneous and respiratory reactions that required treatment with epinephrine.

These five patients were chosen for challenge because parents wanted continual verification of their milk-allergic status and not because of their CM and CM-hydrolysate skin test profiles. Five of eight of the patients in group C who did not undergo oral provocative challenges had sIgE to CM (44, 44, 42, 37, and 36 IU/ml) greater than the two patients in group C (21.70 IU/ml, 26.64 IU/ml) who were challenged. They were reluctant to participate in a challenge

TABLE 2. COW'S MILK ALLERGY CLINICAL PROFILES BY HISTORY

<i>Reaction^a</i>	<i>Group A (n = 8)</i>	<i>Group B (n = 8)</i>	<i>Group C (n = 10)</i>	<i>Total (n = 26)</i>
Urticaria	8 (100%)	8 (100%)	10 (100%)	26 (100%)
Contact	8 (100%)	4 (50%)	7 (70%)	19 (73%)
Generalized	3 (38%)	5 (63%)	9(90%)	17 (65%)
Wheezing (asthma)	4 (50%)	5 (63%)	10 (100%)	19 (73%)
Eczema ^b	3 (38%)	3 (38%)	2 (20%)	8 (31%)

^aExcept for eczema, reactions are immediate reactions to cow's milk that occurred on at least three separate occasions.

^bNot convincingly associated with cow's milk allergy; indicated here to distinguish from other groups that have been studied.

study at the time they were asked. We believe their histories are valid indicators of their severe allergy to CM.

DISCUSSION

Two major observations have been made while investigating the allergenicity of CM whey and casein hydrolysate formulas by skin testing children with a current history of immediate allergic reactions to CM. First, an unexpectedly high frequency of positive prick tests was found to the whey (69%) and to the casein (38%) products, despite the fact that they had been treated by hydrolysis to reduce their allergenicity and previously had been shown to be minimally antigenic

TABLE 3. ORAL PROVOCATIVE CHALLENGE WITH COW'S MILK

<i>Patient</i>	<i>Age (years)</i>	<i>Sex</i>	<i>Group</i>	<i>SIgE (IU/ml)</i>	<i>Amount (ml)</i>	<i>Dilution</i>	<i>Reaction</i>
SQ	4	F	A ^a	0.75	275	Undiluted	4 hives around mouth, 1 on arm
AP	2	M	A	0.65	37	Undiluted	3 hives around mouth, diarrhea
BG	3	M	B ^b	1.86	15	1:1	Hives around mouth, rhinorrhea, sneezing, cough
ML	4	M	C ^c	21.70	21	1:1	Hives around mouth, angioedema of eyelid, sneezing
CS	2	M	C	26.64	7	1:1	Hives around mouth, generalized urticaria, nasal congestion, itchy eyes, cough, wheezing

^aGroup A = prick test (+) to CM.

^bGroup B = prick test (+) to CM, whey hydrolysate (Good Start H.A.).

^cGroup C = prick test (+) to CM, whey hydrolysate (Good Start H.A.), and casein hydrolysate (Nutramigen).

ALLERGIC REACTIONS TO COW'S MILK

and nonallergenic in animals.⁽⁵⁻⁷⁾ Second, the skin test profiles seem to reflect the severity of the immediate allergic reactions to CM as indicated both by history and by provocative challenge.

Severe acute allergic reactions to casein hydrolysate formulas (Pregestimil and Nutramigen) in one child with positive scratch tests to these products have been reported recently by Bock.⁽³⁾ There is also a report of a newborn infant who developed anaphylactic shock, once after ingesting his mother's milk and once after ingesting a formula containing a casein hydrolysate (Pregestimil). The casein hydrolysates in Nutramigen and Pregestimil are similar.

Severe acute reactions to whey hydrolysate formulas also have been reported. Businco et al.⁽²⁾ studied five infants who experienced allergic reactions when they were first fed with a small amount of CM whey protein hydrolysate (Alfaré, Nestlé). Prick tests with Alfaré were positive in all children, and they had high serum concentrations of specific IgE to CM protein (4/5 were greater than 12.8 Phadebas RAST units). Good Start HA (Carnation), a trypsin digest of CM whey, is sold in the United States. We are aware of a few nonfatal acute reactions to Good Start in children. The term "hypoallergenic" was promptly and voluntarily removed from the can label by the manufacturer once these became known and preliminary results of this study became available.

Thus, neither the currently commercially available casein hydrolysate formulas nor the whey hydrolysate formulas should be considered completely safe for all children. Certainly, they should no longer be considered as safe for the child who has had previous adverse IgE-mediated cutaneous (urticaria) and respiratory (asthma) reactions to CM.

This does not mean that under special circumstances, when breastfeeding is not possible, these formulas should not be used to try to prevent the development of sensitization to CM and the occurrence of allergy. On the contrary, in this instance, they indeed may be hypoallergenic.

Zeiger et al.⁽⁸⁾ recently reported that reduced exposure of infants (during pregnancy and lactation, with supplementation) to allergenic foods (milk, egg, peanut, fish), with the use of a casein hydrolysate (Nutramigen), reduced atopic dermatitis, urticaria, and gastrointestinal disease due to food sensitization in the first year of life. Likewise, Chandra et al.⁽⁹⁾ recently reported the results of a prospective double-blind randomized control trial of whey hydrolysate (NAN/HA, available in the United States as Good Start HA), conventional CM formula, soy formula, and exclusive breast-feeding for 4 months in high-risk infants. Among those not breast-fed, feeding the whey hydrolysate formula significantly reduced the incidence of atopic disease. The use of a soy protein formula did not reduce allergic symptoms.

Unexpectedly, in the present study, we found that skin test results separate the patients into three groups that seem to reflect a spectrum of severity of allergic symptoms history, the level of sIgE to CM, and responses to oral provocation challenge. One would expect to find clinically irrelevant false positive CM skin tests at one end of this spectrum and allergic reactions to the feeding of casein hydrolysates at the other end. In between would be found reactions to CM, tolerance to whey hydrolysates, reactions to whey hydrolysates, and tolerance to casein hydrolysates.

The concept of a spectrum of clinical manifestations, associated with adverse reactions to CM in children, is not a new one. Hill et al.^(10,11) have categorized these children into three groups based on nonplacebo-controlled opened CM challenge and the time of clinical reaction after a formal CM challenge. Group I (immediate reactors) patients ($n = 15$) were CM skin test positive, had high IgE anti-CM, and reacted within 45 minutes to small volumes of CM with urticaria, an exacerbation of eczema, wheeze, or vomiting. Group II (intermediate reactors) patients ($n = 24$) were usually skin CM skin test negative, did not have elevated IgE anti-CM, and reacted between 1 and 20 hours after CM ingestion with symptoms of milk enteropathy (vomiting and diarrhea). Group III (late reactors) patients ($n = 8$) were usually skin test negative, only some (slowly evolving eczema) with elevated IgE anti-CM, and reacted more than 20 hours after CM ingestion of normal volumes of milk with symptoms of coughing, diarrhea, eczematoid rashes, or a combination of these. We believe our patients ($n = 26$) most resemble

those in Hill's group I. They all had a history of immediate reactions and had positive prick tests to CM. Based on our finding of a spectrum of skin reactivity to CM and to commercially available CM protein hydrolysates, we propose that immediate reactors with positive skin tests be categorized as groups IA, IB, and IC in future clinical studies.

Sampson⁽¹²⁾ found that atopic children with objectively proven (DBPCFC) immediate cutaneous (13/21), respiratory (12/21), and gastrointestinal (10/21) reactions to CM and positive prick tests (21/21) to CM were able to tolerate a new casein hydrolysate formula (Alimentum) without difficulty except for 1, who developed a single hive on his cheek. It is difficult to compare our patients with Sampson's because he did not indicate that he had skin tested the patients with Alimentum at the time of his report. However, 8 of 10 (80%) of our patients in group C had positive prick tests to Alimentum, the newest casein hydrolysate formula available for infants and children in the United States. In addition, the incidence of occurrence of atopic dermatitis in Sampson's patients appears to be higher than in our patients, 16/21 (76%) vs 8/26 (31%). The occurrence of urticaria was more frequent in our patients, 26/26 (100%) vs 15/21 (71%), as was wheezing 19/26 (73%) vs 12/21 (57%). We have not studied children with predominantly gastrointestinal symptoms from CM. Whether or not some of these children fit into this spectrum, as determined by skin test reactivity, remains to be determined.

Sampson⁽¹²⁾ recommended that "infant formulas promoted as 'hypoallergenic' be tested in milk allergic patients to assess their allergenic potential." To this we would add a corollary—individual milk allergic patients should be tested with infant formulas thought to be "hypoallergenic" to assess the child's level of reactivity before the formula is considered to be safe for that child.

We have not systematically challenged all of our patients with whey and casein hydrolysates. The results of our studies to date indicate that this should be done, but done cautiously in order to make skin testing with CM and CM hydrolysates and measurement of sIgE to CM even more useful for the clinician caring for children. It is expected that these tests will help physicians distinguish the less severe from the more severe reactors to CM.

ACKNOWLEDGMENTS

We would like to thank the many pediatricians and family medicine physicians of the Rochester, NY, community who referred children for confirmation of diagnosis and management. Special thanks also go to Marcia Palumbo, R.N., and Kris Klafhen, L.P.N., who performed the skin testing and to Amy Mincher, R.N., who assisted in the challenge studies. As always, John J. Condemi, M.D., provided encouragement and intellectual guidance. In part, this work was supported by grants from 3M Diagnostic Systems, Inc., and Carnation, Nutritional Division.

REFERENCES

1. 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.
2. 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.
3. Bock SA. Probable allergic reaction to casein hydrolysate formula (Correspondence). *J Allergy Clin Immunol* 1989;84:272.
4. 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.
5. Granati B, Marioni L, Rubaltelli FF. Evaluation in guinea pigs of the allergenic capacity of two infant formulae based on hydrolyzed milk proteins. *Biol Neonate* 1985;48:122-124.

ALLERGIC REACTIONS TO COW'S MILK

6. Gjesing B, Osterballe O, Schwartz B, et al. Allergen-specific IgE antibodies against antigenic components in cow milk and milk substitutes. *Allergy* 1986;41:51-56.
7. Knights RJ. Processing and evaluation of the antigenicity of protein hydrolysates. In: Lifshitz F, ed. *Nutrition for special needs in infancy—Protein hydrolysates*. New York: Marcel Dekker, 1985, Chap 8, pp 105-115.
8. Zeiger RS, Heller S, Mellon MH, et al. Effect of combined maternal and infant food-allergen avoidance on development of atopy in early infancy: A randomized study. *J Allergy Clin Immunol* 1989;84:72-89.
9. Chandra RK, Singh G, Shridhara B. Effect of feeding whey hydrolysate, soy and conventional cow milk formulas on incidence of atopic disease in high-risk infants. *Ann Allergy* 1989;63:102-106.
10. Hill DJ, Ford RPK, Shelton MJ, Hosking CS. A study of 100 infants and young children with cow's milk allergy. *Clin Rev Allergy* 1984;2:125-142.
11. Hill DJ, Firer MA, Ball G, Hosking CS. Recovery from milk allergy in early childhood: Antibody studies. *J Pediatr* 1989;114:761-766.
12. Sampson HA. Safety of casein hydrolysate formula in children with cow's milk hypersensitivity. *Pediatr Res* 1989;25:123A (Abstract 725).

Address reprint requests to:
Robert H. Schwartz, M.D.
Allergy, Asthma, Immunology of Rochester, P.C.
Genesee Valley Medical Center
919 Westfall Road, Building B
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. L. BUSINCO, P. LUCENTI, G. ARCESE, G. ZIRUOLO, A. CANTANI. 1994. Immunogenicity of a so-called hypoallergenic formula in at-risk babies: two case reports. *Clinical & Experimental Allergy* 24:1, 42-45. [[CrossRef](#)]
3. V. Ragno, P. G. Giampietro, G. Bruno, L. Businco. 1993. Allergenicity of milk protein hydrolysate formulae in children with cow's milk allergy. *European Journal of Pediatrics* 152:9, 760-762. [[CrossRef](#)]
4. Luisa Businco, J. Bellintini. 1993. Food allergy in childhood. Hypersensitivity to cows'milk allergens*. *Clinical & Experimental Allergy* 23:6, 481-483. [[CrossRef](#)]
5. 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](#)]
6. Luisa Businco. 1993. Is Soy Allergy Overestimated?Is Soy Allergy Overestimated?. *Pediatric Asthma, Allergy & Immunology* 7:2, 73-76. [[Citation](#)] [[PDF](#)] [[PDF Plus](#)]
7. STANLEY P. GALANT, IRENE B. HAYDIK. 1991. Allergenicity of Cows' Milk Formula Hydrolysates 1. In Vitro Evaluation by Fast InhibitionAllergenicity of Cows' Milk Formula Hydrolysates 1. In Vitro Evaluation by Fast Inhibition. *Pediatric Asthma, Allergy & Immunology* 5:3, 237-244. [[Abstract](#)] [[PDF](#)] [[PDF Plus](#)]
8. ROBERT H. SCHWARTZ, LINDA B. PEERS, MARK S. AMONETTE, STEVEN A. WITHERLY. 1991. Usefulness of a Cow's Milk Whey Infant Formula (Good Start) in the Management of Children with Group 1A (Topical Reactors) IgE-Mediated Cow's Milk AllergyUsefulness of a Cow's Milk Whey Infant Formula (Good Start) in the Management of Children with Group 1A (Topical Reactors) IgE-Mediated Cow's Milk Allergy. *Pediatric Asthma, Allergy & Immunology* 5:4, 305-312. [[Abstract](#)] [[PDF](#)] [[PDF Plus](#)]
9. MARK S. AMONETTE, ROBERT H. SCHWARTZ, LEISA MATTSON, LINDA B. PEERS, DONALD M. ELDREDGE. 1991. 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-OldDouble-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. *Pediatric Asthma, Allergy & Immunology* 5:3, 245-251. [[Abstract](#)] [[PDF](#)] [[PDF Plus](#)]