

Recommendations for Soy Infant Formula: A Review of the Literature and a Survey of Pediatric Allergists

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ABSTRACT

Statements in the pediatric and gastroenterology literature to the effect that use of soybean formula should be avoided because of its high "allergenicity" seem to be unfounded. A review of the literature as well as personal experience in practice and with two dietary prophylactic studies spanning 15 years suggest that the availability of soybean formula constitutes a useful contribution to our knowledge of the handling of many nutritional problems of infants and children. The availability of soybean formula provides parents of infants with cow's milk allergy a nutritional food that can be used in the preparation of many kinds of food dishes and desserts to provide variety for children on restrictive diets. Over the past four decades, the use of soybean formula as a part of a dietary prophylaxis against the development of atopy in children of allergic families has been well accepted by the vast majority of infants who have received it. A survey of pediatric allergists showed the limits of what can be obtained by even the least demanding questionnaire. Given the rarity of reactions and the difficulty in identifying a clear causal agent, the average allergist is "overasked" by even a simple one-page set of questions. If anything, the wide range of answers indicates widespread confusion. A definitive answer about the existence of soybean allergies cannot be obtained without a detailed protocol for reporting and cross-validating such observations in a collaborative study. The use of soybean in infant feeding goes back many centuries in Chinese and Japanese cultures. In modern Japan, soy formula is commonly used either as a substitute for human breast milk or as a postweaning protein source in the first year of life. The first reported use of a soybean preparation for feeding infants with milk allergy was reported by Hill and Stuart in 1929.⁽¹⁾ Yet recommendations for soybean formula have remained controversial. We review the evidence for and against soybean formula and present data from a survey of pediatric allergists.

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INTRODUCTION

History of soybean formula introduction

IN THE 1920s, pediatricians noted that children who were fed egg yolk, either to treat or to avoid iron deficiency anemia, frequently developed classic atopic eczema. They further observed that a majority of these eczematous infants went on to develop major respiratory allergies, such as asthma or allergic rhinitis.⁽²⁾ They also noted that seven times as many infants fed cow's milk developed atopic eczema as did those who had been exclusively breastfed.⁽³⁾

As a result of these observations, Glaser and Hill recommended that one should deliberately withhold from the diet of babies of allergic families those foods suspected of being common allergenic offenders in the development of eczema (J. Glaser and L. Hill, personal communication). These foods included egg, chicken, cow's milk, beef, and wheat. They suggested that these foods be avoided during the first 6–9 months of life as well as during the mother's last trimester of pregnancy and while breastfeeding.

In the first reported trial of dietary prophylaxis, Glaser and Johnstone⁽⁴⁾ recommended strict avoidance of egg, chicken, wheat, and cow products for the first 9 months of life, substituting soybean formula for cow's milk. Few of these infants were breastfed. In this study, infants who were fed such a restrictive diet developed significantly less atopic eczema, and of those who did develop eczema, only 5% went on to develop asthma or allergic rhinitis. By contrast, 60% of their eczematous siblings and controls not on this diet went on to develop major respiratory allergies.

In a second 12-year prospective controlled study of the effects of dietary prophylaxis by Johnstone and Dutton,⁽⁵⁾ 235 infants of atopic families were randomly and prospectively assigned to receive a diet free of milk, beef, egg, chicken, and wheat for the first 9 months of life or to be permitted to have these foods in the first few months of life. Of those on the prophylactic diet, only 10% were breastfed. The only other formula permitted for this group was a soybean-derived formula. The nondiet group received an evaporated milk formula. Mothers of both groups were advised to avoid consumption of milk and egg in the last trimester of their pregnancies and while breastfeeding. Follow-up 10–12 years later revealed that significantly fewer (9 of 112) in the milk-free diet group developed asthma, compared with infants not placed on such a diet (40 of 120). Follow-up 10–12 years later revealed that significantly fewer (9 of 115) in the milk-free diet group developed asthma compared with infants not placed on such a diet (28 of 120).

Other studies have reported the helpfulness of dietary prophylaxis. Businco et al.⁽⁶⁾ reported that environmental controls and reduced maternal intake of milk and eggs gave promising results in preventing atopic disease. Also, Matthew et al.⁽⁷⁾ reported on a study on the prevention of eczema in which 23 children were placed on a diet of exclusive breast milk with soybean formula as complementary feeding or permitted to have cow's milk for the first 6 months of life. They found that significantly fewer infants on the regimen of soy plus breastfeeding developed eczema in the first 12 months of life compared with infants permitted to have cow's milk. However, in reporting on another study of dietary prophylaxis, Zeiger et al.⁽⁸⁾ noted that atopic disease did occasionally develop in spite of reasonable efforts at careful instruction of well-motivated parents. The most obvious factor for failure was parental noncompliance. They found that less than half of highly motivated families adhered to the advice to withhold cow's milk during the mother's last trimester of pregnancy and while nursing her infant.

Recent debate of effectiveness of soybean prophylaxis

Halpern et al.⁽⁹⁾ were unable to confirm the effectiveness of dietary prophylaxis. A detailed critique of the comparison of the findings and interpretation of results of the studies by Johnstone and Dutton and those of Halpern et al. has appeared elsewhere.⁽¹⁰⁾

Two more recent studies failed to replicate the prophylactic advantage of soy vs cow's milk in the prevention of allergic disease. Kjellman and Johansson⁽¹¹⁾ studied 48 children with a bilateral family history of atopy. The soyfed group was breastfed for 2–3 months, and the milkfed group was breastfed 1.5–3 months before milk formula was given. In either group, these children might have become sensitized to cow's milk received either in utero⁽¹²⁾ or via their mothers' breast milk.^(13,14) Follow-up was for 4 years. Kjellman and

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Johansson concluded that withholding cow's milk for 9 months did not reduce the incidence of atopic symptoms of cow's milk intolerance. However, they permitted mothers of both groups to drink milk while breastfeeding and did not specify how long or if solid foods were delayed. Allergy developed in 66.7% of both groups. This prevalence of allergy inordinately exceeds any previously published frequencies of allergic disease^(15,16) found in other studies of the incidence of atopic disease in the general population. They also suggested that the low levels of IgE antisoym antibodies found in a few of the soyfed group seemed to be of no clinical significance.

In a more recent study on the use of soybean formula in a dietary prophylaxis program, Merrett et al.⁽¹⁷⁾ reported a 12-month prospective study of 500 Welsh babies born into allergic families. In the intervention group, 238 mothers of high-risk infants were assigned to withhold from their children all cow's milk products for 4 months, replacing them with soy formula or breastfeeding, with soy complementary feeds. Mothers in this group were advised to restrict their daily milk intake to one-half pint per day. A second group of 249 mothers were advised to offer their children cow's milk after weaning. One third of the soyfed group were breastfed compared with 43% of the cow's milkfed group. By 3 months of age, 26% of the soyfed group had received some cow's milk products. The allergic symptoms reported among the two groups during the first year were similar, but all symptoms were less in infants in either group who had been breastfed. This would suggest, contrary to the findings of Kjellman and Johansson,⁽¹¹⁾ that avoidance of cow's milk was helpful in the intervention of atopic disease in the study groups. Few IgE antisoym antibodies were detected in the sera of the soyfed group. As in Zeiger's study,⁽⁸⁾ these authors found problems with compliance with instructions by parents. At 3 months of age, 37% of the soyfed infants had demonstrable IgG4 milk-specific antibodies in their sera. It is of interest that Merrett et al.⁽¹⁷⁾ stated that "it is just possible that the deleterious effects of cow's milk feeding are yet to show and that the ten-year follow-up trial of Johnstone and Dutton⁽⁵⁾ anticipates this possibility."

Claims about the allergenicity of soybean

In support of the argument against the use of soy formula as a substitute for cow's or breast milk in a dietary prophylaxis regimen, several authors refer to the allergenicity of soybean.^(8,11,18,19) In a survey of American pediatric allergists, several of them told the senior author that they were taught either by the head of their pediatric departments or by pediatric gastroenterologists in their training periods that soy was very allergenic. However, a careful review of the references cited by these physicians and authors revealed that with the exception of a description published in 1961⁽²⁰⁾ of a child with anaphylaxis from ingestion of soy formula, most of the references reported either spruelike or other nonallergic gastrointestinal symptoms.⁽²¹⁻²⁵⁾

A review of allergic reactions to cow's milk⁽²⁶⁾ recommended avoidance of use of soy-derived infant formulas because "the allergenicity of soy proteins is now more readily recognized." To support this thesis, the author quoted two sources.^(27,28) In the first of these, Burks et al.⁽²⁷⁾ demonstrated the immunogenicity of soy proteins using ELISA to reveal antibodies to soy in a few infants with atopic dermatitis. However, the antigens they used were derived from crude soybean. Many of the soybean proteins found in modern day soybean formulas are denatured by heat. This probably explains why some authors have found positive RAST tests in some children who clearly tolerated soybean formula without developing clinical allergic symptoms. Witherly,⁽²⁸⁾ in a letter to the *American Journal of Clinical Nutrition* written to challenge a previous letter suggesting soy was not clinically allergenic, stated that there is abundant evidence of its allergenicity. To support his point, he quotes the report of Eastham et al.⁽²⁹⁾ as evidence that soy protein "is at least as antigenic as cow-milk protein and so should be used with caution." In fact, what Eastham et al. demonstrated was simply that infants who ingested soy protein formed hemagglutinin (i.e., IgG not IgE) antibodies against soy protein. These IgG antibodies Eastham demonstrated have nothing to do with the development of clinical atopic disease. Witherly's letter further quoted the American Academy of Pediatrics Committee on Nutrition⁽³⁰⁾ as recommending against the use of soy formulas in the dietary management of documented allergic reactions to cow's milk. In a reply to Witherly's letter, Erdman⁽³¹⁾ makes two points in refutation. First, he states "We must be careful about drawing broad conclusions from ELISA and other in vitro procedures and assuming those tests directly translate to allergic responses in children fed cow's milk, soy or other foods." Second, he correctly quotes from the Academy of Pediatric Committee on Nutrition⁽³⁰⁾ as stating

"evidence suggests that soy protein may be less allergenic than heat-treated cow's milk protein and is probably a better source of nutrition in allergy-prone infants. However, these infants should be monitored for allergy to soy protein." Witherly also quotes the report of Hill et al.⁽³²⁾ who "found that 50% of infants with cow milk intolerance were also reactive to soy," implying that these infants were allergic to soy. In fact, Hill et al. stated that the "high incidence of soy intolerance [in their study] may have resulted from nonimmune" mechanisms. They also stated that the soy formulas they used contained sucrose and that many of the infants in their study were sucrose intolerant. Similarly, Witherly quoted Lothe et al.⁽³³⁾ as having "demonstrated that 35% of the cow milk-allergic infants were also allergic to soy." In fact, Lothe et al. found that in 29% of the infants in their study, their colic could not be traced to diet and that 18% of the infants with colic became free of symptoms when switched from cow's milk to soy formula. Thus, it seems that Witherly's arguments about the allergenicity of soy do not hold up.

Dannaeus et al.⁽³⁴⁾ studied antibodies to food antigens in 69 children with food allergy and atopic dermatitis. Although none were intolerant of soybean formula, 35 gave positive RAST tests to soy and 5 of 14 tested positive to prick tests to soy. This strongly calls to question the relationship between soy allergy and the presence or absence of positive RAST and skin prick tests to soy protein. Foman⁽³⁵⁾ summed up his 30 years experience using soy protein formulas for infant nutrition and emphasized that less than 1% of the soy formula-fed babies showed adverse reactions of any kind to soy protein. Sampson⁽³⁶⁾ studied 204 patients with atopic dermatitis with double-blind placebo-controlled challenges and found that only 5% showed soy sensitivity. Giampietro et al.⁽³⁷⁾ could find only 4% of 143 children with atopic dermatitis who showed a positive food challenge test to soy.

Asthma from occupational inhalation of soybean dust has been reported.^(38,39) Thus, it was not unexpected that Kjellman and Johansson, in their soy vs milk prophylaxis trial, found no significant IgE antibodies to soybean in their soyfed group.⁽¹¹⁾ In clinical practice, slightly positive skin tests to soybean extract occur not uncommonly, but the incidence of soybean-induced anaphylaxis as a result of an infant's ingesting soy formula is very low or rare.

In the past, the choice for a hypoallergenic formula for at-risk infants as well as for those suspected of having milk allergy was evaporated milk, which was tolerated by some children sensitive only to the heat-labile milk proteins, such as lactalbumin. Wilson and Hamburger⁽⁴⁰⁾ suggested that a formula with even less potential for allergy than soybean is a formula whose protein source is enzymatically hydrolyzed casein. Unfortunately, these casein hydrolysate formulas have been shown capable of causing anaphylaxis in a subset of infants exquisitely sensitive to milk proteins.⁽⁴¹⁻⁴⁵⁾ Businco and Catani⁽⁴⁶⁾ reported the results of an interesting experiment. They studied the sensitizing effect via breast milk of partially hydrolyzed whey protein hypoallergenic formula. They gave 400 mL/day of the whey hydrolysate formula to 39 nursing high-risk mothers throughout the first 6 months of nursing. A second group of 39 control high-risk mothers were given 400 mL/day of cow's milk. At 1 year of age, babies of both groups had no significant differences in the cumulative incidence of atopic disease. However, the prevalence of babies at 12 months of age with specific anticow's milk IgE antibodies in their sera and total IgE was significantly higher in the group of babies whose mothers received the hydrolyzed whey hypoallergenic formula. This shows that the hydrolyzed formula not only contains peptides that are able to sensitize high-risk babies via breast milk but also, as Businco and Catani commented, "it seems even more sensitizing than cow's milk."

The findings of Businco and Catani⁽⁴⁶⁾ are not surprising in view of the report of Seban et al.⁽⁴⁷⁾ They pointed out in 1977 that because hydrolysis of milk proteins may be incomplete and a number of potentially allergenic macromolecules may be present in such formulas, manifestations of milk intolerance or allergy may occur in infants with extreme sensitivity if they are fed such hydrolysate formulas. These same authors showed that although manufacturers of casein hydrolysis formulas claimed that they were produced only from casein, injection of such formula into animals resulted in the production of precipitating antibodies against at least three whey proteins as well as against casein.

MATERIALS AND METHODS

This review of the literature on which type of infant formula is optimal, either for dietary prophylaxis of atopic disease in at-risk newborns or for the treatment of cow's milk allergy, suggests that there is a wide range

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of opinion on the subject. For this reason, we conducted a survey of pediatric allergists to find out what their experience had been over the years of clinical practice.

We sent questionnaires to 1450 pediatric allergists in the United States, Canada, Mexico, South America, France, Denmark, Sweden, Italy, Japan, Germany, Egypt, Saudi Arabia, and Indonesia. The questionnaire first asked each physician to *estimate the percentage* of all infants experiencing IgE-mediated allergic reactions to *cow's milk formula* and *how many* infants he or she had seen personally, or had direct knowledge of who had experienced anaphylaxis from drinking cow's milk formula. Specifically, we asked about the numbers of children seen with such symptoms as flareup of popliteal or antecubital eczema, asthmatic wheezing, circumoral contact dermatitis, allergic rhinitis, or anaphylactic shock within minutes of drinking milk. Next, the same set of questions was asked with regard to drinking *soybean formula*. Then, experience with milk *hydrolysates* such as Nutramogen, Goodstart, and Alfaré was probed, although, not in the same detail as for cow's milk and soybean formula. Finally, each physician was asked to state the number of years they had been in practice.

The objectives of the survey were limited, but we used very precise terminology. On a one-page questionnaire, we asked about IgE-mediated allergic reactions, not about food intolerance. We asked about personal, cumulative lifetime experiences, not about knowledge obtained from articles or lectures. We were interested in experiences in normal practice settings, not in the selective caseloads from highly specialized medical centers. Yet we realized that recall of practice events from the past is limited and asked "*approximately* what percentage of all infants" or "*approximately* how many cases of. . ." have you seen. We were interested in the range of responses rather than in a precise count or true/false test.

Had we been interested in incidence and prevalence, we would have used a long questionnaire inquiring about their patient load and referral population, the rate of breastfeeding in this population, the marked share of cow's milk, soybean, and hydrolyte formulas, and the confirmation of allergic reactions through RAST tests. All questions would have specified a clearly defined recent time period, such as "during the calendar year 1990" or "within the last 12 months." We would also have used persistent follow-up to raise the response rate as high as possible rather than use anonymous returns to a single mailing with optional self-identification. Such a long questionnaire was considered overkill for our purposes. Instead, we settled for the limited objectives of an unfunded research project.

RESULTS

There were 402 complete responses available for analysis, for a response rate of about 28%. Some respondents were personally interviewed by the senior author at a scientific meeting. Those who identified themselves were followed by telephone to check how "hard" their answers were. The general impression was that even the limited objectives of our survey were difficult to meet for most respondents. Frequently, some questions were left unanswered. Many of the quantitative questions ("How many cases of. . .") were answered qualitatively ("dozens," "several," and so on). Frequently, the answers were given with qualifiers ("less than. . .") or as ranges ("5%–10%"). The response rate of 28% is average for a one-mailing only survey.⁽⁴⁸⁾ Our impression was that the primary reason for nonresponse was lack of detailed knowledge rather than unwillingness to respond. Had we pressed for higher returns, the proportion of unanswered questions would have increased. The answers provided give, in our opinion, a fairly accurate picture of the prevailing experiences and views of pediatric allergists.

The 402 respondents represented a wide range of practice lengths (Table 1), ranging from 1 to 50 years, for a total of over 6731 years of experience (19 respondents did not answer the question). The average was 17.5 years of practice. Nearly half (43%) volunteered a single-value estimate of the incidence of allergic response to cow's milk formula (Table 2). About a quarter did not answer this question, most likely because they could not even give an estimate, and another quarter gave a qualified estimate, such as "less than X%." The remaining respondents gave a range, such as "between X% and Y%," or a qualitative response, such as "very few." For those who gave a single-value estimate we computed summary statistics. The average estimate was 3.4%, based on 2935 years of experience. For soybean formula, the estimate averaged 1.1%, based on 2521 years of experience. More interesting is that nearly 40% could not provide an estimate.

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TABLE 1. YEARS IN PRACTICE

<i>Years in practice</i>	<i>n</i>	<i>%</i>
1-5	49	12.8
6-10	74	19.3
11-15	69	18.0
16-20	74	19.3
21-25	35	9.2
26-30	37	9.7
31-50	45	11.7
Missing	19	—
Total	402	100.0
Summary statistics		
Mean $\pm$ SE	17.57 $\pm$ 0.559	
Median	15	
Mode	10	
Minimum	1	
Maximum	50	
<i>n</i>	383	
Sum	6731 years of experience	

The most frequently observed reaction to cow's milk was eczema, for which the average respondent reported seeing 18 cases, or about 1 case per year (Table 3). Allergic rhinitis was next with an average of 14.6 cases, or slightly less than 1 case a year. Circumoral dermatitis and asthma were less frequent with an average of 6.7 cases for dermatitis and 7.5 cases for asthma—that is it took over 2 years of experience to see 1 case. Shock as a reaction to cow's milk was extremely rare, with less than 1 case per respondent reported, or nearly 18 years of experience needed per case. Reported cases of allergic reactions for soybean formula were only about one-sixth the number of reactions to cow's milk (Table 4). Over their whole practice experience,

TABLE 2. REPORTED INCIDENCE ESTIMATES

<i>Answer type</i>	<i>Cow's milk</i>		<i>Soy bean</i>	
	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>
No answer	94	23.7	155	39.0
Single value ^a	171	43.1	148	37.3
Qualified single	92	23.2	72	18.1
Range	37	9.2	21	5.3
Qualitative	3	.8	1	.3
Missing	5	—	5	—
Total	402	100.0	402	100.0
Summary statistics, single-value answers				
Mean $\pm$ SE	3.37 $\pm$ 0.51		1.05 $\pm$ 0.20	
Median	1		0.005	
Mode	1		0	
Minimum	0		0	
Maximum	60		20	
<i>n</i>	171		148	
Years of experience	2935		2521	

^a Includes 0 values.

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TABLE 3. NUMBER OF REACTIONS OBSERVED TO COW'S MILK FORMULA

	Asthma		Eczema		Rhinitis		Circumoral dermatitis		Shock	
	n	%	n	%	n	%	n	%	n	%
Answer type	41	10.3	69	17.3	102	25.5	105	26.3	57	14.3
No answer	311	77.8	278	69.5	264	66.0	266	66.5	330	82.7
Absolute, single ^a	23	5.8	23	5.8	18	4.5	13	3.3	5	1.3
Absolute, range	5	1.3	8	2.0	9	2.3	5	1.3	1	.3
Percent, single	4	1.0	4	1.0	1	.3	1	.3	1	.3
Percent, range	16	4.0	18	4.0	6	1.5	10	2.5	5	1.3
Qualitative	2	—	2	—	2	—	2	—	3	—
Missing	402	100	402	100	402	100	402	100	402	100
Total										
Summary statistics absolute, single										
Mean $\pm$ SE	7.45 $\pm$ 0.83		18.34 $\pm$ 2.1		14.64 $\pm$ 2.20		6.66 $\pm$ 0.94		0.96 $\pm$ 0.11	
Median	2		5		2		1		0	
Mode	0		0		0		0		0	
Minimum	0		0		0		0		0	
Maximum	100		303		303		100		20	
n	311		278		264		266		330	
Years experience	5181		4518		4428		4250		5615	
Cases/year of experience	0.44		1.13		0.87		0.42		0.06	

^aIncludes 0 values.

TABLE 4. NUMBER OF REACTIONS OBSERVED TO SOYBEAN FORMULA

	<i>Asthma</i>		<i>Eczema</i>		<i>Rhinitis</i>		<i>Circumoral dermatitis</i>		<i>Shock</i>	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Answer type										
No answer	22	5.5	31	7.7	48	12.0	43	10.8	23	5.8
Absolute, single ^a	375	93.3	345	86.05	347	86.5	355	88.8	375	93.8
Absolute, range	1	0.2	16	4.0	4	1.0	1	0.3	1	0.3
Percent, single	1	0.2	2	0.5	1	0.2	0	0	0	0
Percent, range	1	0.2	3	0.7	0	0.0	0	0	0	0
Qualitative	1	0.2	4	1.0	1	0.2	1	0.3	1	0.3
Missing	1	—	1	—	1	—	2	—	2	—
Total	402	100	402	100	402	100	402	100	402	100
Summary statistics absolute, single										
Mean $\pm$ SE	1.33 $\pm$ 0.19		2.76 $\pm$ 0.43		2.548 $\pm$ 0.43		0.910 $\pm$ 0.224		0.107 $\pm$ 0.022	
Median	0		0		0		1		0	
Mode	0		0		0		0		0	
Minimum	0		0		0		0		0	
Maximum	40		90		150		50		5	
<i>n</i>	375		345		347		355	375	375	
Years experience	6368		5769		5834		5923		6393	
Cases/year of experience	0.08		0.26		0.15		0.05		0.006	

^a Includes 0 values.

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respondents averaged 2.8 cases of eczema, 2.5 cases of rhinitis, 1.3 cases of asthma, and 0.9 cases of circumoral dermatitis. Only one tenth of reporting respondents had seen a case of shock during their entire practice period. It would take 167 years for the average pediatric allergist to see 1 case.

Reactions to hydrolytes were even rarer than to soybean formula (Table 5). The average allergist reported 0.4 case for Nutramogen and 0.6 case for Goodstart. Only 3 of the 402 respondents reported reactions to Alfaré. On the average, the respondents had only seen 1 case of hydrolyte reaction during their entire practice period.

DISCUSSION

The main finding of our survey is the rarity of allergic reactions to soybean formula and hydrolytes. Most respondents reported zero cases. The arithmetic average was somewhere around 1 case every 3 years. We have strong suspicions that even this figure is highly inflated. First, the arithmetic mean is strongly affected by a few outliers who reported extraordinarily high observations, such as 90 cases of eczema, 150 cases of rhinitis, and 50 cases of circumoral dermatitis. We suspect that either these cases were observed intolerances rather than IgE-mediated reactions, or the respondent represented a highly specialized referral center. As this was an anonymous survey, we could not check the validity of such responses. Second, many respondents failed to provide an answer to specific reactions, giving us missing values. We suspect that most likely such "no answer" means "no observations," but again, we could not check the validity of the response and had to take the response at its face value. Third, for those respondents who signed their questionnaires, the senior author conducted follow-up interviews to check how hard the evidence for reactions to cow's milk and soybean formula was. Such retesting gave consistent evidence for cow's milk reactions but not for soybean reactions. Estimates were frequently revised down. Literature or lectures rather than clinical experience proved the source of such data.

TABLE 5. NUMBER OF REACTIONS OBSERVED TO HYDROLYTES

	<i>Nutramogen</i>		<i>Goodstart</i>		<i>AlfaRé</i>	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Answer type						
No answer	75	18.8	75	18.8	75	18.8
Absolute, single ^a	320	80.0	312	78.0	324	81.0
Absolute, range	3	0.8	6	1.5	1	0.3
Percent, single	1	0.3	1	0.3	0	0
Percent, range	0	0	0	0	0	0
Qualitative	1	0.3	6	1.5	0	—
Missing	2	—	2	—	2	—
Total	402	100	402	100	402	100
Summary statistics absolute, single						
Mean $\pm$ SE	0.438 $\pm$ 0.117		0.593 $\pm$ 0.187		0.049 $\pm$ 0.034	
Median	0		0		0	
Mode	0		0		0	
Minimum	0		0		0	
Maximum	30		50		105	
<i>n</i>	320		312		324	
Years experience	5459		5348		5523	
Cases/year of exp.	0.03		0.03		0.003	

^aIncludes 0 values.

However, the data may also be biased to the low side because of limited recall. Respondents often answered not with an estimate of their lifetime experience but with an estimate per year. We converted those responses to lifetime experiences if the years in practice was known. Research on recall periods clearly shows that rare events tend to be telescoped into more recent periods and underreported for events beyond 15–20 years.⁽⁴⁹⁾ We, therefore, suspect that older respondents with long practice periods underreported events and that the estimates only reflect experiences during the last 15 practice years. Our data actually show evidence for such recall bias. When the number of observed reactions are tabulated by length of practice, we see a steady increase of observations for up to 15 years of experience but not after 15 years.

Given the large measurement error obviously present in the data, it is difficult to draw conclusions about the true incidence of allergic reactions. Some consistency checks are, however, possible. If we assume a community like Rochester with about 10,000 births/year, a 50% breastfeeding rate, and a market for formula that is 75% cow's milk and 25% soybean based, and apply our derived estimates (Table 2) of 3.37% for cow's milk reactions and 1.05% for soybean reactions, we should experience 12 cases of soybean reaction and 126 cases of cow's milk reactions per year that may or may not be reported to the primary care physician, who may or may not make a referral to a pediatric allergist. If we further use our rates of observed reactions/year (about 3 for cow's milk, about 0.5 for soybean formula), we would expect about three full-time pediatric allergists in the community to see 9 cases of cow's milk reaction and 1.5 cases of soybean reactions. The implications are that only about 10% of infants with allergic reactions are seen by pediatric allergists.

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