

Correspondence

Probable allergic reaction to casein hydrolysate formula

To the Editor:

I would like to describe a food reaction that has been reported anecdotally but has not been well documented. This young man was first observed at age 5 months when his parents came seeking advice on infant feeding because of their highly atopic family history. His diet from birth to 5 months of age included breast milk, soy formula, rice cereal, and sweet potatoes. Symptoms had included mild wheezing, atopic dermatitis, and urticaria, beginning at age 2 weeks and slowly progressing up to the time of the initial evaluation. Because of concern that the onset of intermittent but regularly recurring wheezing might be due to the soy formula, since he was sensitized to soy (as determined by skin testing), his first trial of casein hydrolysate formula (Nutramigen) was administered at 7½ months of age. He appeared to dislike this immediately, and he vomited for about 45 minutes. Soy formula was returned to the diet, but almost daily wheezing continued despite oral bronchodilators. Skepticism that the casein hydrolysate was the problem resulted in a second feeding at 8 months of age with Pregestimil, one-fourth strength (exact quantity unknown). Within minutes he vomited and then exhibited choking, coughing, and wheezing, becoming quite breathless.

Subsequently, he started receiving Vivonex that he tolerated without difficulty. Because of continuing skepticism that casein hydrolysate was responsible for his symptoms after ingestion of that substance, 6 weeks later a double-blind food challenge with Pregestimil was administered. Two portions of Vivonex were prepared and placed in opaque baby bottles. One portion contained only Vivonex, and the other portion contained 0.5 cc of Pregestimil mixed in the same amount of Vivonex. These portions were coded and then administered by a blinded observer. The non-Pregestimil-containing Vivonex produced no reaction. The Pregestimil-containing Vivonex produced immediate (in seconds) vomiting followed promptly by an urticarial rash on the abdomen, neck, and face. No wheezing was detected. Skin testing was then undertaken with Nutramigen and Pregestimil. Four, 1 cm scratches were made on the patient's arm, and one drop of Nutramigen, one drop of Pregestimil, one drop of diluent control, and one drop of histamine (1 mg/ml) were placed on the scratches. The Nutramigen and Pregestimil each elicited an immediate wheal-and-flare reaction with the wheal being >15 mm in diameter. The control was negative, and the histamine produced a wheal 5 mm in diameter. The mother, physician, and a nurse were each used as control subjects, having the identical tests performed. Each control subject had a significant whealing reaction to the histamine, but no wheal appeared at the site of the control test or the test with the two formulas. Previous skin testing of this child with commercially available extracts to food produced the following results: egg, 25 mm (wheal diameter); cow's milk, 10 mm; wheat, 6 mm; soy, 6 mm; and squash, 4 mm.

We have previously observed youngsters who reportedly reacted to casein hydrolysate-containing formulas, but challenges in all preceding cases did not confirm these suspicions. I have been unable to find another documented case similar to this case. Seban et al.¹ have reported sensitization of rabbits by injection with casein hydrolysates, thus, providing an animal model to support the fact that these peptides are immunogenic to the mammalian immune system. Jarmoc and Primack² reported a milk-allergic youngster with two episodes of anaphylaxis after cutaneous application of casein-containing ointment to inflamed skin. Their patient had elevated RAST titers to milk proteins. The youngster reported here represents a double-blind, placebo-controlled, food-challenge proved example of reaction to casein hydrolysate-containing formula. Since he was highly sensitized to the formula by skin testing, it appears likely that this reaction was IgE mediated. Of course, it is possible that he was reacting to something else in the formula, but examination of the contents of these formulas does not reveal any other likely candidate.

I share this case with my colleagues so that other care providers who have not observed this phenomenon will be less skeptical than I about its possible existence and will attempt to confirm observations, such as this occurrence, by carefully controlled blind challenges and appropriate laboratory tests to confirm the mechanism when it is indicated.

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REFERENCES

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Benzalkonium chloride and bronchoconstriction

To the Editor:

Paradoxical responses to inhaled bronchodilators are well-recognized potential complications of nebulization therapy for asthma.¹⁻³ Recent articles⁴⁻⁶ have focused on the role of preservatives in nebulizer solutions as mediators of adverse reactions. First sulfites,^{7,8} and more recently, benzalkonium chloride (BKC),⁹⁻¹¹ have been demonstrated to induce dose-dependent bronchoconstriction. Albuterol nebulizer solution, recently introduced in the United States, contains BKC. Until this product became available, an injectable, unpreserved form of terbutaline sulfate adminis-