

after the initial challenge; he again showed no evidence of an adverse drug reaction.

To our knowledge, this is the first report of a celecoxib-specific anaphylactic or anaphylactoid reaction, given that the patient could safely take another NSAID, Naprosyn, another COX-2 inhibitor, Vioxx, and a sulfonamide-containing drug.

Two important observations devolve from this case study. First, the anaphylactic/anaphylactoid reaction to celecoxib is not necessarily due to the COX-2 inhibitory activity of the drug, and other medications of the same class can be well tolerated. This is consistent with the observations of Stevenson⁵ that anaphylactoid reactions to NSAIDs are usually selective for a single agent. In like fashion, cross-reactivity between NSAIDs and cyclooxygenase inhibitor is rare. Again, our patient tolerates Naprosyn, suggesting that a selective mechanism is involved with celecoxib sparing COX-1 inhibitors. On the other hand, the exact mechanism of COX-2 hypersensitivity is still unclear, inasmuch as a case of cross-reactivity between COX-1 and COX-2 inhibitors has been reported.⁶ Second, the hypersensitivity was not related to sulfonamide allergy, inasmuch as the patient tolerated a full dose of Septra.

This case report also demonstrates that celecoxib, like other sulfonamide group-containing agents (eg, many of the diuretics), has a low propensity for cross-allergenicity with sulfonamide antimicrobials.^{7,8} In general, these observations are important in the management of patients who have had allergic reactions to celecoxib in that systematic avoidance of all COX-2 inhibitors and sulfonamide-related medications might well not be necessary. Hence, the decision on how to proceed with therapy after a patient has had an adverse reaction to celecoxib must be taken on a case-by-case basis after appropriate challenges have been performed.

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Atopy and allergic respiratory diseases in multitransfused patients: A new insight into the increase in the prevalence of atopy

To the Editor:

In 173 patients affected by major β -thalassemia (BT) and a control group of 253 blood donors, we performed skin prick tests (SPTs) with glycerinate extracts (1/20 w/v; Bayropharm, Milan, Italy) of the most common inhalant substances (*Dermatophagoides pteronyssinus*, cat and dog allergens, *Alternaria alternata*, grass pollen, *Parietaria officinalis*, and olive) according to the recommendations of the European Academy of Allergology and Clinical Immunology.¹ The presence of asthma and/or rhinitis was investigated through use of a standardized questionnaire (ISAAC).²

The data were analyzed on an IBM-compatible personal computer with the statistical package program SPSS for Windows; we used the χ^2 test or multiple logistic regression as indicated. A *P* value of less than .05 was considered significant.

The 173 patients affected by BT had a mean ($\pm$ SD) age of 28 ($\pm$ 6) years (range, 8-42 years). Eighty-six (49.7%) of the patients were male; the other 87 (50.3%) were female. The patients had had their first transfusions at a mean ($\pm$ SD) age of 18.7 ($\pm$ 4.2) months, and they had been transfused regularly for a mean ($\pm$ SD) period of 27 ($\pm$ 6.5) years. Sixty percent of the patients underwent splenectomy; 90% were hepatitis C virus-positive. The control population had a mean ($\pm$ SD) age of 30 ($\pm$ 4) years (range 20-46 years); 129 were male and 124 were female. The prevalence of atopy (at least 1 positive SPT result for major inhalant allergens) was significantly lower in patients with BT than in the control population (28% [49/173 vs 45.28% [114/253]; *P* < .00001). Even when corrected for sex and age in a multiple logistic regression, subjects with BT were still protected for the development of atopy (*P* = .0045). Also significantly lower in the patients with BT than in the control group were the prevalence of asthma (3% vs 13%; *P* < .00001) and the prevalence of rhinitis (18% vs 31%; *P* < .0001). Patients who underwent splenectomy were not significantly different from patients who did not with respect to frequency of atopy (24.2% vs 34.2%; *P* = .15), rhinitis (14.2% vs 24.2%; *P* = .071), or asthma (1.9% vs 4.2%; *P* = .36).

A few years ago our group studied the prevalence of atopy among patients with BT compared with a control population of the same age. At that time, the subjects with BT had a mean age of 11.8 years and the prevalence of positive SPT results was 10%, which compared with 21% for the control population.³ In the present study, the mean age of the patients with BT was 28 years and the

prevalence of positive SPT results was 28%, which compared with 45.2% for the control group. This study also shows that the frequency of positive results of SPTs to aeroallergens and of respiratory atopic diseases increased even in this population considered at low risk of developing atopy, probably as consequence of both the normal increase in positive SPT results with age and the increase of atopy and allergic diseases observed in the last 20 years in our region.⁴

It has been speculated that the lower prevalence of atopy in patients with BT might be due to allergen-specific IgG acquired early in life through transfusions, which could suppress the synthesis of allergen-specific IgE,³ or to chronic viral infections.⁵ The role of splenectomy remains unclear. Theoretically, the higher incidence of bacterial infection after splenectomy might deviate T-cell cytokine response toward the T_H1 phenotype and a lower incidence of atopy. In this study, we found that splenectomy in patients with BT is associated with a lower incidence of atopy and atopic diseases, though the difference was not significant.

In conclusion, at a mean age of 28 years, patients with BT are still less atopic than the members of a general population. It seems that the atopy inhibitory factor (or factors) that acts in the first years of life has a long-term effect or is still active in adult life.

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Severe anaphylaxis to kiwi fruit: Immunologic changes related to successful sublingual allergen immunotherapy

To the Editor:

Sublingual swallow allergen immunotherapy (SLIT) with standardized extracts has been shown to reduce clinical symptoms in a variety of IgE-mediated respiratory allergic diseases.¹⁻⁴ Although it appears also as a reasonable route of allergen delivery for desensitization protocols in food-induced allergic reactions, it is usually not applied because of the lack of standardized extracts, the inconsistency in allergen uptake, and the possibility of therapy-related life-threatening anaphylactic symptoms in such patients.

We present the case of a 29-year-old white woman who had several episodes of severe anaphylaxis after consumption of kiwi fruit, including 3 episodes of allergic shock with loss of consciousness and subsequent hospitalization. For the first 2 episodes, the symptoms started shortly after ingestion of pure fresh kiwi preparations without concomitant consumption of additional foods, pointing to the causative role of kiwi. Most remarkably, in a third episode anaphylaxis had been elicited by minute amounts of kiwi left on a knife that was subsequently used to prepare a strawberry dessert served to the patient in a restaurant.

In addition, the patient had a 15-year history of seasonal rhinitis during the grass pollen season. Her physical examination revealed an otherwise healthy patient. Allergy diagnosis included positive skin prick test (SPT) reactions to kiwi, grass pollen, house dust mite, and crab meat (extracts from Allergopharma, Reinbek, Germany). A large panel of routinely tested seasonal and perennial aeroallergens, as well as food allergens, including birch pollen and latex, elicited negative results. When SPTs were performed with undiluted fresh kiwi extract, the patient had severe systemic symptoms, such as pharyngeal swelling and generalized urticaria. In the patient's serum specific IgE (CAP-FEIA; Pharmacia, Uppsala, Sweden) was found against kiwi (*Actinidia chinensis*; 28.0 kU/L; normal range, <0.35 kU/L), crab meat (*Peneaus indicus*; 3.18 kU/L), and timothy grass pollen (*Phleum pratense*; 29.0 kU/L; Fig 1).⁵ Western blot analysis of kiwi and timothy pollen extracts revealed specific IgE reactivity to the 30-kd major kiwi allergen, previously identified as Act c 1,⁶⁻⁸ and various IgE reactivities to timothy grass pollen allergens (Fig 2). A subsequent detailed analysis with recombinant allergens revealed dominant IgE reactivity with the *P pratense* allergens Phl p 1 and Phl p 4. SPTs and serologic analysis for specific IgE against a variety of other allergens, including birch pollen and latex, showed negative results.

Because of the life-threatening nature of anaphylaxis and the impossibility of allergen avoidance (unawareness of kiwi exposure in prepared meals), indication for immunotherapy was given, and SLIT was started with kiwi fruit extract. To this end, a stock solution was prepared by means of homogenization and filtration of fresh