

AUTHORS' RESPONSE TO IS ANGIOEDEMA A CLASS SIDE-EFFECT OF THE ANGIOTENSIN-CONVERTING ENZYME INHIBITORS?

To the Editor:

Drs Karagiannis, Tziomalos, and Athyros describe a patient who developed severe upper airway angioedema that necessitated an emergency tracheostomy.^{1,2} The patient had been treated with ramipril for the previous 3 years. After recovery, another physician administered trandolapril, and within 2 days, angioedema recurred. In our article,³ as noted in Table 1, 4 patients had experienced episodes of angiotensin-converting enzyme inhibitor (ACEI)-associated angioedema before presentation to the hospital. In fact, 2 patients had reported 2 prior episodes of angioedema, and 2 patients had experienced a single episode before presentation. All 4 patients had developed angioedema while receiving lisinopril or ramipril in the past and continued to receive these medications until hospitalization for a more serious episode of angioedema. These findings are consistent with earlier reports of a 10-fold increase of recurrent angioedema in patients who continued receiving ACEIs after already experiencing the initial attack.⁴ Furthermore, using a pharmaceutical database that provided experiences of 14 patients who had received both captopril and enalapril, 7 patients developed angioedema or urticaria with both medications.⁵ Three other patients reacted initially to enalapril but not subsequent captopril, and 4 patients who had tolerated captopril then had angioedema or urticaria from enalapril.⁵ The conclusions by Slater et al⁵ in 1988 remain true today. The angioedema is much more likely to recur in patients who have already developed angioedema from an ACEI should ACEIs be readministered. The case description by Drs Karagiannis, Tziomalos, and Athyros^{1,2} emphasizes the seriousness of the upper airway angioedema. Avoidance of ACEIs remains best!

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MITIGATED BINDING OF IgE TO THIOREDOXIN-TREATED SALT-SOLUBLE WHEAT ALLERGENS IN A CHILD WITH BAKER'S ASTHMA

To the Editor:

Baker's asthma is a common occupational disease among bakery workers¹; however, only 1 case of this disorder in children has been described.² During the past 3 years, a 6-year-old girl developed asthma, dermatitis, rhinitis, and conjunctivitis. Clinically, all of her symptoms were believed to be related to domestic exposure, because confectioneries were made and sold in her home since her birth.

Since the salt-soluble wheat fraction contains the IgE-binding proteins involved in baker's asthma,³ inhalation challenges were performed in the girl with a commercial salt-soluble wheat solution (Torii, Tokyo, Japan). The solution consisted of wheat grain defatted with ether and then extracted with 20 volumes of 5% saline (pH 7.1, 4.1 mg/mL of protein). A significant asthmatic reaction occurred on application of 0.02 mL of the solution, together with itchy eyes and a runny nose. The same test was performed on 2 asthmatic children not sensitized to wheat; however, these children did not respond.

Thioredoxin is a ubiquitous 12-kDa protein with a highly conserved catalytically active disulfide group. The role of thioredoxin in allergy is controversial. A previous study⁴ has demonstrated thioredoxin-linked mitigation of allergic responses to wheat in atopic dogs; however, another recent study⁵ showed that thioredoxins have allergic potential. Therefore, the present study was undertaken to evaluate the role of thioredoxin in the girl and the patients with other clinical symptoms of IgE-mediated wheat allergy.

Five patients were enrolled in this study. Four of them had experienced rash, respiratory distress, or collapse after the ingestion of wheat-containing foods; however, one of them had no symptoms when ingestion was not followed by exercise. One patient was a baker with generalized chronic dermatitis, which greatly improved after suspension of work followed by aggravation after resumption of work. Oxidized thioredoxin was purchased from Wako Chemicals, Osaka, Japan. Dithiothreitol was used for reduction of thioredoxin⁴ and then removed by centrifugation on a Bio-Spin 6 column (Bio-Rad, Hercules, CA). One hundred milliliters of the salt-soluble wheat solution was treated with 8 μ L of 0.3 mg/mL of oxidized thioredoxin or the same dose of reduced thioredoxin. The skin prick tests were performed with plastic bifurcate needles (Lincoln Diagnostics, Decatur, IL), and the diameters of the wheals were determined after 15 minutes. The concentrations of specific IgE to salt-soluble wheat were determined with CAP-FEIA (Phadia, Uppsala, Sweden). For the inhibition assays in CAP-FEIA, 200 μ L of serum was incubated overnight with 20 μ L of each of the wheat fractions before the measurements.

The skin wheal reactions with the salt-soluble wheat were markedly decreased with reduced thioredoxin in the present girl. In addition, the in vitro binding of IgE to wheat was

Table 1. SPT and CAP-FEIA Inhibition Test Results After Treating Salt-Soluble Wheat Preparations With Catalytically Active Thioredoxin in Patients With Wheat-Related Allergies

Patient No. (age/sex)	Clinical features	SPT result, wheat diameter in mm			CAP-FEIA, kU/L (%)*			
		Untreated	ReTh	OxTh	Negative	Untreated	ReTh	OxTh
Present case (6 y/F)	Baker's asthma	10	4	13	24.2	1.0 (96)†	6.1 (75)	1.0 (96)
1 (7 mo/M)	Generalized urticaria	16	19	15	16.4	7.3 (55)	6.7 (59)	6.8 (59)
2 (9 y/M)	Rash and chest tightness with wheezing	24	24	24	>100.0	38.7 (>60)	41.6 (>58)	43.1 (>57)
3 (2 y/M)	Anaphylactic shock	10	9	8	2.2	<0.3 (>86)	<0.3 (>86)	<0.3 (>86)
4 (37 y/F)	Anaphylactic shock after exercise	5	4	4	3.4	0.5 (85)	0.6 (82)	0.4 (88)
5 (46 y/M)	Baker with generalized chronic dermatitis	0	1	0	66.3	19.9 (70)	16.3 (75)	18.3 (72)

Abbreviations: ReTh, reduced thioredoxin-treated salt-soluble wheat fraction; SPT, skin prick test; OxTh, oxidized thioredoxin-treated salt-soluble wheat fraction.

* The percentages in parentheses indicate the percentage of inhibition in CAP-FEIA: $(1 - \text{serum with wheat preparation} / \text{serum without wheat preparation}) \times 100$.

found to be hampered on treatment with reduced thioredoxin in the CAP-FEIA inhibition study. The results for patients with other clinical symptoms were not different in the skin reactions or in the CAP-FEIA inhibition studies (Table 1). Since thioredoxin can modulate intramolecular disulfide bonds,⁴ the structural features of proteins in the salt-soluble wheat fraction might be involved in the pathogenesis of childhood baker's asthma.

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ANAPHYLAXIS TO MARE'S MILK

To the Editor:

Allergic reactions to mare's milk (MM) are very uncommon. Mare's milk is used as an alternative in children allergic to cow's milk (CM)^{1,2} or with atopic dermatitis.³

A 53-year-old woman with rhinoconjunctivitis and mild asthma sensitized to horse epithelium (HE) developed pruritus on the palms and soles, generalized erythema, conjunctivitis, and intense dyspnea 45 minutes after her first MM intake, although she had good tolerance to goat's milk (GM) and CM before and afterward. She was evaluated 2 months after the reaction using prick-by-prick tests,⁴ and she underwent soluble and basophil surface IgE determination by means of radioallergosorbent tests (RASTs)⁵ and basophil activation tests,⁶ cross-reactivity by RAST inhibition assay,⁵ and allergenic proteins by immunoblotting⁵ using native MM, CM, and GM plus commercial HE and solid-phase disks conjugated to MM or HE. Controls consisted of 5 patients allergic to HE (group A) and 10 nonatopic persons (group B).

Good agreement was found between results of skin testing, basophil activation testing, and RAST inhibition, confirming the presence of specific IgE antibodies to MM and HE in 4 cases (the patient and controls 1, 2, and 3) and only to HE in 2 (controls 4 and 5) (Table 1). The RAST inhibition results showed that in the patient, using MM in the solid phase, the stronger inhibitor was MM, with less recognition with HE. These results were reversed with HE in the solid phase. Immunoblotting with the patient's serum showed 3 bands of MM recognized by IgE antibodies (caseins [23–36 kDa], β -lactoglobulin [18 kDa], and α -lactalbumin [15 kDa]) and only 1 band of HE (EquC1 [19 kDa] or EquC2 [18 kDa]). All 5 group A controls had the same pattern of HE recognition as

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