

between 199 and 1107 ng/m³.⁵ The cumulative inhaled NRL dose for asthmagogenesis among these subjects ranged between 25 and 515 ng, with exposure durations of 3 to 114 minutes.⁵

This study is the first to quantify NRL bioaerosol concentrations in ambulances (model Citrôen Jumper). Latex aeroallergens were captured with an area air sampler (AAS) (Quan-Tec-Air, Inc, Rochester, Minn) operated for 1 hour at a flow rate of 2.5 L/s and personal breathing zone (PBZ) air-sampling pumps (SKC Inc, Eighty Four, Pa) at a flow rate of 3 L/min. Airborne particles were collected onto polytetrafluoroethylene 0.3-μm filters rated 99.9% efficient. The filters were extracted in 0.1 mol/L phosphate buffer and assayed immunochemically.³ PBZ air-sampling pumps were worn by paramedics during their work shift and were operated only inside the ambulance confinement (approximately 9 m³) for 5 to 6 hours. The NRL aeroallergens were quantified (ng/m³) as a time-weighted average by a competitive IgE immunoassay by using sera from latex-sensitive individuals.³ The limit of detection was approximately 1 ng/m³ for AAS and 5 ng/m³ for PBZ air samplers. Differences in allergen detection limits are related to collection volumes.

A brand-new, so-called latex-free, ambulance was developed by the Emergency Health System (Servicio de Urgencias Médicas de Madrid) from Madrid (Spain) to attend patients allergic to NRL. All structural materials and medical equipment used in this ambulance were latex free, as certified by the suppliers. Only synthetic gloves were used in this ambulance.

The NRL aeroallergen concentration in the so-called latex-free ambulance was undetectable with the AAS. In an ordinary ambulance that had been in use for several years, the NRL aeroallergen concentration after a 24-hour shift of continuous activity (with intense use of powdered NRL gloves) was 4364 ng/m³. The NRL aeroallergen concentration measured over a 24-hour period in the ambulance headquarters coordination office, a large room of approximately 100 m² where NRL gloves were very seldom used, was 1 ng/m³. With PBZ sampling pumps, the concentrations of NRL aeroallergen in 4 ordinary ambulances during their regular work activities were 159, 23, 107, and 30 ng/m³.

These results show that ordinary ambulances in which powdered NRL gloves are used show moderate (10-50 ng/m³), high (>50 ng/m³), or even very high latex aeroallergen concentrations. A latex-free ambulance can be developed by avoiding all latex equipment, which provides a safe environment for both health-care workers and patients who are allergic to NRL. Notwithstanding, because powdered NRL gloves are the major contributor to airborne latex,³⁻⁶ by using powder-free NRL gloves and thoroughly cleaning vehicle surfaces likely to serve as allergen repositories, the latex aeroallergen concentration can be decreased to acceptable levels.^{4,7,8} Strict avoidance of direct contact with all NRL objects should be still applied for subjects who are allergic to NRL.

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REFERENCES

1. Vandenplas O, Delwiche JP, Evrard G, Aimont P, van der Brempt X, Jamart J, et al. Prevalence of occupational asthma due to latex among hospital personnel. *Am J Respir Crit Care Med* 1995;151:54-60.
2. Heilman DK, Jones RT, Swanson MC, Yunginger JW. A prospective controlled study showing that rubber gloves are the major contributor to latex aeroallergen levels in the operating room. *J Allergy Clin Immunol* 1996;98:325-30.
3. Swanson MC, Bubak ME, Hunt LW, Yunginger JW, Warner MA, Reed CE. Quantification of occupational latex aeroallergens in a medical center. *J Allergy Clin Immunol* 1994;94:445-51.
4. Tarlo SM, Sussman G, Contala A, Swanson MC. Control of airborne latex by use of powder-free latex gloves. *J Allergy Clin Immunol* 1994;93:985-9.
5. Quirce S, Swanson MC, Fernandez-Nieto M, de las Heras M, Cuesta J, Sastre J. Quantified environmental challenge with absorbable dusting powder aerosol from natural rubber latex gloves. *J Allergy Clin Immunol* 2003;111:788-94.
6. Heilman DK, Jones RT, Swanson MC, Yunginger JW. A prospective, controlled study showing that rubber gloves are the major contributor to latex aeroallergen levels in operating room. *J Allergy Clin Immunol* 1996;98:325-30.
7. Allmers H, Brehler R, Chen Z, Raul-Heimsoth M, Fels H, Baur X. Reduction of latex aeroallergens and latex-specific IgE antibodies in sensitized workers after removal of powdered natural rubber latex gloves in a hospital. *J Allergy Clin Immunol* 1998;102:841-6.
8. Charous BL, Schuenemann PJ, Swanson MC. Passive dispersion of latex aeroallergen in a healthcare facility. *Ann Allergy Asthma Immunol* 2000;85:285-90.

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Anaphylaxis to mizolastine

To the Editor:

Modern antihistamines are essential in the treatment of type I allergic diseases.¹ Mizolastine (Mizollen; Sanofi-Synthelabo GmbH, Berlin, Germany; Zolim, Schwarz Pharma GmbH, Monheim, Germany) is a peripherally acting selective H₁-receptor antagonist used worldwide for the symptomatic relief of seasonal allergic rhinoconjunctivitis (hay fever), perennial allergic rhinoconjunctivitis, and urticaria. Its efficacy and tolerance in humans have been demonstrated in many studies.²⁻⁴ H₁-antihistamines generally have the potential to produce a wide variety of short-term and long-term adverse effects.⁵ The most common side effects reported for the second-generation H₁-antagonist mizolastine are drowsiness and fatigue.^{2,4} Other adverse effects listed in the "Summary of

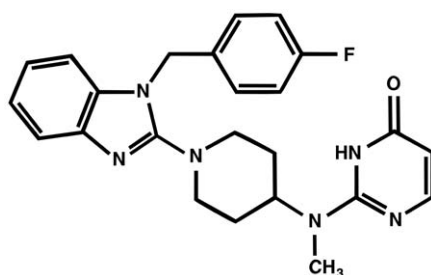


FIG 1. Chemical structure of mizolastine.

Product Characteristics” include dry mouth, diarrhea, dyspepsia, and increased appetite (associated with weight gain in some individuals). Fig 1 shows the chemical structure of mizolastine.

Here we present the case of a 47-year-old Caucasian woman who experienced generalized urticaria with respiratory distress, hypotension (80/40 mm Hg), and dizziness 2 hours after intake of 10 mg of mizolastine (Mizollen), with subsequent hospitalization and emergency treatment (dimethindene, prednisolone, and epinephrine). No food or other medication had been ingested before the reaction.

The patient had a 8-year history of seasonal allergic rhinitis during the grass pollen season which had been treated with several antihistamines. She had taken Mizollen for the first time but could not rule out having received Zolim before.

Physical and routine laboratory examination on admission revealed an otherwise healthy patient. Routine allergy diagnosis with a large panel of aeroallergens and food allergens showed positive skin prick test (SPT) reactions to grass, rye, birch, beech, oak, and hazel pollen, as well as celery. In the patient’s serum, specific IgE (CAP-FEIA; Pharmacia, Uppsala, Sweden) was found against birch, hazel, alder, and mixed grass pollen. Total serum IgE was 61.2 kU/L.

Further SPTs showed positive reactions to suspensions of Mizollen (10 mg of mizolastine) and Zolim (10 mg of mizolastine), but not to the other ingredients of Mizollen (lactose, cellulose, tartaric acid, povidone, silicon dioxide, castor oil, magnesium stearate, hypromellose, propylene glycol, and titanium oxide) suspended in PBS.

SPTs to a variety of common antihistamines suspended in PBS—including Zyrtec (cetirizine), Allegra (fexofenadine), and Lisino (loratadine), as well as the first-generation Fenistil—(dimethindene) yielded negative results.

After obtaining the patient’s written informed consent, we performed double-blind, placebo-controlled oral challenge tests with increasing doses of several anti-H₁ drugs at 2-hour intervals until an adverse reaction was observed or a therapeutic dose was achieved. Full emergency cover was provided. Oral exposure to cetirizine, fexofenadine, loratadine, and dimethindene was tolerated without problems. In contrast, within 1 hour after a cumulative dose of 10 mg of mizolastine, the patient developed laryngeal

edema, dyspnea, hypotension (80/50 mm Hg), and tachycardia. Immediate treatment with intravenous fluid, dimethindene and prednisolone was provided, and symptoms rapidly disappeared and the reaction completely resolved over the next few hours without the need to administer epinephrine.

Anaphylaxis is a clinical syndrome that represents the most severe and life-threatening systemic allergic reaction. It is caused by the immunologically induced release of mast cell and/or basophil mediators upon exposure to a specific antigen in sensitized persons.⁶

Usually, the term *anaphylaxis* is restricted to IgE-dependent events, whereas the term *anaphylactoid* is often used to describe clinically similar, but IgE-independent, reactions. The most common and often initial clinical manifestations of anaphylaxis are generalized urticaria and angioedema.

To test for the nature of the observed adverse reaction, we screened for specific IgE antibodies in the patient’s and several control sera. Because of the lack of commercially available serologic assay reagents, we performed a modified nitrocellulose (Schleicher and Schuell, Dassel, Germany) Dot-Blot by spotting 1 mg of mizolastine (Mizollen dissolved in PBS) on nitrocellulose membranes and incubated the blot with serial dilutions of the patient’s serum and 5 control sera of patients with rhinoconjunctivitis and healthy control individuals. This test showed no specific reaction of the patient’s serum and no reactivity with the control sera. We therefore conclude that with available laboratory techniques, mizolastine-specific IgE was not detectable in our patient.

There are single reports about urticarial reactions to cetirizine,⁷⁻¹⁰ which also belongs to the family of second-generation antihistamines. However, in these cases, the lack of other symptoms of anaphylaxis, negative SPTs, and failure to detect specific IgE suggest nonimmunologic intolerance reactions.

Although in this case the immediate clinical symptoms (urticaria, angioedema, and hypotension), the positive SPT results to both Mizollen and Zolim but not the other ingredients of Mizollen, and the positive oral challenge test indicate that mizolastine was the cause of the clinical symptoms and support the assumption of an anaphylactic type of response. In addition, the route of sensitization remains unclear, because the patient had never taken Mizollen before. However, it could not be excluded that she had received Zolim containing mizolastine before.

To our knowledge, this is the first report of anaphylaxis to mizolastine in the literature. We urge physicians to be aware of the rare possibility of allergic reactions to “antiallergic” drugs, especially in view of their widespread use.

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REFERENCES

1. Simons FE. H₁-antihistamines: more relevant than ever in the treatment of allergic disorders. *J Allergy Clin Immunol* 2003;112(4 suppl):S42-S52.
2. Leynadier F, Bousquet J, Murrieta M, Attali P. Efficacy and safety of mizolastine in seasonal allergic rhinitis. *Ann Allergy Asthma Immunol* 1996;76:163-8.
3. Brostoff J, Fitzharris P, Dunmore C, Theron M, Blondin P. Efficacy of mizolastine, a new antihistamine, compared with placebo in the treatment of chronic idiopathic urticaria. *J Immunol* 1996;51:320-5.
4. Bachert C, Vovolis V, Margari P, Murrieta-Aguttes M, Santoni JP. Mizolastine in the treatment of seasonal allergic rhinoconjunctivitis: a European clinical experience with 5408 patients managed in daily practice (PANEOS SAR study). *Allergy* 2001;56:653-9.
5. Simons FER. Non-cardiac adverse effects of antihistamines (H₁ receptor antagonists). *Clin Exp Allergy* 1999;29:125-32.
6. Ellis KE, Day JH. Diagnosis and management of anaphylaxis. *CMAJ* 2003;169:307-12.
7. Karamfilov T, Wilmer A, Hipler UC, Wollina U. Cetirizine-induced urticarial reaction. *Br J Dermatol* 2001;140:979-80.
8. Calista D, Schlanchi S, Morri M. Urticaria induced by cetirizine. *Br J Dermatol* 2001;144:196.
9. Tella R, Gaig P, Bartra J, Garcia-Ortega P. Urticaria to cetirizine. *J Investig Allergol Clin Immunol* 2002;12:136-7.
10. Schröter S, Damveld B, Marsch WC. Urticarial intolerance reaction to cetirizine. *Clin Exp Dermatol* 2002;27:185-7.

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Staphylococcus aureus colonization and IgE antibody formation to enterotoxins is increased in nasal polyposis

To the Editor:

The role of bacterial colonization or infection in chronic rhinosinusitis (CRS) is unclear and has not been thoroughly investigated in CRS with nasal polyps (NPs), a subgroup of patients with often severe eosinophilic inflammation, a high recurrence rate, and frequent asthma comorbidity and aspirin sensitivity.¹ In the whole group of patients with CRS, a *Staphylococcus aureus* carriage rate of 35% was observed at the middle meatus.² *S aureus* also frequently colonizes the nostrils in healthy subjects and may form enterotoxins, which under appropriate conditions can penetrate the mucosal barrier and possibly act as superantigens on T and B lymphocytes. This can induce a polyclonal stimulation with consecutive eosinophilic inflammation and IgE formation. We have recently shown that in approximately 50% of nasal tissue homogenates derived from NPs, IgE antibodies specific to classical staphylococcal enterotoxins (*Staphylococcus aureus*-derived enterotoxins [SAEs] A and/or B) could be found. This was linked to high concentrations of total IgE and a local polyclonal IgE antibody formation against various inhalant allergens.³ Furthermore, in polyp samples with SAE-specific IgE antibodies, a severe eosinophilic in-

flammation was present, demonstrated by the upregulation of IL-5, eotaxin, eosinophil-cationic protein (ECP), and cysteinyl-leukotriene synthesis. In addition, most of these patients had asthma and aspirin hypersensitivity.³ The presence of IgE antibodies to SAEs A, C, and toxic shock syndrome toxin 1 (SAE mix) has also been studied in healthy controls, in subjects with mild asthma, and in patients with severe asthma, defined by the need for regular high-dose inhaled corticosteroid therapy and, despite this treatment, persistently impaired lung function.⁴ In these groups, IgE antibodies to SAE mix were found significantly more often in serum from patients with asthma compared with controls, especially when comparing patients with severe asthma with controls (62% vs 13%; $P = .01$). This suggests a relationship between the presence of IgE antibodies to SAEs in serum and the severity of asthma.

In this study, we aimed to investigate the rate of colonization of the middle nasal meatus by *S aureus* in controls ($n = 9$, 4 males, 5 females; mean age, 38.4 years), subjects with CRS ($n = 22$, 11 males, 11 females; mean age, 49 years) and subjects with NP ($n = 55$, 36 males, 19 females; mean age, 48 years), as well as subgroups of the latter characterized by comorbid asthma ($n = 18$) and aspirin sensitivity ($n = 8$). Only 1 of the patients with asthma had current atopic dermatitis but was not colonized. None of the other patients had previous or current atopic dermatitis in their medical history.

The tissue was homogenized with a mechanical homogenizer (B. Braun, Melsungen, Germany) at 1000 rpm for 5 minutes on ice. After homogenization, the suspensions were centrifuged at 3000 rpm for 10 minutes at 4°C, after which the supernatants were separated and stored at -80°C until analysis. Blood samples were clotted at room temperature for 20 minutes and centrifuged at 1500 for 10 minutes at 4°C, and the serum was separated. ECP and total IgE and specific IgE against *Staphylococcus* enterotoxin A, *Staphylococcus* enterotoxin C, and toxic shock syndrome toxin 1 (SAE mix) levels were measured in tissue and serum using the Uni-CAP system (Pharmacia & Upjohn, Uppsala, Sweden).⁵ Immunocap coated with human serum albumin or glycine was used to evaluate any nonspecific binding of IgE.

Colonization rates in controls and subjects with CRS were 33.3% and 27.3%, whereas 63.6% ($P < .05$ vs CRS) of all subjects with NP were colonized with *S aureus*, with rates of 66.7% and 87.5% in the NP subgroups with asthma and aspirin sensitivity ($P < .05$ vs CRS for both), respectively (Fig 1, A). Repeated swabbing of the middle meatus in 8 subjects with NP suggested long-term colonization with *S aureus*. However, the factors that determine carrier and noncarrier status are largely unknown, and this question awaits further prospective studies.

The prevalence of IgE antibodies to SAEs in tissue homogenates paralleled colonization rates (Fig 1, B) but was always lower. Probably not only colonization with *S aureus* but also another event, which could be a viral infection, is necessary to induce this specific immune