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Allergy to meat

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Key words: bovine serum albumin; bronchial asthma; meat allergy.

ALLERGY TO mammalian meats has rarely been reported in the literature (1,2). Hypersensitivity reactions (3) after intake of these foods pose a serious problem to the patients suffering them since they make up one of the principal foods in all but vegetarian diets.

Serum albumin is a panallergen.

Patient 1. A 3-year-old boy developed erythema and peribuccal pruritus after eating veal. He was tolerated milk, chicken, turkey, pork and lamb.

Patient 2. A 45-year-old woman presented with severe corticosteroid-dependant bronchial asthma. She reported that her bronchial symptoms worsened when she was in the presence of a cat in her usual home. Over the last 2 years, she has presented labial angioedema, abdominal pain, and erythematous papule lesions in her upper limbs, dyspnea, and occasional vomiting after eating cured ham, cured loin of pork, and veal, lamb, rabbit, or pork, mainly if they are undercooked. She tolerated mortadella, cooked ham, milk, chicken, and turkey. Her personal background includes IgE-mediated asthma (3), with a severe obstructive spirometric pattern.

Skin prick tests were performed in both patients according to the Subcommittee on Skin Tests of the European Academy of Allergology and Clinical Immunology with commercial extracts of common aeroallergens, milk and fractions, mammalian (veal, bovine, horse, pork, rabbit), chicken and turkey meats, and bovine serum albumin (BSA). Total IgE and IgE antibodies (kU/l) were determined with the CAP System-Pharmacia technique (Table 1).

We performed sodium-dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE) in 12.5% acrylamide gel, followed by immunoblotting. In Patient 1, a large number of IgE-binding protein bands between 25 and 95 kDa were observed to veal and bovine meat extracts. This did not occur for the lamb extracts, in which only one protein band of approximately 65 kDa was recognized. On the other hand, serum from the woman only recognized a protein band of about 65 kDa all extracts.

The serum of Patient 2 against cat dander produced an intense protein band of around 60 kDa, which would correspond to a serum albumin. All types of mammalian meats were eliminated from her diet. The beginning of this diet was accompanied by a significant improvement in bronchial symptoms, and the digestive symptoms disappeared. Beef was eliminated from the diet of the boy, and the he remained without symptoms.

BSA is responsible for much of the cross-reactivity between different types of mammalian meat (1) and dander. Both patients' sera contained IgE that showed binding to a protein band of approximately 65 kDa, most likely albumin.

Significant sensitivity to animal dander was observed in Patient 2. In SDS-PAGE performed with the cat dander extract, her serum recognized serum albumin. Her symptoms were less pronounced when she ate well-cooked meat. In most of the studies (2,4) BSA stands out as a thermolabile protein.

On the other hand, we believe that Patient 1 presents IgE-mediated allergy (3) to veal and bovine meat and is not exclusively sensitized to BSA due to the large number of protein bands recognized by his serum in the veal and bovine meat extracts, and his good tolerance to other meats.

Table 1. Results of skin prick tests and total and specific IgE quantification in both patients

	Patient 1	Patient 2
Prick test positive	Grass and arizonic pollens Dog and cat dander Meats	*Dermatophagoides pteronyssinus* and *D. farinae* Dog and cat dander Meats Whole milk and fractions Bovine serum albumin
IgE total	234	534
Specific IgE		
whole milk	16.1	2.57
lactoalbumin	2.51	< 0.35
lactoglobullin	2.86	< 0.35
casein	2.52	1.35
veal	23.1	1.35
bovine	0.5	< 0.35
lamb	0.7	1.35
pork	< 0.35	5.2
rabbit	< 0.35	2.03
dog dander		> 100
cat dander		> 100
D. pteronyssinus		5.2

In conclusion, we present two clinical cases of allergy to meats that are clinically and immunologically different. The serum albumin would thus be a panallergen and should be considered as such in cases of allergy to mammalian meats and to dander.

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Caffeine hypersensitivity

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Key words: analgesic; caffeine; coffee; urticaria.

We present the case of a 69-year-old woman who had developed generalized urticaria after intake of the over-the-counter (OTC) pain medication Thomapyrin (250 mg aspirin, 200 mg paracetamol, 50 mg caffeine) two months prior to presentation at our Allergy unit.

Generalized urticaria after caffeine intake.

Skin prick testing (SPT) and oral challenge with aspirin, paracetamol, and rofecoxib were performed, with negative results. The patient also reported generalized urticaria on six independent occasions with itching of the palms, lip edema and dizziness after one cup of coffee, requiring admission to the hospital once. She denied any use of sweetener in combination with coffee.

SPT with freshly brewed coffee was negative. Oral challenge test with encapsulated caffeine did not induce urticaria at a dose of 1, 2, 5, 10 and 20 mg given at 30 min intervals. On the following day the patient also tolerated 50 and 100 mg caffeine. But 20 min after oral challenge with 150 mg caffeine the patient noticed generalized pruritus and within minutes large areas of the skin were covered by confluent wheals. Caffeine hypersensitivity was diagnosed and antiallergic treatment was initiated resulting in complete recovery.

To confirm the dose-dependency of the test reaction, SPT with a caffeine citrate dissolved in glycerine at 1–100 mg/ml was performed 2 weeks later. Wheal formation could not be observed at 1, 2 and 5 mg caffeine/ml. At 10, 20, 50 and 100 mg caffeine/ml wheal diameter increased from 3 mm to 6, 7, and 8 mm, respectively, accompanied by substantially increasing local erythema.

As a control, caffeine SPT with different concentrations (1–100 mg/ml) was negative in five healthy individuals (age 28–30 years, three women, two men) demonstrating the absence of nonspecific reactivity.

To investigate whether leukotriene release is involved in the observed caffeine-induced generalized urticaria, the patient's leukocytes and those obtained from four healthy controls (two men, two women; 18–53 years) were stimulated with 100 μg caffeine/ml using the cellular allergy stimulaton test (CAST-ELISA, DPC Biermann, Bad Nauheim, Germany) (1). Stimulation of the patient's leukocytes with caffeine (100 μg/ml) resulted in higher leukotriene release compared to leukotriene release from the leukocytes of healthy controls (81% *vs* 6%) when leukotriene release upon stimulation with IgE-receptor antibody was set at 100%. Western blot analysis for caffeine-specific IgE was negative (DPC Biermann, Germany).

So far, only four cases of caffeine-induced hypersensitivity symptoms presenting with urticaria or even cardiac arrest have been described in the literature (2–5). Due to the wide distribution of caffeine in soft drinks, certain types of chocolate, and OTC pain medications, as well as potential life-threatening implications, it is important to identify caffeine as the culprit agent. We demonstrated here, by SPT and oral challenge test, that caffeine-induced urticaria was dose-dependent. By history, one cup of coffee with approximately 100 mg caffeine induced a systemic reaction in our patient, which is a lower amount than that needed for induction of urticaria in the oral challenge test (6). This discrepancy may be due to short time intervals between the oral provocations, suggesting that caffeine absorption in the gastrointestinal tract may contribute to delayed appearance of urticaria upon oral administration with 100 mg caffeine.

Although we observed greater leukotriene release from leukocytes of the patient following incubation with caffeine, compared to control leukocytes, it remains to be seen whether caffeine-induced urticaria represents IgE-mediated type I allergy or nonallergic hypersensitivity (7). In the absence of caffeine-specific IgE as a positive control, our results giving a negative Western blot for caffeine-specific IgE is difficult to assess. Further studies are required to investigate the exact pathogenesis of caffeine induced urticaria.

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Anaphylaxis to antitetanus toxoid serum

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Key words: albumin; anaphylaxis; horse antitetanus toxoid serum.

Sensitization to horse (*Equus caballus*) is often responsible for severe rhinoconjunctivitis and asthma. There are three major horse allergens, Equ c 1, Equ c 2 and Equ c 3, present in the horse skin, dander, sweat and urine (1,2). Other allergenic fractions, including albumin, are considered as minor allergens. We report the case of a patient sensitized to horse albumin, with a severe anaphylactic shock when injected with horse antitetanus toxoid serum.

A 38-year-old woman had suffered for 10 years from moderate persistent asthma and moderate rhinitis. These were well controlled by a combination of inhaled glucocorticosteroids and long-acting β_2-agonists and her forced expiratory volume in 1 s (FEV_1) was 70–80% of predictive value. Contact with her own horse and cats gave her no symptoms or variation in peak-flow records.

Due to IgE antibodies to horse serum albumin from inhalation allergy.

On 2 November 1999 this patient was wounded above the eye. The emergency services administered an injection of horse antitetanus toxoid serum (Mérieux-Pasteur, France) because she had never been vaccinated against tetanus infection. She had not received horse serum previously. Within minutes of this injection she experienced a very severe anaphylactic shock with cardiorespiratory arrest. Emergency treatment consisting of epinephrine (adrenaline), plasma expanders and intubation enabled her to recover within an hour. An allergic reaction to the proteins present in the horse serum was thus suspected.

Performed under strict hospital surveillance, skin prick test (SPT) with pure antiserum and intradermal tests with 1/100 dilution of horse antitetanus toxoid serum were positive; and they were negative in five nonatopic subjects. SPT were positive for horse, cat and dog dander extracts but not for other common regional aeroallergens (Stallergènes, Antony, France). Serum-specific IgE levels, measured by ELISA (1,2), were undetectable for horse allergen Equ c 1 and were highly positive for horse, cat and dog serum albumins (Fig. 1). Electrophoresis and immunoblot to cat proteins showed IgE against cat serum albumin but not against Fel d 1.

This case report is a rare but informative observation of anaphylaxis to horse antitetanus toxoid serum related to IgE to horse serum albumin. Major horse allergens Equ c 1, Equ c 2, and Equ c 3 are extremely powerful allergens, responsible for upper and lower respiratory symptoms in sensitized patients.

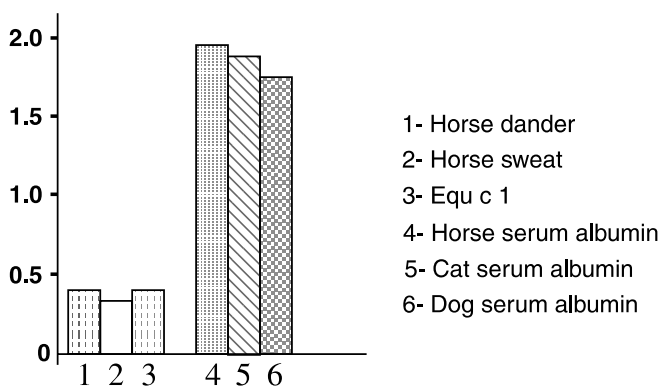

Figure 1. Specific IgE measurement by direct ELISA.

IgE analysis has proved that patients suffering from respiratory horse allergies react mainly to these major allergens and not very much to the minor allergen albumin (3). Cross-antigenicity between horse, cat and dog serum albumins has clearly been shown (1,3). Because it was not our aim to demonstrate this for our patient, RAST inhibition studies were not performed. The presence of IgE directed against horse, cat, and dog albumins in our patient probably explains the anaphylactic shock with the horse antitetanus toxoid serum. Since she had never received horse serum before, her sensitization was most likely caused by exposure to her own animals. Moreover, the absence of IgE directed against the major horse allergens and Fel d 1 may explain the absence of respiratory symptoms when in contact with her own horse and cats.

The earliest signs after allergen contact are rhinitis and conjunctivitis. The diagnosis of animal respiratory allergies is simple, based on clinical history, SPT with standardized extracts and specific-IgE dosage if needed. The biologist's main interest in the case of animal allergy is in the major allergens. However, sensitization to minor allergens, as in the case of horse albumin, can expose the patient to serious anaphylactic reactions when injected with serum containing horse proteins.

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Prevalence of allergy to Cypress

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Key words: Cypress; IgE sensitization; pollinosis; retrospective study.

Pollinosis is a disease of high and constantly increasing prevalence all over the world. Grasses, weeds, Urticaceae and trees are the most frequently responsible agents for the clinical manifestations. During the last 10 years, some pollens, usually considered minor allergens, have been claimed to become more and more important causes of both sensitization and clinical symptoms, and in fact they have been termed "emerging allergens" (1). Within these emerging allergens, pollens from trees belonging to the family of Cupressaceae have received noticeable attention (2). The Cupressaceae family (16 genera and 140 species) is widely distributed throughout the world, the most represented species being cypress, mountain cedar and *Cryptomeria japonica*. The cypress tree (*Cupressus sempervirens*) is the most abundant plant in the Mediterranean areas.

A 10-year retrospective survey on sensitization and pollinosis in Western Liguria.

We describe the results of a retrospective survey on the prevalence and characteristics of sensitization to cypress in a large patient population referred to our Service for respiratory diseases during a 10-year period (from 1990 to 2000). Our service covers patients in an area of about 9600 km^2 surrounding the town of Alassio, in the Western Ligurian Riviera, located at 44°N and 8°10′E. In this geographic area, cypresses are part of the spontaneous flora and they are also cultivated and planted for ornamental and gardening purposes.

A total of 1735 patients suffering from respiratory allergy, and living in the surrounding area were seen between 1990 and 2000. All patients underwent skin tests with a standard panel of allergens (DHS, Bayropharm, Milan, Italy) including: grasses, Parietaria, ragweed, olive, cypress, dust mite, cat and dog dander, *Aspergillus* and *Alternaria*. Positive and negative control allowed grading of skin reactivity as recommended in the international guidelines. The mean of the major diameter of the wheal plus its orthogonal was considered and expressed from 0 to + + + +. A skin reaction of + + or more was considered positive. Assays for IgE antibodies were performed only in selected cases. During the examined period, pollen count was continuously performed by means of a Hirst-like volumetric spore trap (Burkard) placed on the roof of the hospital, 20 m above ground level and 300 m from the sea.

Out of 1735 patients, only 18 (1.04%) had positive skin tests to cypress. Notably, out of these 18 patients only five were monosensitized, whereas the remaining 13 patients showed concurrent sensitizations (five to grasses, six to Parietaria, two to mites). Therefore the overall prevalence of single sensitization to cypress was 0.29%. In the five patients with single sensitization, the symptoms paralleled the pollen season of cypress. Rhinitis (rhinoconjunctivitis) was the more frequent disease (Table 1). In the remaining patients, with multiple sensitizations, symptoms were not clearly related to the cypress pollen season, but rather to other pollens. The Cupressaceae pollen counts were high (sometimes more than 500/mm^3) during the pollen season (usually January to March) with a trend to increase during the last four years.

The data collected in this large population show that the prevalence of sensitization to cypress, at least in this geographic region, is very low despite the large diffusion of the source of pollens and of the high pollen peaks. This contrasts partly with data reported in previous surveys (3,4). For instance, in a study by Ariano and colleagues (4), performed in another area of the Ligurian Riviera, the pollen counts referred to Cupressaceae and the rate of sensitizations were somewhat higher. In addition, the clinical relevance of cypress in terms of symptoms seems to be even lower, since in poly-sensitized patients the clinical manifestations were preferably related to the presence of other relevant pollens.

We conclude that in the area studied, cypress *per se* is rarely a cause of sensitization and is responsible even more rarely for clinical symptoms.

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Table 1. Demographics and clinical characteristics of the study population

	n (%)	Male/ female	Mean age (range)	Disease	Associated sensitizations
Single sexsnsitization	5/1735	4/1	17.2	3 rhinoconjunctivitis 1 asthma 1 asthma + rhinitis	—
Multiple sensitization	13/1735	9/4	20.1	11 rhinoconjunctivitis 1 asthma 1 asthma + rhinitis	5 Parietaria 6 Gramineae 2 mites
Total	18/1735	13/5	18.65	14 rhinoconjunctivitis 2 asthma 2 asthma + rhinitis	

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Fatal dextran-induced allergic anaphylaxis

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Key words: anaphylaxis; antibodies; complement; dextrans.

Dextrans may provoke severe reactions that result from the presence of high titres of dextran-reactive antibodies (DRAs) (1). The formation of immune complexes between dextran and DRAs has been proposed as the mechanism of dextran-induced anaphylactic reactions (DIARs).

Dextran antibodies could be detected before but not after the reaction.

A 54-year-old man developed generalized pruritus, dyspnea and sudden hemodynamic shock with cardiac and respiratory arrest 8 h after the resection of a hepatic hydatid cyst, while being administered intravenously dextran 40. He had no prior history of atopy or adverse drug reactions. The hydatid cyst resection had been performed with macroscopic integrity of the cyst wall. Despite intensive reanimation therapy the patient remained unconscious and hemodynamically unstable. In the following days he became septic, with progressive renal function impairment and died on the fifth day.

Total serum IgE was 34 kU/l. Tests (CAP^{TM} System, Pharmacia & Upjohn, Uppsala, Sweden) for IgE antibody and indirect hemagglutination for *Echinococcus granulosus* were negative (< 0.35 kU/l and < 1/80, respectively). A serum tryptase level taken 16 h after the reaction was 12.2 μg/l (UniCAP Tryptase System, Pharmacia & Upjohn, Uppsala, Sweden; normal values < 10 μg/l). Serum complement levels measured by nephelometry were C_3: 42 mg/dL (normal 83–177 mg/dL) and C_4: 7 mg/dL (normal 15–45 mg/dL) after 6 h of the reaction and C_3: 27 mg/dL and C_4: 7 mg/dL after 24 h. Serum C_3 and C_4 levels measured before the operation were normal (C_3: 167 mg/dL; C_4: 26 mg/dL).

DRAs could be detected by passive hemagglutination (2) in a serum sample drawn before the reaction but were undetectable after it. The addition of a normal serum, as a source of complement proteins, restored the hemagglutinating activity.

The demonstration of DRAs and the evidence of complement protein consumption suggested that DRAs formed immune complexes with the dextran leading to complement activation and anaphylaxis mediator release. Tryptase serum levels were slightly increased after the adverse reaction indicating the involvement of mast cell degranulation.

Previous studies have demonstrated that DRAs are predominantly of the IgG class and ruled out the participation of IgE antibodies in case of severe DIARs (3). The occurrence of these antibodies has not been related to a previous administration of dextran because most patients developing DIARs have never received dextran infusions before as occurred to our patient. Moreover, a high prevalence (81%) of low titres of DRAs has been demonstrated in normal individuals (4). The induction of DRAs has not been yet elucidated and might be due to sensitization to dextran cross-reactive polysaccharides present in bacteria such as streptococci, pneumococci, lactobacilli, etc.

Titration of DRAs prior to the administration of dextrans would provide the possibility of identifying those individuals at risk of DIARs. Furthermore, the administration of a monovalent hapten dextran (Promit®, Pharmacia & Upjohn, Uppsala, Sweden) before the infusion of dextran has been proven that reduces the risk of DIARs (5).

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Occupational asthma due to liquorice roots

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Key words: occupational asthma; asthma.

We describe the case of an herbalist who developed occupational asthma due to liquorice roots as confirmed by specific inhalation challenges.

Many high-molecular-weight agents have been reported as causes of occupational asthma (OA) (1) (asthmanet.com, asthme.csst.qc.ca).

An herbalist with an IgE-mediated allergy.

A 33-year-old woman started to work as an herbalist 13 years ago. In her workplace, she was exposed to several natural products. She started suffering from asthma 8–9 years before being referred. She reported that her asthma symptoms were worse at work and improved on weekends and during a maternity leave. She also had rhinoconjunctivitis symptoms at work. She mentioned that several products brought on asthmatic symptoms when she handled them in powder form at work, including liquorice root. Her FEV_1 varied from 1.5 to 2.2 L (pred = 3.2 l) and the concentration of methacholine causing a 20% fall in FEV_1 (PC20 values), from 0.5 to 2.0 mg/ml (slight to moderate airway hyperresponsiveness (2) when she was assessed while at work. Peak expiratory flows showed greater fluctuations in some instances during periods at work. Skin-prick tests with a liquorice extract showed an 8 mm immediate weal. Skin-prick tests were also positive (= 3 mm weal) to common inhalants (pollens, mites) and to other products handled at her workplace, including echinacea, nettle, hop and thistle. Specific inhalation challenges carried out by exposing the subject with a dry aerosol generator (3,4) to liquorice root powder at concentrations lower than 10 mg/m^3 and for progressively increasing periods up to a total of 90 min induced a 25% immediate fall in FEV_1 without significant late reaction (Fig. 1). PC20 did not change significantly in the afternoon of the challenge day to liquorice roots (PC20 at 1.3 mg/ml by comparison with a value of 2.0 mg/ml before exposure). The patient was removed from her workplace with improvement in her symptoms.

This case report shows that liquorice roots can cause OA through an apparently IgE-mediated mechanism as seen by immediate skin reactivity reaction to the diluted powder of liquorice root.
The subject also presented symptoms of occupational rhinoconjunctivitis, which is commonly encountered in the case of high-molecular-weight agents (5). Herbalists are typically at risk of developing IgE-mediated allergic conditions (6), as they are exposed to several seeds, herbs and derivatives of vegetal products.
Other vegetal roots can cause OA. Vandenplas and co-workers indeed described an interesting case of OA due to sarsaparilla root dust (7).

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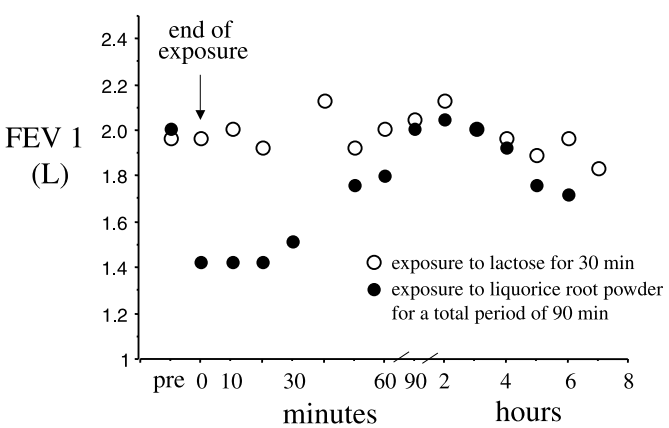

Figure 1. Values of Fev1 as a function of time after exposure to lactose and liquorice roots.

Playing cards as a carrier for peanut allergens

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Key words: peanut allergy; playing cards; hidden food allergens.

Peanuts and tree nuts are responsible for the majority of fatalities due to food-induced anaphylaxis in the USA (1). Even very small amounts can cause symptoms (2). In this context hidden food allergens are of great impact for the patients concerned (3). We describe for the first time playing cards as a carrier for peanut allergens provoking severe symptoms.

Extremely small amounts of allergen can cause an IgE-mediated reaction.

Here we report the case of a 32-year-old male (pharmacist) with known history of allergy to peanut and tree nuts. He suffered from the Atopic Eczema Dermatitis Syndrome during childhood and from allergic rhinitis and allergic asthma since the age of six. In the past, he had developed recurrent severe reactions after ingestion of sweets, cakes, salads and other food containing nuts or peanuts. Even being exposed to the breath of someone who had eaten peanuts before caused symptoms of oral allergy syndrome and shortness of breath.

One evening the patient was sitting together with friends playing skat, a typical German card playing. After one hour the patient felt swelling of lips and tongue as well as shortness of breath. He had to be treated with antihistamines and glucocorticosteroids.

The patient himself did not eat anything during this evening and since everybody knew that the patient was allergic to peanuts, the peanuts were put away and not eaten in front of him.

After this episode he visited our outpatient clinic. He showed sensitizations to grass, tree and weed pollen, house dust mites and animals. Total IgE was elevated with 1303 kU/l. Skin-prick-test showed a wheal to histamine of 5 mm diameter, to hazelnut of 7 mm and to peanut of 4 mm and no reaction to the negative control. Using CAP-RAST we found IgE- antibodies specific to peanut (8.4 kU/L/class 4) and to hazelnut (13.1 kU/L/class 3).

Still the patient persisted that he had not eaten anything. However, then he showed how he had touched the cards. As the cards often stuck together he licked off his thumb before putting them on the table. This typical movement is called threshing the skat. We suppose that the cards contained on their surface small amounts of peanut protein from the fingers of the friends eating peanuts during the playing. The patient got in contact with these proteins when he licked off his thumb. Knowing that 100 μg peanut protein may provoke symptoms (2), we suppose that the amount of peanut allergens displaced from the fingers of the players on the playing cards was sufficient enough to cause the patient's problems.

Hourihane et al. showed that skin-prick testing and peanut-specific IgE antibody levels do not predict clinical severity (4). Therefore, peanut seems to be the provoking allergen although the patient had a small wheal at skin-prick testing and a moderately elevated of IgE antibodies to peanut level. A comparable case was reported from Wüthrich et al. (5) who described a patient developing symptoms after a kiss of his friend who had eaten peanuts before.

In conclusion not only patients with peanut allergy have to avoid peanuts and peanut containing food but also their relatives and friends if they get in direct and indirect contact with them.

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Allergic contact dermatitis to nebivolol

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Key words: Beta-blocking agents; nebivolol; patch-testing; systemic contact dermatitis.

Nebivolol is a highly selective beta1-adrenergic blocking agent which has vasodilator properties by modulating nitric oxide (NO) release. For this dual mechanism of action, it is used in the management of patients affected by mild to moderate uncomplicated essential hypertension with a highly favorable tolerance profile (1). We report about a patient affected by systemic contact dermatitis due to nebivolol.

A case of systemic exposure to a beta-blocking agent.

A 60-year-old woman complained of a three year history of eczematous lesions in the periorbital areas. This dermatitis appeared from December to April; year after year it became wider and the itching was severer; the last year, eyelid angiedema also occurred. During the first two years, the symptoms improved as a result of the use of systemic antihistamines (cetirizine) and local corticosteroids (mometasone); the third year, this treatment was ineffective and an oral corticosteroid (deflazacort) was needed. The patient had no history of atopy.

During the last four years, because of mild essential hypertension, she had been prescribed treatment with oral nebivolol

at the dosage of 2.5 mg once daily. The patient interrupted this therapy each year late in spring and in summer because the pressure values turned spontaneously back to normal range; remittance of the eczematous lesions and of the angiedema occurred in this period.

Skin-prick-tests for the most common inhalant and food allergens (Alk-Abelló, Milan, Italy) were negative; patch testing with the European standard series, the cosmetic and preservative battery and the dental material series (Merck, Milan, Italy) were negative. The total IgE level was 83 UI/ml. Patch testing with nebivolol was performed at the concentrations of 20% in vaseline and 20% in physiologic saline solution and read at 48, 72 and 96 h with positive results at 72 and 96 h (+/++). At 84 h, the patient also reported a pruritic, erythematous, microvesicular eruption with mild eyelid angiedema in the periorbital areas. This dermatitis recovered spontaneously five days after the removal of the patch testing. The patient also underwent patch testing with timolol, labetalol, carvedilol, metoprolol, all at 20% in vaseline and 20% in physiologic saline solution with negative results at 72, 96 and 120 h. Single-blind oral challenge tests with increasing doses of timolol, labetalol, carvedilol, metoprolol, until the therapeutic doses, were negative. Patch testing and single-blind oral challenge tests with nebivolol were negative in six control subjects.

On the basis of clinical history and patch testing, the diagnosis of systemic contact dermatitis, due to cell mediated allergy to nebivolol, was made. We have not performed oral challenge with nebivolol given the exacerbation of dermatitis during the patch test. Negative patch tests and oral challenge tests with other beta-blockers indicate that there is no cross-reactivity among nebivolol and these other beta-blocking agents, probably due to the peculiar chemical structure of nebivolol, which is a racemic mixture of d- and l-enantiomers (1). In literature, cross reactions have instead been described among beta-blockers used in the long term topical treatment of open-angle glaucoma. In all these cases, the patients presented local contact dermatitis (2). Systemic cutaneous reactions due to beta-blockers are very rare and they are not usually due to delayed hypersensitivity reactions. In fact, a case of Stevens–Johnson syndrome was associated to carvedilol therapy (3), a case of cutaneous vasculitis and another of generalized fixed drug eruption were described after atenolol therapy (4,5); an urticarial nonallergic anaphylactic reaction and a case of severe angiedema were reported after administration of metoprolol (6,7).

To the best of our knowledge, our report is the first case of allergic reaction to nebivolol and also of systemic contact dermatitis due to a beta-blocking agent.

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Beta-thalassemic patients are not at risk for latex allergy

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Key words: Beta-thalassemic; latex allergy; IgE antibody.

Beta-thalassemic (BT) are a group of multitransfused patients, who have regular contact with latex devices for example, parts of blood filters, catheters or deflussors since the second year of life. Therefore they may be considered a group at risk for the presence of latex specific IgE antibodies (LISA) as well as latex IgE mediated allergy (LIMA) (1).

Despite significant exposure they do not get IgE sensitized.

The aim of this study was to compare the prevalence of LISA in 174 patients affected by major beta-thalassemia compared with a control group of 205 blood donors (BD). The concentration of IgE antibodies to latex in serum was measured by an automated system (CAP Pharmacia, Uppsala, Sweden) according to the manufacturer's instructions.

The 174 BT patients and the 205 BD had a mean age of 28 years [(± 6 SD); range 8–51] and of 32 years [(± 8 SD); range 18–50], respectively. BT patients had their first transfusion at a mean age of 18.7 months (± 4.2 SD) and they had been transfused regularly for a mean period of 30 years (± 6.5 SD). Sixty percent of them underwent splenectomy and 90% of them were Hepatitis C Virus (HCV) positive. Seven out of 174 (4.0%) BT patients and eight out of 205 (3.9%) BD had IgE specific to latex ($p = 0.8$, chi-square test). Most patients were classified in Class I (2/7 in the BT patients and 2/8 in the BD) or II (4/7 in BT patients and 5/8 in the BD). Only one subject in both groups had IgE specific to latex in the Class III, and none in the other classes. None of the subjects with IgE specific to latex referred symptoms after latex exposure.

In this study we found similar prevalence of LISA in patients with beta-thalassemia and BD. The relatively low prevalence of LISA in BT patients, despite their frequent contact with latex devices, was rather surprising and needs some comment.

First, it might be that the level of exposure in patients with beta-thalassemia was not high enough to determine LISA. In fact, they don't have a high number of operations, which is considered an important risk factor for sensitization and allergy to latex in children with spina bifida (2). Moreover BT patients have splenectomy in late child-

hood or beginning of adolescence, when the organ is compromised, whereas surgery is a risk factor for LISA in those patients who undergo multiple surgical procedures early in life, such as children with spina bifida.

If the exposure to latex might not be sufficient to cause LISA and thus develop LIMA, it might indicate that BT patients are less likely to develop IgE-mediated allergy in general. In fact, it has been reported that positive skin-prick-tests to common inhalant allergens and the frequency of respiratory atopic diseases were significantly less frequent in BT patients than in their relatives and controls, and it has been speculated that in beta-thalassemic patients, allergen specific IgG acquired early in life through transfusion could suppress the synthesis of allergen-specific IgE (3). Moreover, beta-thalassemic patients have many immune alterations in T-cell responses, such as higher CD8/CD4 ratio, lower T-cell activity, higher INFγ and TNF secretion (4). The above immune abnormalities may in part account for a lower tendency to LISA in beta-thalassemic patients, if an increased exposure to latex products was assumed.

In conclusion BT patients have a similar frequency of LISA than BD, and therefore they should not be considered at risk for latex allergy despite their potential increased exposure. Further studies are needed to establish if these results are due to the altered immune response of BT patients or if the level of exposure to latex is not high enough to induce sensitization.

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Occupational contact dermatitis to dill

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Key words: contact, dermatitis; dill; occupational.

Foods and spices of the parsley family (*Umbelliferae*, formerly *Apiaceae*) include anise, caraway, coriander, cumin, celery, lovage, fennel, parsley, carrot, and dill. Some of these have been associated with various allergic reactions, including contact dermatitis, anaphylaxis, gastroenteritis, and asthma (1–4). We report a case of occupational contact dermatitis in a cook who handled several different plants.

IgE antibodies and positive patch test.

A 43-year-old man with no personal history of atopy was studied in our department. He reported that during the previous two years, he developed symptoms when handling dill plants, improving during holiday periods. The patient had held this job for the previous nine years.

At the time of the study, the clinical examination and the hemogram of the patient were normal. There was no history of allergic eczema/dermatitis syndrome (AEDS), rhinitis, asthma, or urticaria.

Serum total IgE was 35 kU/l (HYCOR Biomedical Inc.-IZASA, Barcelona, Spain). IgE specific to dill (and other allergens) was detected with enzyme-linked immunoassay (ELISA), which was performed with the commercial kit (HYCOR), using activated paper disc as solid phase. The allergenic extract was specially prepared at 5% w/v in phosphate buffered saline (PBS) (0.15 M). We did not detect IgE specific either to dill or to other members of the parsley family. Skin prick tests were negative to these extracts. The patient had negative skin prick test (Bial-Arístegui, Bilbao, Spain) and IgE specific (HYCOR) to a battery of allergens (house-dust mites, pollens, foods, moulds, and animal dander). Both skin tests and ELISA to salmon were negative.

Patch tests with extracts of dill and other members of the parsley family were applied for 2 days (D), and readings made at D2, D3, and D7. The dill extract was clearly positive, and the other extracts were negative. All these extracts were negative in six nonatopic and in six atopic control subjects.

Contact dermatitis from plants is a worldwide problem, extending from the Nordic countries to the tropics. The number of plants that can cause contact dermatitis is very high. The occupations at greatest risk regarding contact dermatitis from plants are florists, horticultural workers, cooks, and cabinet-makers, carpenters and others who work with wood. Direct contact with *Compositae* plants is probably the primary mode of sensitization, and, in general, contact with cultivated plants must be assumed to occur more often than with weeds. The high prevalence of positive weed reactions (similar to or higher than that of some cultivated plants) could be at least partially attributable to cross-reactions.

The family *Umbelliferae* is very widespread with close to 3000 species of aromatic herbs (some of which are poisonous), shrubs, and trees with small flowers. The increase in contact dermatitis from members of the family *Umbelliferae* is due to the growing use of species and flavours in foods and cosmetics in Western countries. Investigation of contact or delayed-type hypersensitivity to herbs and spices is important for several reasons. First, the cause of cheilitis, gingivostomatitis, gastrointestinal or perianal problems in some patients may be elucidated. Cinnamon oil and cinnamic aldehyde in dentifrices, tooth-

pastes, and medical and cosmetic preparations, and cardamom, oil of mustard, oil of cloves, allspice, ginger, coriander, nutmeg, and curry have all been reported as causes of allergic contact dermatitis (5,6). Second, in growers and handlers of spices, and cooks who have frequent contact with spices, hand eczema may be due to contact allergy to spices. Garlic and onion cause contact dermatitis in food handlers, and vegetables such as lettuce, endive, parsley, and carrots are also reported as being responsible for contact dermatitis in cooks and catering workers (7).

The various members of the parsley family have antigens that either are in common or cross-react (4). The patient reported here demonstrated no reactive patch tests to other members of the *Umbelliferae* apart from dill.

To our knowledge, this is the first case report of allergic contact dermatitis caused by dill. The patient no longer had symptoms after avoiding further contact with dill.

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Coronary vasospasm during an acute allergic reaction

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Key words: anaphylactic reaction; coronary vasospasm; drug hypersensitivity; food hypersensitivity.

Food- and drug-induced hypersensitivity reactions (1) are responsible for a wide spectrum of clinical manifestations involving skin, gastrointestinal tract, and respiratory tract. Acute urticaria and angiedema are believed to be among the most common manifestations of IgE-mediated food allergy. Food allergies are often involved in the pathogenesis of generalized anaphylaxis seen in hospital emergency departments. Indeed, in addition to cutaneous, respiratory and gastrointestinal symptoms, patients suffering from food-induced anaphylaxis may accuse cardiovascular symptoms, including hypotension, vascular collapse, cardiac disrhythmias and chest pain, presumably caused by massive mast cell mediator release (2). The onset of symptoms may be very rapid, appearing a few minutes after food allergen ingestion.

A patient with an IgE-mediated food allergy and ASA hypersensitivity.

In some patients the foods allergy and drugs hypersensitivity coexist. The possible clinical consequences are even more important. Few patients without anamnestic manifestations of hypersensitivity develop urticaria/angiedema, as well as anaphylaxis, after intaking ASA and/or NSAIDs. The mechanisms involved are not completely known yet, although it is widely accepted that cyclo-oxygenase (COX) inhibition is the central event. Recently, it has been proposed that prostaglandin E2 (PGE2) exerts a direct inhibitory effect on the 5-LO pathway and deficiency of PGE2, as a consequence of COX inhibition, causes both the removal of the suppressive effect and a rise in cysteinil-leukotrienes (Cys-LTs). Additional mechanisms have been suggested such as mast cell activation, neurohormonal acetylation, altered response of kinin receptors, tissue enzyme activation and activation of the complement alternative pathway.

A 53-year-old-man was hospitalized approximately 3 h after the intake of ASA and nimesulide with a generalized pruriginous macopapular rash and angiedema with glottis involvement. The clinical manifestations rapidly evolve into a severe malaise with moderate hypotension, tachycardia, and chest pain. The electrocardiography (ECG) examination showed a S-T segment displacement. For these reasons, the patient was submitted to both echocardiography and coronary arteriography, but neither of these revealed any meaningful alterations. The patient's condition rapidly improved after corticosteroid and antihistamine parenteral treatment with fast normalization of ECG. The urticaria eruption cleared 3 h later.

The detection of serum IgE antibodies (Pharmacia CAP RAST FEIA) revealed the existence of a sensitization toward some animal proteins such as beef (13 KUA/l), pork (13.1 KUA/l), and lamb (3.68 KUA/l), the total serum IgE level being 142 KU/l. IgE antibodies specific for cat (13.2 KUA/l) and dog (21.4 KUA/l) danders, in the absence of any clinical manifestation of rhinitis and bronchial asthma, were also detected. The patient denied any hypersensitivity reaction to food ingestion in the past. It is noteworthy that the patient was not affected by heart diseases. In the past, the patient had developed three other episodes of urticaria/angiedema after eating even relatively small amounts of foods found to be responsible for the present sensitization.

The involvement of the cardiovascular system represents a very important clinical finding during an hypersensitivity reaction. The mast cell activation and the subsequent release of mediators represent a central pathogenetic event in the induction of anaphylactic reactions. Moreover, the high number of mast cells in heart tissue allows us to understand the reason why mast cell activation is responsible for the cardiovascular alterations. In this patient, the simultaneous involvement of different factors able to induce the activation and degranulation of mast cells, acting via both IgE-mediated (food allergy) and non-specific mechanisms (non-allergic drug hypersensitivity) probably caused the

mentioned complex clinical manifestations.

In this report it is of note that whereas histamine is mainly responsible for the tachycardia and other arrhythmias, the alterations of coronary flow are usually determined by the action of other mediators such as Cys-LTs (LT)-C4, LT-D4, and LTE4. In humans, intravenous injection of a low dose of Cys-LTs is followed by increases in coronary arteriolar resistance (3).

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Does SIT to Der p protect from snail sensitization?

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Key words: *Helix* spp.; house-dust mite; snail allergy; specific immunotherapy.

Food allergy induced by snails has been described both in adults and in children (1) in significant association with house-dust mite (HDM) allergy. Both tropomyosin (2) and haemocyanin (3) are implicated in this cross-reactivity. The main problem was asthma (1,4–6), but even rhinitis (5,6), cough (1), urticaria (1,4,5), angioedema and anaphylaxis (4) were observed.

Specific immunotherapy seems protective in children.

Another link between Der p and snail allergy is the possible induction of snail sensitization caused by subcutaneous specific immunotherapy (SIT) with Der p extracts in patients who have never eaten snails before (5).

The snail species involved were *Euparipha pisana, Helix* spp., *Limax agrestis, Eobania vermiculata, and Cernualla virgata* (2,3).

Our aim was to evaluate whether SIT against Der p can induce skin prick test (SPT) positivity to snail extracts in atopic children.

One hundred and eighty-three symptomatic atopic children were enrolled (117 males, median age 8.5 years). They had to have at least a positive SPT for Der p. The symptoms were asthma (67%), rhinitis (81%), conjunctivitis (23%), atopic dermatitis (19%), urticaria (10%), contact dermatitis (1%), and systemic anaphylaxis (1%).

The children were divided in two groups. Group 1 ($n = 101$) children had never undergone SIT (or other kinds of immunotherapy) with Der p. Group 2 ($n = 82$) children had undergone SIT with Der p for at least 12 months (range 12–57 months, mean 29 months). In particular, 8/82 children had stopped SIT and 74/82 were having SIT at the moment of enrolment.

Besides standard SPTs with commercial common inhalant and food allergens, the children underwent SPTs with two different land snail extracts (*Helix aperta* and *H. pomatia,* weight/volume ratio 2%; Lofarma – Italy) chosen because commonly found and eaten in Italy.

No difference was found between the two groups except for SPT positivity to *Lolium perenne* and asthma, both more frequent in the group 2 children ($P < 0.01$).

In the group 1 children, 3/101 (3%) were positive to *H. pomatia,* and 5/101 (5%) to *H. aperta*. No group 2 child was positive either to *H. pomatia*, or to *H. aperta*. Therefore all the 8 children indifferently positive to both the *Helix* spp. belonged to the group who had never had SIT (group 1). This difference (8/101 vs. 0/82) was significant ($P < 0.01$).

Overall, 35/183 children (19%) had previously eaten snails (19 children of group 1 and 16 of group 2), but only 2/183 (1.1%) developed clinical symptoms (vomiting and asthma with urticaria). It is worth noticing that neither had received SIT and both were negative to the species of snails tested.

Only 1/8 children testing positive to *Helix* spp. had previously eaten snails, without symptoms.

Serum IgE antibodies against snails in 17 adult patients receiving SIT for HDM allergy were tested by van Ree et al. (5). Fourteen to twenty months later, although the average IgE response to Der p did not alter significantly, the average IgE response to snails showed a considerable increase.

Since these data may cause concern about the safety of SIT against Der p, it was decided to evaluate whether SIT against Der p, caused by the cross-reactivity, could induce SPT positivity to snail.

Surprisingly, and unlike the results in adult populations (2,3,5), the data seem to indicate that SIT with Der p extract, administered for about two and a half years (mean), could even have a protective effect against possible sensitization to snails, at least during childhood. In fact, the only snail SPT positivity found, was identified in children who had never practised SIT against Der p.

Group 1 and 2 allergens are the most important mite allergens, but several other proteins have been described and tropomyosin belongs to the Der p 10 group of mite allergens (7). Since total culture extracts and whole-body extracts are generally used for SIT, a different IgE antibody response for each allergen in different people and in children with respect to adults, may be expected.

The increase in IgE antibody against snails after Der p SIT does not mean, as a strict consequence, that any symptom will arise after snail ingestion. Even in the adult population studied by van Ree none of the subjects with IgE antibody to snail had symptoms after snail ingestion (5).

It can be concluded that the link between snail and HDM allergy does exist, but that it should be reconsidered in order to clarify: (a) the shared allergens between Der p and snails; (b) why SIT more than natural sensitization to Der p can lead to snail sensitization; (c) whether SIT in chil-

dren has the same effect as in adults; and (d) if the extraction methodology (presence of tropomyosin or other shared allergens) in SIT preparation may influence subsequent snail sensitization.

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Unusual IgE-mediated allergy to fish bait

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Key words: allergy; fish bait; *Galleria mellonella*; late reaction.

A case of late reaction (angioedema and urticaria) to the exposure of *Galleria mellonella* larvae used as bait by an amateur fisherman is described.

Fishing baits are known to be potential sensitizing agents among fishers, usually those at an amateur level. There are case reports of rhinoconjunctivitis and asthma provoked by *Asticot* maggots (1), by larvae of *Lucilia caesar* (2,3), *G. mellonella,* and *Tenebrio molitor* (4,5). Dermorespiratory allergy (angioedema, rhinitis, asthma) to fishing baits is also reported for the marine worm *Marphysa sanguinea* (6), and to *Eisenia foetida* (7). In these clinical reports, the symptoms occurred immediately after exposure to bait, and skin tests and *in vitro* tests confirmed an IgE-mediated mechanism. One case is reported of a late-asthmatic reaction (asthmatic attacks during the night or day after a fishing competition), IgE-mediated, due to larvae of *Calliphora erytrocephala* (8).

A late reaction to *Galleria mellonella* larvae.

A 58-year-old amateur fisherman came to the outpatients' allergology department of the first of authors, referring angioedema to the face and urticaria of the whole body whenever he went fishing in fresh water. The symptoms appeared about 3 h after he began fishing, sometimes after 6–8 h, when he was back at home. Past history was negative for atopic dermatitis in childhood, and positive for slight oculorhinitis in spring and autumn, which started 5 years before.

IgE detection. The patient underwent skin prick tests (SPT) with a standard panel of pollen, mite and mould extracts, revealing slight positivity to mites and grass pollen. The detection of specific IgE by RAST (Sferikit, Lofarma SpA, Milan, Italy) confirmed the SPT results: Der p 1, Der f 2, grass mix class 2, other pollens, and mould negative. As he had used larvae *of G. mellonella* for bait, a specific antigen was prepared to detect IgE antibodies. Briefly, the larvae were homogenized, extracted overnight at 5% weight/volume ratio in phosphate buffered saline, centrifuged, and the supernatant was filtered on Millipore membranes and exhaustively dialyzed. The antigen was covalently bound to polystyrene balls as solid phase and tested according to the common RAST procedure (Sferikit) with the patient's serum and with sera of healthy individuals, and other patients allergic to common allergens as negative controls. The RAST for the patient's serum resulted positive with 15.3 RAST-units, corresponding to class 3 (in a range from 1 to 4), and negative with control sera.

Patch test. Considering the delay from allergen exposure to the appearance of symptoms, we made a patch test with a small amount of homogenized larvae, put directly on to a plaster. The reading of skin reactions was made after 30 min and 48 h. Two control subjects were tested in the same way, one atopic and one healthy. The patient had a clear positive reaction after 48 h (characterized by erythema and infiltrate), while the test was negative after 30 min The two control subjects resulted negative after 30 min and 48 h.

The IgE-mediated sensitization to *G. mellonella* larvae was confirmed. The peculiar aspects of this clinical case are 1) the exclusively dermatological symptoms, angioedema and urticaria, without rhinitis or asthma; and 2) the late onset of the symptoms, confirmed by the late reaction at patch testing. This sensitization is clearly attributable to an IgE-mediated mechanism involving allergenic proteins; indeed, only proteins are able to bound the solid phase and therefore be revealed by RAST. Many protein allergens from animal and vegetable sources (like latex, mites, and some foods) have been shown to be able to develop protein contact dermatitis (9). It is quite difficult to explain the late reaction, as observed in our patient, considering the IgE-mediated nature of his sensitization.

This phenomenon has also been observed in other sensitizations, such as allergy to ingested snails, where severe asthma often appears 1–2 h after ingestion (10). It can be argued that in these cases the delayed appearance of symptoms could be due to slowed absorption of responsible allergens.

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Are hospitals safe for latex allergic patients?

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Key words: anaphylaxis; epinephrine; natural rubber latex.

IgE-mediated allergy to natural rubber latex is a cause of severe hypersensitivity reactions. There is widespread ignorance of the problems of latex allergy among healthcare professionals (1).

There is no evidenced-based guidance on management of patients with severe IgE-mediated anaphylaxis to latex outside hospitals. Current practice follows similar lines to other severe hypersensitivity: allergen avoidance and provision of self-treatment packages, including the provision of epinephrine (adrenaline) for self-injection where serious reactions have occurred, oral antihistamines, and possibly oral steroids (2, 3). Advice to patients is that the epinephrine (adrenaline) is for "first-aid" only and the patient must go immediately to the nearest emergency medical facility, preferably in a paramedic ambulance, for further treatment (4).

Optimum management should not include recourse to hospital.

Our experience of a number of patients with severe IgE-mediated anaphylaxis to latex, leading to multiple episodes of anaphylaxis, has indicated that this may not be the most appropriate approach to management, and that flexibility in the approach to self-treatment with additional training of family and friends may be safer.

Case 1. This woman was referred at the age of 33 in 1993 with anaphylaxis triggered by latex exposure. She had been in contact with latex seat covering and gave a clear history of previous generalized urticaria on contact with latex. There was no history of atopic disease. When she arrived in hospital, she was treated with oxygen by mask and developed an extension of her rash at the site of the mask and became much more wheezy. She had a history of reactions to tomatoes. She had IgE antibodies to Latex [Pharmacia CAP-RAST]. She continued to have severe allergic reactions to latex and had multiple casualty attendances after using epinephrine (adrenaline). She became very reluctant to go out of her house because of her reactions to environmental latex and became very depressed about her health. She preferred to manage her reactions without recourse to hospital.

Case 2. This 22-year-old woman was referred from the occupational health department of the hospital where she worked as a trainee laboratory scientist in 1998. Her case has been published previously (2). She was highly atopic and markedly dermographic. However there was a history of severe allergic reactions after contact with latex household items and with latex-containing laboratory equipment, including gloves. She was also allergic to latex-related foods. However, IgE antibodies to latex were not detected and skin prick testing was not possible due to continuing antiallergic treatment. Blind challenge with a latex glove led to a moderate reaction. Despite aximal antiallergic therapy she continued to have repeated severe reactions to latex, with one or two admissions with anaphylaxis per week and several admissions to ITU. Large doses of epinephrine (adrenaline) were required to reverse reactions (1–4 mg). The illness caused her significant stress. A policy of nonattendance at hospital was instituted and her partner was trained to administer all emergency drugs. She was reminded that failure to respond appropriately to treatment would still require attendance at hospital. It then became apparent that previously she would delay administration of epinephrine (adrenaline) in the hope of avoiding the need to attend hospital, leading to more severe reactions. Her epinephrine (adrenaline) requirements dropped dramatically after the "nonattendance at hospital" was introduced, even though reactions continued.

Case 3. This woman was 34 when first referred for allergic asthma, allergic rhinitis and "irritable bowel", but gave a clear history of IgE-mediated latex allergy, confirmed by skin prick testing [ALK-Abello]. Anaphylaxis only developed after latex avoidance was instituted (5), although her asthma, rhinitis, and bowel symptoms resolved. Initially there were significant difficulties over acute medical care with the ambulance service and the local casualty unit, because of staff wearing latex gloves. This caused significant stress and led to an acute depressive illness. A policy of nonattendance was instituted and she and her partner were trained to self-administer all medical treatments in the community. This led to a significant improvement in her confidence.

Our survey of hospital healthcare workers, including casualty staff and emergency medical staff, has shown very poor knowledge of the problems that may arise in the management of all types of latex hypersensitivity (1). This means that patients may be at greater risk of

prolongation or worsening of reactions through hospital attendance. This engenders increased anxiety in patients, and gradual erosion of confidence in the emergency medical services. All the people described here had severe depressive illnesses related to their severe reactions and ''loss of control'', worsened by medical insistence on hospital attendance. The insistence on attendance at hospital after using epinephrine (adrenaline) self-injection devices causes patients to delay using them, in an attempt to avoid hospital attendance—thus leading to more severe reactions.

We have therefore changed to a policy for severe latex allergic patients where emergency attendance at hospital is avoided unless self-treatment is ineffective. Patients are encouraged to use epinephrine (adrenaline) early, accompanied by oral prednisolone (20 mg) or intramuscular hydrocortisone sodium succinate (100 mg). Provided that there is a good response (as evidenced by resolution of angioedema, breathing difficulty and dizziness), hospital attendance is not required. Failure to respond to 2×0.3 mg epinephrine subcutaneously, or 1 mg epinephrine by nebuliser, or recurrence of symptoms, is viewed as an indication for transfer to hospital. Nurse specialists provide training to the patient and family on use of corticosteroids and epinephrine (adrenaline) and provide a latex-free medical kit, including a supply of drugs for self-treatment. This has significantly improved patient confidence, re-established patients' control over their disease, and led to earlier and better treatment. Although patients should feel safe in hospitals, until legislation eliminates latex from this environment, patients with severe IgE-mediated anaphylaxis to latex may be best managed away from hospital.

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