

SPECIFIC IMMUNOTHERAPY FOR SEVERE LATEX ALLERGY

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Summary

ABSTRACT : We studied 4 patients (3 adult females + 13y old boy) with latex allergy. All patients had anaphylaxis related with latex and oral-latex-fruit syndrome. All 3 females had severe symptoms in the workplace. The boy had spina bifida with 9 previous surgeries and needed further surgical interventions. Positive skin prick tests (SPT), the presence of serum latex specific IgE (CAP-RAST, Pharmacia-Upjohn, Sweden- class 3 in the 3 females and class 4 in the boy) demonstrated the sensitization.

All 4 patients were treated with specific immunotherapy (SIT) with aqueous extract (ALK-ALK-ABELLÓ SA, Spain) administered subcutaneously at the hospital, by a modified rush schedule. A maintenance dose (MD) of 0.35_g protein was established according to the magnitude of local reactions (LRs). In one patient a higher dose induced the appearance of a systemic reaction (SR) 40 min after administration, which promptly remitted with treatment. After reaching MD, all 3 females remained asymptomatic at workplace. A challenge test with latex gloves was performed. Two months after MD was reached 2 females had no symptoms and one other had mild symptoms of rhinoconjunctivitis. The boy was subjected to a surgical intervention with no allergic reaction. We also observed a reduction on skin reactivity to latex in all patients by prick tests.

We consider SIT with latex to be highly effective, safe and well tolerated provided we use this dose of the allergenic extract.

Key-words: Latex - Hypersensitivity - Immunotherapy - Anaphylaxis - Occupational disease.

INTRODUCTION

Latex is a complex mixture of allergenic proteins ranging in molecular weight from 5 to 100 kDa (1). The major allergens appear to be rubber elongation factors, hevein and prohevein (2, 4). Latex allergy, first described in the English literature in 1979, has become a significant problem because of its increasing prevalence as an occupational disorder among health care professionals, and its association with other occupational or clinical situations such as spina bifida, severe urological malformations, employment in the rubber industry, and individual atopy (5). An association between latex allergy and hypersensitivity to certain fruits and nuts (latex-fruit syndrome) is also frequently seen; this relationship is the result of cross-reactivity between *Hevea brasiliensis* and common antigens in some foods (6). Irritant dermatitis,

contact dermatitis and rhinoconjunctivitis are the most frequent clinical manifestations (1). Asthma and anaphylaxis are more uncommon, although they are being reported with increasing frequency (7).

Since the first report, latex allergy has turned into an increasingly recognized occupational disease, particularly in health care workers (8). The prevalence in different groups of individuals who frequently handle latex gloves and other medical-surgical materials containing latex, ranges from 12 to 18%, with different clinical manifestations (9, 10). Studies in Portugal have found a prevalence of 11 to 14% among health care workers (11-13).

Unfortunately, for latex-allergic health care workers, especially those working in technical areas or departments, a latex-free environment is almost impossible to achieve: in addition to gloves, many clinical instruments contain latex parts. Thus latex allergy represents a serious social and occupational problem for individuals with severe symptoms (14).

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Anaphylaxis is the most severe clinical pattern of latex allergy, often appearing in health care workers or in some patients with latex-fruit syndrome. For those individuals, allergen avoidance may not be sufficient because latex is an ubiquitous material in everyday activities. Immunotherapy must be considered in these selected cases, always under close supervision by hospital allergist (15). Our group applied the first successful SIT schedule with a latex extract in one patient in 1997.

SUBJECT AND METHODS

The Hospital's Ethics Committee approved the desensitisation protocol with latex allergen extract, and all patients gave fully informed written consent to the treatment. Since 1997, we are involved in the follow-up of 4 patients who were included in this study (3 in Coimbra and 1 in Lisbon).

PATIENTS

PATIENT 1

31-year-old caucasian woman, radiology technician since the age of 24. She reported lid edema, burning and itching of the nose and eyes of about 2 years duration. The symptoms appeared while she was at work, particularly when she spent time in areas where latex gloves had been used. Symptoms became progressively more severe, with urticaria, rhinitis and conjunctivitis, with a clear clinical correlation between the appearance of symptoms and exposure to latex in the work environment. Although the patient tried to avoid areas of high exposure, her symptoms at work did not remit completely. In March 1997 the patient had two acute anaphylactic episodes related to food ingestion: figs and chestnuts. For both accidents a short-term hospitalisation was required.

She had previous intestinal surgery in 1992 and cesarian delivery in 1996, both uneventful. There was no family history of atopy.

She was referred to Coimbra Allergology Department in April 1997.

PATIENT 2

36 year old female, surgical nurse-assistant since the age of 30. In 1990 we observed this patient for chro-

nic urticaria (2 years), with one anaphylactic episode. At this time we demonstrated food allergy to banana (specific IgE and positive skin prick test), without latex or other food allergies. An open oral provocation test to banana induced anaphylaxis, which promptly remitted with treatment.

In 1996 she started complaining of rhinitis and conjunctivitis at workplace, with increasing severity. Two years later, after a rectal manoeuvre with latex gloves she had a severe anaphylactic episode, needing intensive care support. No family history of atopy was found. She was referred to our Department in July 1998.

PATIENT 3

25 years old female, working as swimming trainer since the age of 23. She had daily contact with swimming hoods and other latex materials. Since she started working (2 years before), she reported frequent crisis of angioedema of face and hands, rhinoconjunctivitis and, recently, several anaphylactic episodes during swimming class. No syncope accidents were noted but emergency care was needed on several occasions, with administration of epinephrine, systemic steroids and antihistamines. No personal or familiar atopic status was noted.

The first observation in Coimbra University Hospital occurred in August 1998.

PATIENT 4

13-year old boy with spina bifida who had 9 surgical interventions, 5 of them during the first year of life. Latex allergy was suspected from the age of 6, when he started having angioedema of the lips when blowing rubber balloons, but the allergological work-up at that time was negative. After avoiding contact with balloons the symptoms did not recur. At the age of 12, during an orthopaedic surgery for osteomyelitis, in which latex gloves were used, the child had an anaphylactic reaction.

He was referred in December 1999 to Santa Maria Hospital (Lisbon), to clinical evaluation. At this time skin prick test to latex was positive and the child had also clinically silent positive skin prick tests (SPT) to some foods (avocado, chestnut and other tree nuts, peach, spinach, passion fruit and peanut) already described in latex-allergic patients. Additionally, he had developed in the previous year a clinically relevant food allergy, manifested by dysphonia and pruritus of the perioral region, lips and tongue, immediately after eating chickpeas. SPT with chickpea extract was exuberantly positive, but there were no positive SPT to

other foods from Leguminosae family. Chickpeas evic-tion led to symptom remission and two open food chal-lenges confirmed the aetiology.

However an additional orthopaedic surgery was necessary and a complete latex free surgical environ-ment was not possible to guarantee.

METHODOLOGY

All patients were subjected to the following procedures.

ALLERGIC EVALUATION

As *in vivo* tests we used cutaneous SPT with allergenic extracts (ALK- ABELLÓ SA, Spain), applied to forearm skin. The reactions were scored 20 minutes after punc-ture. Histamine chlorhydrate (10 mg/ml) was used as positive control, and saline solution as negative control. The standard set of aeroallergens consisted of dust mites, dog and cat dander, cockroach, mixed grasses, *Parietaria judaica*, *Artemisia vulgaris*, *Olea europaea*, *Quercus robur*, *Platanus orientalis* and *Pinus radiata*.

A second set of allergens (Leti, Spain) was applied to test food allergen extracts, including: fruits (orange, pineapple, kiwi, strawberry, peach, pear, banana, grape, melon, watermelon, coconut, lemon, medlar, avocado, passion fruit, tangerine, fig, raspberry, cher-ry, prune, mango, apple; nuts (chestnut, walnut, pista-chio, hazelnut, pine nut).

We tested latex allergen extracts from two suppliers: ALK- ABELLÓ SA, (Spain) and Stallergenes (France).

Skin tests for latex and food allergens were repeated along the desensitization protocol: during build-up phase before each increment of the allergen dose and several times during maintenance phase.

For *in vitro* measurements of latex specific IgE and IgG, we stored at -70°C two aliquots of each patient's serum.

Specific latex IgE was measured by fluorescent enzy-me immunoassay (Pharmacia UniCAP System, Uppsala, Sweden) and specific IgG was measured by latex-specific fluorescent enzyme immunoassay (Pharmacia CAP FEIA, Uppsala, Sweden).

ALLERGENIC EXTRACT

Latex extract was prepared from an ammonia latex particle suspension by neutralization, semi-purification

and concentration, essentially as previously described by Morales *et al.* (10).

The protein profile obtained by SDS-PAGE and subse-quent immunoblotting analysis displayed a characte-ristic profile with allergenic bands similar in molecular weight to most relevant latex allergens found in pooled sera from latex-allergic patients (data not shown). Final adjustment to 0.5 mg/ml of protein was used for SPT diagnosis.

Treatment extract (ALK-ABELLÓ SA, Spain) was dosed in 10% glycerol 0.9% NaCl buffer at 10-fold dilutions, the highest potency being 100mg/ml. Vials were labelled A' (0.01 µg/ml), A (0.1 µg/ml), B (1 µg/ml), C (10 µg/ml) and D (100 µg/ml).

IMMUNOTHERAPY SCHEDULE

All patients were on short-term hospital admission in order to allow the administration of the allergenic extracts exclusively by allergists, in the Immunoallergy Department and under close sur-veillance. The Guidelines of the Position Paper of the European Immunotherapy Academy were followed (17); exposure to latex was minimal, and staff mem-bers of our department were permanently in contact with the emergency room during treatment.

After subcutaneous administration of the extract, the patient remained under observation in the hospital for 4 h (a period much longer than that recommended for SIT with other allergens) (17), and general condition and vital signs were monitored closely. Local and sys-temic adverse reactions were classified according to European Guidelines (17).

For the first patient, lacking any reference, we establi-shed the MD as the dose immediately previous to the one that caused a SR that being the maximum tolera-ted dose. Initially, during the build-up phase, a single weekly dose was given, but the progression was acce-lerated at the patient's request after starting the 1 µg/ml concentration vial. For the other patients, a rush-modified schedule was decided.

SAFETY

To evaluate the safety of the extract and integrity of the immune system, venous blood was collected for hemo-gram and white blood cell counts, blood biochemistry, liver enzyme studies and ionogram. Glycemia and renal function were also determined, and proteins were studied electrophoretically. Complete urinalysis was done. We measured serum IgG, IgA, IgM (nephe-lometry) and IgE (Pharmacia UniCAP System,

Uppsala, Sweden) and lymphocyte subpopulations. Membrane surface antigens (anti-CD2, CD4, CD8, CD7, CD29, CD14 and CD45RA) were studied with a Coulter-Immunoprep. All analyses were performed in the hospital's laboratory. Before starting SIT, an electrocardiogram was obtained in every patient.

CLINICAL EFFICACY

During each visit the patient's clinical symptoms (nose, eyes, lungs and skin) were carefully checked. The severity of the allergic disease in these patients constituted an ethical limitation to provocation tests. However, we planned a controlled provocation test after reaching MD. The test consisted in the following: the patient entered a 1m³ air-tight cabin and handled four pairs of latex gloves for 15 minutes; clinical symptoms were evaluated during the following 6 hours.

RESULTS

All patients had a history of severe SRs to latex products. In table 1 we present the results of allergological evaluation. Before immunotherapy latex-specific IgG was not detectable in any of the patients.

Concerning safety there were no anaphylactic episodes during SIT. However in patient 1 at the 4th day of week 9, at a dose of 0.5ml of the vial B (1_g/ml), a SR was observed 40 minutes after the injection. The reaction remitted promptly under adequate treatment. This reaction led us to reduce the dose to 0.35ml, which was later increased to 0.40ml and well tolerated. This administration continued each week from the 11th to the 17th week, and quarterly till week 29. A 3-weeks interval between injections was established till week 35, when an increase in LR_s (60mm) was observed. Therefore it was decided to maintain a maximum dose of 0.35_g of protein. From the 44th to the 89th week the patient received a monthly injection and each 5 weeks after week 88.

In the other 3 patients SIT was well tolerated, no SRs were observed and LR_s never exceeded a wheal diameter of 18mm.

We emphasize patient's excellent tolerance to treatment, and full compliance with the schedule of allergen extract administration.

Immunotherapy with this latex extract produced no changes in laboratory values, all of which remained within normal limits in both blood and urine. No changes were seen in the main lymphocyte subpopu-

lations nor in serum levels of immunoglobulins (IgG, IgA, IgM and total IgE).

All electrocardiograms were considered normal.

Regarding cutaneous responses to latex during SIT, we observed a reduction in the mean diameter of the SPT papule with both commercial extracts tested. There were parallel decreases in the reactions to food allergens (figure 1).

Specific IgE to latex showed a decrease in all patients; additionally there was a clear rise in specific IgG to latex. Specific IgE for foods clearly decreased during treatment.

Clinical symptoms improved steadily in all the patients. Acquisition of environmental tolerance at the workplace was gradual during SIT, being more pronounced once the MD was reached.

	Patient 1	Patient 2	Patient 3	Patient 4
Sex	Female	Female	Male	Male
Age (years)	31	36	25	31
Prick test				
Latex	Positive	Positive	Positive	Positive
Chestnut	Positive			
Banana		Positive		Positive
Chickpea				Positive
Total IgE (UI/ml)	51	56	63	124
Specific IgE (KU/L)				
Latex	5.79	6.32	7.1	46.3
Chestnut	0.71			1.7
Banana		1.33		1.52
Chickpea				2.12
Avocado				1.74
Passion fruit				2.92
Peach				0.60
Latex specific IgG (mg/l)	Negative	Negative	Negative	Negative
Treatment (months)	63	52	52	30
Serologic measurements				
Total IgE (UI/ml)	41	34	64	
Specific IgE (KU/L)				
Latex	1.5	5.8	4.1	32.5
Chestnut	<0.35			0.60
Banana		<0.35		1.00
Chickpea				0.60
Avocado				0.80
Passion fruit				0.70
Peach				<0.35
Latex specific IgG (mg/l)	6.6	3.3	2.2	17.5

Table 1 : Allergological study results before and after active treatment.

	Week (day)	Dose (mg protein)	Wheal (mm)	Erythema (mm)
Vial A' (0.01 µg/ml)	0	0.003	0	37
	1	0.005	20	32
	2	0.008	10	35
Vial A (0.1 µg/ml)	3	0.01	10	25
	4	0.02	12	27
	5	0.04	10	32
	6	0.05	14	27
	7	0.07	11	34
	8	0.08	15	36
	9 (1)	0.10	15	22
Vial B (1 µg/ml)	9 (2)	0.20	12	20
	9 (2)	0.25	8	17
	9 (3)	0.35	8	18
	9 (3)	0.40	14	23
	9 (4)	0.40	18	23
	9 (4)	0.50+	11	27
	9 (5)	0.35	12	22
	10 (1)	0.35	13	20
	10 (2)	0.40	20	28
	10 (4)	0.40	60	82
	11	0.40	25	30
	12	0.40	20	25
	13	0.40	22	28
	14	0.40	25	33
	15	0.40	30	40
	17*	0.40	33	42
	19	0.40	35	40
	21	0.40	10	21
	23	0.40	15	24
	25	0.40	12	18
	27	0.40	30	40
	29**	0.40	33	42
	32	0.40	35	50
	35	0.40	41	60
	38	0.35	15	24
	41	0.35	12	18
	44***	0.35	14	20
	48	0.35	10	19
	52	0.35	15	22
	56	0.35	20	25
	60	0.35	12	17
	64	0.35	8	19
	68	0.35	12	21
	72	0.35	11	22
	76	0.35	10	16
	80	0.35	10	21
	84	0.35	15	24
	88****	0.35	12	18
	93	0.35	14	20

Table 1 : Patient 1 - Therapeutical schedule and local reactions.

+ Late systemic reaction.

* frequency 2 weeks.

** frequency 3 weeks.

*** frequency 4 weeks.

**** frequency 5 weeks.

Week (day)		Dose	Wheal			Erythema		
			Patient 2	Patient 3	Patient 4	Patient 2	Patient 3	Patient 4
0.01mg/ml	0 (1)	0.002	0	3	3	5	12	7
	0 (2)	0.004	2	2	0	7	8	6
	0 (3)	0.006	10	5	2	16	16	8
	0 (4)	0.008	3	6	3	6	10	6
0.1mg/ml	1 (1)	0.01	2	5	4	3	8	7
	1 (2)	0.02	3	7	0	4	9	3
	1 (3)	0.04	3	6	5	4	10	10
	1 (4)	0.06	3	6	3	4	11	8
1mg/ml	1 (5)	0.08	3	8	4	4	15	7
	1 (6)	0.06	4	6	6	6	10	10
	2 (1)	0.06	10	7	4	12	17	9
	2 (2)	0.10	5	8	6	6	15	9
	2 (3)	0.20	5	8	5	10	19	10
	2 (4)	0.25	5	10	6	7	22	10
	2 (5)	0.30	5	10	6	8	25	9
	3 (1)	0.35	12	15	4	16	24	7
	3 (2)	0.35	12	18	5	16	27	9
	3 (5)	0.35	4	15	3	9	24	6
	4	0.35	4	15	4	6	24	8
	5*	0.35	3	14	0	8	20	5
	12**	0.35	3	10	0	9	15	0
	24***	0.35	4	12	2	10	18	4
	71****	0.35	4	9	2	11	17	3

Table 1 : Therapeutical schedule and local reactions. Patients 2, 3 and 4.

* frequency 2 weeks.

** frequency 3 weeks.

*** frequency 4 weeks.

**** frequency 5 weeks.

The provocation test performed 2 months after MD didn't induce any symptoms in patient 1 and 2, and induced only mild symptoms of rhino-conjunctivitis in patient 3, 20 minutes later. No rescue medication was needed. We did not subject the boy to a provocation test in the standard cabine. However after 10 months since the beginning of treatment he underwent a surgical intervention. No complications were recorded during surgery or during the hospitalization period. After surgery, the boy had also occasional contact with rubber balloons that did not induce any allergic reaction.

In 2002, Patient 3 became pregnant but we maintained SIT, with a reduced monthly dose of 0.20_g protein. She was closely watched during the whole pregnancy and the delivery was performed in latex-reduced environment. There were no complications for the mother or the baby. Measurement of latex specific IgE in cord blood was negative.

All patients are still in desensitization program (more than five years for patient 1, four years and a half for patients 2 and 3 and two years and a half for patient 4).

DISCUSSION

Latex allergy is a really worrisome problem with an increasing number of reports of severe reactions. Latex avoidance is a balance between disease prevention, lifestyle choices and livelihood (18). A complete latex free environment for patients with high risk of anaphylaxis, although desirable is frequently unattainable, and could be extremely limitative. Furthermore, for health care workers, latex allergy can result in a restriction of their occupation and career.

Another problem is the well known latex-fruit syndrome due, among other factors, to the hevein molecule

(Hev b 6.02) that has striking homology with class-1 chitinase, widely present in plants (19). Several fruits and other foods of plant origin have a risk of cross-reactivity with several allergens identified in *Hevea brasiliensis*. The increase of cross reactivities to different foods in a same patient is an issue that has been alluded to in recent papers, even despite prophylactic measures and dietetic avoidance (20).

Besides classical risk groups to latex allergy, such as spina bifida, the increase of surgical procedures during childhood could explain the increased number of reports of severe cases in paediatric ages. These compile an extremely vulnerable group because further surgical interventions are often needed.

All patients selected for the treatment with SIT were severe cases of latex allergy. For these, avoidance measures are frequently not enough to guarantee a low risk of future allergic accidents. For the 3 females, the maintenance of their regular occupation was also a social-clinical problem. On the other side, the boy had serious orthopaedic problems with clinical indication to a programmed surgery. These are the major reasons for which we decided to start this kind of therapy. In 1997 when we considered this therapeutic strategy with the first patient, there was only one report of desensitization of 3 patients by oral ammoniated latex form (21). The severity of these patients was not comparable to the recent anaphylactic episodes of our first health care worker.

We strongly believe that there are clinical and pathophysiological similarities between latex anaphylaxis and bee venom allergy, in which subcutaneous SIT is the gold standard treatment. In close cooperation with ALK-ABELLÓ SA, Spain, an aqueous allergenic extract obtained from latex suspension was prepared and 5 different concentrations supplied (15), although we ended up not using the two highest concentration vials. When we started latex SIT in the first patient, we had no idea of the allergenic potency of the extract and what would be the maximum tolerated dose, so we chose to establish a MD as the highest dose that did not cause a SR. The first patient freely consented to participate in the study, after being informed of the risks of immunotherapy, especially those involved in the use of a new allergenic extract that had not previously been injected in human subjects. Initially we planned to perform a conservative desensitisation schedule, with weekly injections of the allergenic extract, but we changed this approach in response to several factors. The most important factor was the patient's request; because she lived 150 km away, frequent trips to the hospital were inconvenient and costly. Once we had confirmed that the first two vials had been well

tolerated, we changed to a semi-rush schedule that reduced the number of trips the patient had to make. This part of the treatment schedule was undertaken with maximum precautions.

For the other patients, we learned from our previous experience and decided to follow a modified rush schedule immunotherapy. The 0.35mg of protein was defined as the maximum dose and it was also the MD.

Tolerance was excellent, and like other authors who used accelerated schedules (22), we established the MD on the basis of the appearance of a SR. We felt this to be the most prudent approach, in contrast with other studies in which the appearance of a SR led only to a change in the dose schedule (23, 24). The MD in our patients was significantly lower than in the group of Leynadier F. *et al.* (25), but our group had different clinical manifestations of latex allergy. In Leynadier's group only one patient had history of anaphylactic shock and the reactions following injection of allergenic extract were significantly higher.

One recent paper from Sastre J. *et al.* describes a double-blind placebo controlled study using a standardised extract adsorbed in alum on 16 out of 24 latex allergic patients (19). In this study a subcutaneous cluster schedule was administered and the doses

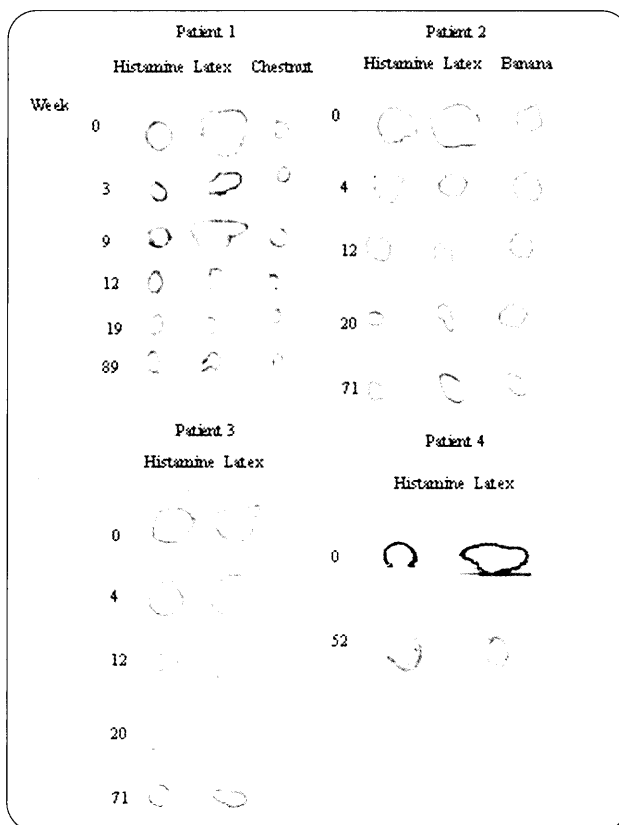


Figure 1 : Skin prick tests results during treatment.

were also higher than in our patients, but with more frequent SRs. Furthermore, patients in Sastre's group had less severe clinical manifestations (rhinitis and conjunctivitis, asthma and contact urticaria), apparently without any case of anaphylaxis.

In our study only the first patient experienced a SR, with a dose which was probably too high. We believe that the allergenic extract is safe, at least in concentrations up to 0.35 µg latex protein. This conclusion is also based on the absence of changes in laboratory values or in other cellular and hormonal biological measurements. We stress the fact that our patients are still in treatment (2 years and 6 months/5 years and 4 months) with no adverse reactions after allergen injections. Regarding clinical efficacy, patients remain asymptomatic in areas that formerly triggered intense symptoms; the orthopaedic surgery in the boy and the delivery in patient 3 did not cause any allergic reactions.

We did not perform a specific provocation test to confirm the clinical diagnosis before starting SIT, because we considered natural allergenic provocation at workplace to be sensitive and specific enough for diagnosis. However, we used this test in the 3 adult females to demonstrate SIT efficacy, after MD had been reached. The allergen provocation test, which attempts to simulate natural exposure, confirmed the absence of cutaneous, ocular, nasal or bronchial symptoms during the 6 h following exposure to the allergen in two-thirds of the patients, with only slight symptoms of rhino-conjunctivitis in patient 3. The boy was not subject to the provocation test, but absence of symptoms with rubber balloons, that previously induced symptoms, was considered sufficient.

Skin tests were used along the study, not to demonstrate clinical and therapeutic efficacy, but because they are a routine follow-up measure for patients undergoing SIT in our department. If skin tests are not performed by duplicate with several different dilutions, it is not possible to quantify the results with the parallel line assay (26), and our analysis would be limited to the use of descriptive statistics. Although cutaneous reactions decreased we could not demonstrate statistical significance. A decrease in skin reactivity to food allergens was also observed in all patients.

We found that specific IgE decreased and IgG increased during treatment, as is generally observed in SIT with other extracts; however, how significantly these changes relate to clinical improvement is unclear (24, 27, 28). Specific IgG was absent in the beginning of SIT and its expected increase was only observed after several months of active treatment, as this immunoglo-

bulin generally appears after prolonged exposure to antigens (29).

More recently, some studies have used non-injectable SIT, all showing clinical efficacy and reduced skin reactivity in prick tests to latex (30, 31, 32). Another study from Patriarca G. et coll. reported clinical improvement using a schedule of progressively increasing exposure (33). The sublingual route has demonstrated efficacy in allergic diseases, but till now its use is restricted only for mild to moderate forms of allergic diseases. Furthermore, this strategy was never applied to the most dangerous IgE mediated allergy, such as hymenoptera venom anaphylaxis. In fact, our patients had anaphylactic crises with a clinical pattern quite similar to those. However, we believe that the sublingual route could be an excellent choice for minor symptoms of patients with occupational latex allergy. We are highly convinced that subcutaneous SIT, under close surveillance by hospital allergists with training in hymenoptera venom immunotherapy, is indicated to patients with severe latex allergy. With the doses we used, we had not any SRs, in contrast to the reports of other authors (19, 34). Local and SRs found in the group of patients studied by Leynadier F et al could be explained by the higher doses injected (25).

The most noteworthy feature of our report is the substantial reduction in clinical allergic symptoms, which allowed patients to continue to perform their daily work with no significant limitations and no relevant adverse effects. Future developments in allergenic extracts, peptide immunotherapy, recombinant allergens or conjugation of allergens to immunostimulatory sequences of DNA (19), will probably contribute further to a better management of patients with latex anaphylaxis.

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