

Allergy to Latex

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INTRODUCTION

The first case of immediate hypersensitivity (urticaria) resulting from latex of *Hevea brasiliensis* (LHB) was reported in 1979 by Nutter (1). This new side effect of rubber was clearly different from the frequent and well-known contact dermatitis (eczema) induced by a delayed hypersensitivity to low molecular chemical additives (vulcanizers, stabilizers, accelerators, and antioxidants). In this case, the diagnosis was obtained by patch tests, which became positive 48 h after contact (2). Since 1979, several observations of immediate allergy to LHB have been reported, mainly contact urticaria (3-21).

In 1984, the two first case of anaphylactic reactions to surgeons' latex gloves during an operation were described by Turjanmaa et al. (22). About 30 cases of anaphylaxis to LHB have been published. They were induced by vaginal examination with LHB gloves, dental treatment (latex cofferdam), or by blowing up a rubber balloon. These cases were most frequently observed during surgical operations (3,9,11,14,15,18,20,21).

Since 1987, we have observed in our department 18 cases of anaphylaxis to LHB during operations (Table 1). They represent about 10% of all cases of anaphylaxis to anesthetic drugs seen during the same period. Three possible explanations for the increasing frequency of immediate allergy to LHB in the past few years are: a better knowledge of the clinical picture, the increase in use of latex

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Table 1
Eighteen Patients with Anaphylaxis to Latex During Operation

Case	Sex	Age	Atopy personal	Occupation	Allergy to latex since, year	Food allergy	Prick Test, latex	RAST, class	IgE, KU/L	HBDT
1a	F	30	No	Cook	10	Pineapple	+	2	980	+
2	F	47	Yes	Clerk	>10	Cabbage	+	4	40	ND
3	F	32	No	Nurse	8	None	+	3	303	+
4a	F	35	No	Clerk	3	Banana, avocado, pear	+	2	136	+
5	F	34	No	Assist. nurse	2	None	+	3	122	+
6a	F	29	No	Assist. nurse	10	Tomato, grape, banana, avocado, pear	+	2	225	+
7	M	16	No	None		None	+	4	905	+
8	F	32	No	Nurse	5	Passion fruit, pimento	+	3	1664	+
9	F	56	No	Cook	<1	Fish	+	2	80	+
10	M	9	No	None		None	+	4	3300	-
11	F	31	Yes	Accountant	6	Nut	+	2	561	+
12	F	32	No	Nurse	2	Strawberry	+	2	75	ND
13	F	30	Yes	Saleswoman	>10	Orange	+	0	72	-
14	F	40	No	Saleswoman	6	None	+	0	7	-
15	F	44	No	None	6	Banana, avocado, pear, nut	+	1	126	+
16	F	57	No	None		None	+	0	95	-
17	F	28	No	Dentist	4	None	+	1	ND	-
18	F	26	Yes	Secretary	6	None	+	3	185	+

a: Two shocks to latex.
ND: Not done.
HBDT: Human basophil degranulation test.

gloves, and condoms and/or some modifications of the manufacturing process or of the *Hevea brasiliensis* culture.

CLINICAL ASPECTS

Anaphylaxis to LHB occurs mainly in women (more than 80% of cases) who also previously suffered from contact urticaria to LHB in 83% of our 18 cases (Table 1). As reported by Wrangsjo et al. (20), urticaria may be isolated (23%) and not spontaneously mentioned by patients, or it may be associated with mild (40%) or severe distant symptoms (36%), such as facial edema, rhinitis, conjunctivitis, dyspnea, tachycardia, generalized urticaria, asthma, or even shock.

The sensitization is probably acquired by repeated contacts with LHB gloves. It is not surprising that women working as health personnel represented 6 out of our 18 cases (33%) (Table 1). In their report about contact urticaria, Wrangsjo et al. (20) indicated that 43% of patients were working in a medical occupation. LHB immediate allergy occurs in 7.5% of doctors and 5.6% of nurses working in operating departments. (23).

In our two cases of anaphylaxis in children, as in the two cases of Slater (15), the sensitization probably resulted from the multi-operated children having several contacts with surgeons' LHB gloves. However, frequent exposure to LHB of balloons, pacifiers, and bottles may explain some sensitizations in children (4,20).

Atopic disease (atopic dermatitis, asthma, and/or rhinitis) is frequent (53–74% of cases) in contact urticaria (20,23), but was observed in only 22% of our cases (Table 1). It is remarkable that the association with food allergy is frequent: 76% of cases for Wrangsjo et al. (20) and 56% in our cases. A crossallergenicity between some LHB proteins and exotic fruits, particularly the banana, is probable. A history of immediate allergy to drugs not previously mentioned in the literature appeared in 33% of our patients (penicillin: 3 cases, aspirin:1, glafenine: 1, and indometacine: 1).

In the 19 reported cases of shock during operations, as in our 18 cases (5 of which were previously published) (11), approx 50% were observed during gynecological intervention, mainly delivery by

caesarean section, and about 20 and 10%, respectively, during abdominal and orthopedic surgery. In the other 20%, the shock appeared after contact with a rubber tube (tracheal intubation or urethral catheterization) placed by an anesthetist or a nurse who wore latex gloves.

The first symptoms occurred generally more than 15 min after the injection of anesthetic drugs and even at the end of the surgical intervention. Urticaria, angioedema, and tachycardia were the first symptoms, followed in a few minutes by a collapse and in some cases bronchospasm. In most cases, adrenaline was necessary to correct the collapse. To our knowledge, no death has been reported. The delay between the injection of drugs and the symptoms, on one hand, and the progressive worsening of symptoms, on the other, is a serious argument against anaphylaxis to anesthetics, as further confirmed by the negative skin tests with these drugs.

DIAGNOSTIC METHODS

The prick tests with natural LHB are specific and sensitive: 100% of our 18 patients have a positive prick test (wheal ≥ 5 mm, flare ≥ 10 mm) with a commercially available extract at 1/1000 or if negative at 1/100 (vol/vol) (Stallergenes 94264 FRESNES, France). No false-positive test was observed in more than 200 control subjects. The same results were obtained by Turjanmaa et al. (24) and Wrangsjö et al. (20). In previous works, prick tests have been carried out through surgical gloves or with different commercial prevulcanized LHB, containing chemical additives. These techniques were less sensitive (24): not all surgical gloves are equally allergenic (25) and, on the other hand, skin tests may be negative when the glove has been washed (14).

The scratch-chamber tests are less specific than prick tests (false-positive results) (23,24). Provocation tests by wearing a surgical glove can be dangerous and, in some cases, negative (20).

This IgE-mediated allergy can be tested in vitro either by detecting serum-specific IgE (Radio-allergo-sorbent test, RAST) or by measurement of basophil degranulation or basophil histamine release (BHR) (26). RAST was positive in 53–83% of cases (20,24). In our 18 patients, the RAST was clearly positive (Class II–IV) in 72% only.

Human basophil degranulation test (Allergolam® procedure, Diagnostic Pasteur, Marnes-la-Coquette, France) proved to be as sensitive as the BHR test (27). This test was negative for LHB in 5 out of our 16 tested patients (Table 1).

BHR was positive in 13 out of 14 patients tested by Turjanmaa et al. (26) and in the 2 cases reported by Slater (15). However, this technique is more expensive than the basophil degranulation test, and certainly more so than prick tests. Finally, the lymphocyte proliferation test was positive in 20% of patients studied by Turjanmaa et al. (26), and patch tests were negative except when delayed allergy (eczema) to rubber chemicals was present (20,25,28).

In summary, the prick test with natural extract of LHB appears clearly sufficient for a diagnostic purpose. It is sensitive, specific, cheap, and easy to perform, even by a nontrained nurse or doctor.

ALLERGENS OF LHB

Some authors have ascribed rubber immediate allergy to the powder (29,30), to a chemical additive (31), to a bicyclic terpene (32), or to lycopodium spores (33). However, it is now clearly established that the natural LHB itself is responsible in almost all cases.

The fresh LHB contains about 1.5–2.8% protein (34), and the commercial latex “low-ammonia” about 1.65%. For example, Morales et al. (14) found that the protein content of nondialyzed serum latex obtained from natural latex “high-ammonia” was 4.5 mg/mL in dialyzed serum. They observed by isoelectric focusing, that latex contained several proteins, most of which were focused in the acidic zone. Some of these proteins persisted after rubber manufacturing. After incubation of glove pieces for 30 min in physiological saline (1 g of glove/mL), the amount of protein was 25–280 µg/g of glove (25). In a recent work, we obtained a protein content of about 100–1200 µg/g after incubation of different commercial gloves for 3 h in physiological saline (stirred on a roller).

As supposed by Meding and Fregert (12) and Carillo et al. (5), it has been clearly demonstrated that these proteins were the allergens of immediate allergy (14,26). Recently, Turjanmaa et al. (17,25) have conducted studies with high-pressure liquid chromatography (HPLC) on gloves or latex condoms. The protein profile was quite

similar to that observed with natural LHB. Positive prick tests were obtained with fractions corresponding to mol wt of 2, 5, and 30 kDa. Morales et al. (14) using sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE) observed at least four protein bands (approx mol wt 10, 24, 35, and 100 kDa), with the ability to bind human IgE.

In our unpublished results conducted on six patients with the SDS-PAGE, we observed a great variability between patients. However, a 30-kDa protein was the most frequently recognized by specific IgE. It should be noted that a high peak of a 30-kDa protein was observed by HPLC in a cleaning glove (25). On the other hand, we confirmed the IgE heterogenous responses of patients using the basophil degranulation test with different fractions of LHB obtained by gel filtration on Sephadex G 75 (Pharmacia, France) or by ion exchanger chromatography on DEAE (LKB, France). The basophils of each patient were able to degranulate for at least three or more fractions, which were not always the same among patients.

This variability in IgE responses may reflect, at least in part, the variability in allergenic properties and in protein content of the different commercial gloves (25). Taken together, these results suggest that the manufacturing process is an important factor that contributes to the recent increase in immediate allergy to LHB. As suggested by Turjanmaa et al. (25), "it is necessary to develop glove manufacturing processes in which the latex allergen is totally eliminated."

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