

Patch testing with natural rubber latex

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Immediate-type hypersensitivity to natural rubber latex (NRL) may be associated with chronic eczema, and it has recently been suggested that NRL should be used as a patch-test allergen. However, a standardized preparation does not exist, and experience of patch testing with this substance is extremely limited. The aims of our study were to investigate the patch-test response to different preparations of NRL amongst patients with suspected contact dermatitis. 608 patients were patch tested with a latex series which included wet and dry preparations of undiluted high-ammonia (HA) NRL and low-ammonia thiuram-containing NRL. Cutaneous reactions to 1 or more NRL patches were noted in 24 patients. None of these were strong allergic reactions ($> +$), and in 15 patients, the responses were only doubtful ($?+$). Positive patch tests were observed in 9 patients, and were probably due to concurrent thiuram allergy in 6. In the remaining 3 patients, the reactions had subsided by the 2nd reading and may have represented false positives. None of the patients showed consistent allergic reactions to all NRL patches, and most of the doubtful readings had resolved within 4 days, suggesting that they were irritant rather than weak allergic responses. Patch testing to dry HA latex was associated with the least number of reactions. We conclude that allergic patch test reactions to NRL are uncommon, and as reactions are usually weak and difficult to interpret, we suggest that patch testing with NRL should remain experimental until further studies have been undertaken.

Key words: allergic contact dermatitis; patch testing technique; natural rubber latex; ammoniated latex; prick test. © Munksgaard, 1999.

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Natural rubber latex (NRL) is a frequent cause of immediate-type hypersensitivity, with symptoms ranging from contact urticaria to anaphylaxis (1, 2). Several important allergenic proteins have been identified and characterized (3), and at-risk groups have been defined (4). As some latex-allergic individuals present with chronic eczema, it has been suggested that a delayed-type hypersensitivity to latex proteins can also occur. This might represent so-called protein contact dermatitis (5), a diagnosis conventionally confirmed by prick testing rather than patch testing. There have been isolated reports of positive patch tests to latex, with (1, 6–7) and without (8–10) coexistent contact urticaria. More recently, a significantly high frequency of positive patch tests (1.2%) to natural rubber latex was reported amongst a teaching hospital patch-tested population (11). However, experience in patch testing with NRL is very limited, and a standardized patch-test preparation does not exist. The aims of our study were to investigate the prevalence of positive reactions to different formulations of natural latex among a patch-tested population.

Materials and Methods

During an 8-month period, consecutive adult patients seen in the department for suspected contact dermatitis were patch tested to a natural latex series in addition to an extended European standard series, and other allergens as clinically indicated. Our latex series comprised an additive-free aqueous latex suspension preserved solely with ammonia (HA latex), a low-ammonia latex-containing zinc oxide and tetramethylthiuram disulfide (LATZ latex) (kind gift of the Malaysian Rubber Producers' Research Association, London), and tetramethylthiuram disulphide 0.025% pet. Latex formulations were tested undiluted as both wet and dry patches, the latter having been left exposed to the air overnight to dry. The latex was applied to filter paper discs in Finn Chambers® on Scanpor® tape to the upper back, and patches were removed after 2 days. Readings were carried out on days 2 and 4, 2 and 5 or 3 and 5, and scored according to standard criteria, doubtful reactions being recorded as $?+$.

Table 1. Clinical details, patch- and prick-test reactions of patients who reacted to latex series

Sex, age (years) reading		HAd	LAd	HAw	LAW	Tmix	TMTD	SptL	Final diagnosis and body site
F41	R1	—	—	?+	—	—	—	—	suture reaction
	R2	—	—	—	—	—	—	—	chest
M30	R1	—	—	—	+	++	+	—	ACD thiurams
	R2	—	—	—	+	+	+	—	hand
F24	R1	—	?+	?+	?+	—	—	—	endogenous eczema
	R2	—	?+	?+	?+	—	—	—	hand and foot
F53	R1	—	—	—	?+	—	—	—	psoriasis, ICD
	R2	—	—	—	—	—	—	—	hand
M89	R1	—	—	+	+	++	++	NT	ACD thiurams
	R2	—	—	?+	+	++	++	—	hand and arm
F38	R1	—	?+	?+	?+	—	—	+ve	atopic eczema, ACD chromate, Type I latex
	R2	—	—	—	—	—	—	—	widespread and hand
F66	R1	?+	?+	?+	?+	—	—	NT	unclassified eczema
	R2	IR	IR	IR	IR	—	—	—	widespread
F30	R1	?+	—	?+	?+	++	++	NT	atopic eczema, ACD thiurams
	R2	—	—	—	+	+	+	—	hand
F23	R1	?+	?+	—	—	—	—	NT	atopic eczema
	R2	?+	—	—	—	—	—	—	widespread
M26	R1	—	—	?+	—	—	—	NT	endogenous eczema
	R2	—	—	—	—	—	—	—	hand & foot
F19	R1	?+	—	?+	?+	—	—	NT	atopic eczema, ICD
	R2	—	—	—	—	—	—	—	hand
M19	R1	—	?+	—	?+	—	—	NT	atopic eczema, ICD
	R2	—	—	—	—	—	—	—	hand
F35	R1	—	?+	?+	?+	—	—	NT	endogenous, ICD
	R2	—	—	—	—	—	—	—	hand
F35	R1	—	—	—	—	—	—	NT	ACD nickel
	R2	—	?+	?+	—	—	—	—	trunk
F28	R1	—	?+	?+	?+	—	—	+ve	atopic eczema, Type I latex
	R2	—	—	—	—	—	—	—	hand and face
F50	R1	—	—	—	—	—	—	+ve	ACD glutaraldehyde, Type I latex
	R2	—	—	—	—	—	—	—	hand
M64	R1	—	?+	—	?+	—	—	NT	endogenous eczema, ACD lactones
	R2	—	—	—	—	—	—	—	hand & foot
F47	R1	—	—	+	?+	—	—	NT	ACD chromate
	R2	—	—	—	—	—	—	—	hand and foot
M27	R1	—	?+	—	—	—	—	NT	seborrhoeic eczema
	R2	—	—	—	—	—	—	—	face
F39	R1	—	—	—	+	+	?+	NT	ACD thiurams
	R2	—	—	—	—	+	—	—	hand
M69	R1	—	—	+	+	++	+	—	endogenous eczema, ACD thiurams
	R2	?+	?+	?+	?+	++	+	—	widespread and hand
M30	R1	—	+	?+	+	+	++	+ve	atopic eczema, ACD thiurams, Type I latex
	R2	—	+	—	—	+	++	—	widespread and hand
M38	R1	—	—	?+	—	—	—	—	endogenous eczema
	R2	—	—	—	—	—	—	—	hand
F29	R1	+	—	+	—	—	—	NT	atopic eczema
	R2	—	—	—	—	—	—	—	widespread
F51	R1	—	—	+	?+	—	—	NT	endogenous eczema
	R2	—	—	—	—	—	—	—	hand

HAd=dry HA latex; LAd=dry LATZ latex; HAw=wet HA latex; LAW=wet LATZ latex; Tmix=thiuram mix; TMTD=tetramethylthiuram disulphide; SptL=skin prick test to latex; R1=1st reading (day 2 or 3); R2=2nd reading (day 4 or 5); ACD=allergic contact dermatitis; ICD=irritant contact dermatitis; IR=irritant reaction; ?+=doubtful positive reaction; NT=not tested.

Individuals with a history suggestive of immediate-type hypersensitivity to latex were investigated by prick testing on the volar aspect of the forearm to a fresh non-commercial aqueous solution of latex glove eluate. This was obtained by incubating small pieces of a freshly cut thin latex glove in 1–2 ml of sterile water for 30 min. A positive control

(histamine 10 mg/ml) and a negative control (normal saline) were included. The criterion for a positive reaction was a wheal size of 0.3 cm diameter greater than the negative control at 20 min. Patients who had a history of asthma, systemic symptoms or anaphylactic reactions to rubber latex were excluded, and those with widespread urtica-

rial reactions on prick testing were not patch tested, due to the risk of precipitating an anaphylactic reaction by prolonged contact with the latex. Prick-test-positive patients who were patch tested remained in the department under observation for 30 min after patch application.

Children were omitted from the study, unless their history was suggestive of allergic contact dermatitis from rubber, and patients who required testing to a large series of allergens or those in whom there was limited clear space on the upper back were also excluded. Demographic details were recorded of patients' age, sex, atopic eczema status, and primary body site affected.

Results

608 patients (232 male (38%) and 376 female) were patch tested with the latex series. The mean age of these individuals was 41 years (range 3–89), and the median age 46 years. The most frequent primary sites of dermatitis were hands (34%), facial (22%) or generalized (16%), and a current or recent history of atopic eczema was noted in 123 patients (20%).

58 patients were prick tested to latex over the study period. The results were negative in 43 patients and positive in 15, 11 of whom were not patch tested with the latex series. There were no immediate adverse reactions to the latex patches, and all had solidified by the time of their removal.

Patch-test reactions to 1 or more of the latex patches were observed in 24 patients, and these included 3 of the prick-test-positive patients. The 4th prick-test-positive patient did not show any reaction to the patches. These patients' ages ranged from 19–89 years, 8 (32%) had atopic eczema, and hand involvement was noted in 19 (76%). The majority of the reactions to the latex series were reported as doubtful (?+) and no strongly positive reactions (++ or +++) were observed (Table 1). No patient showed allergic reactions to all 4 latex patches. Concurrent allergic patch test reactions, which were considered to be relevant, included thiurams ($n=6$), chromate ($n=2$), glutaraldehyde ($n=1$), and nickel ($n=1$). Patients who were found to be allergic to thiurams, but did not show any reaction to the latex patches, are not reported.

The results of testing with the individual latex formulations were as follows:

Dry HA latex

This elicited the lowest number of reactions. 4 patients showed doubtful (?+) reactions on the 1st reading (R1) which resolved by the 2nd reading (R2) ($n=3$), or evolved to irritant reactions ($n=1$), and 1 patient developed a ?+ reaction at R2.

1 patient had a positive reaction to both dry and wet HA latex at R1 without any reaction to the LATZ patches, but these had cleared by R2, and another showed a ?+ reaction at R2 in conjunction with thiuram allergy.

Dry LATZ latex

11 patients showed ?+ reactions, mostly on R1 only ($n=7$), and only 1 allergic reaction was observed. This was in a patient with atopic eczema, who was allergic to thiurams, and had a positive latex prick test.

Wet HA latex

11 patients showed ?+ reactions on R1, and in most, these had cleared by R2 ($n=9$). 1 patient had a ?+ reaction to both HA wet and LATZ dry on R2 (Fig. 1). Positive reactions were reported in 5 patients on R1, but most of these patients did not react to the dry HA preparation, and all reactions had diminished ($n=2$) or cleared ($n=3$) by R2.

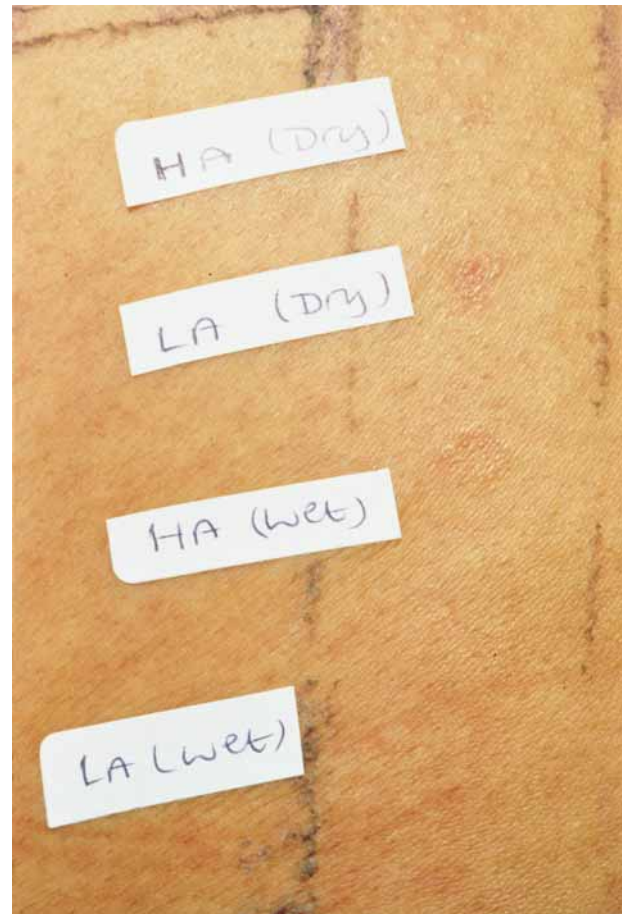


Fig. 1. Doubtful (?+) reactions to dry LA latex and wet HA latex on R2.

Wet LATZ latex

10 patients showed ?+ reactions on R1, and in most, these had cleared by R2 ($n=8$). Allergic reactions were noted on R1 or R2 in 6 patients, all of whom were allergic to thiurams.

Discussion

The risks of developing immediate-type hypersensitivity to latex proteins amongst those regularly exposed to NRL, especially in gloves and medical devices, are significant and firmly established. Delayed hypersensitivity reactions to a wide range of rubber additives are also well recognized, but the importance of natural latex as a Type IV allergen is unclear. In the vast majority of patients with rubber glove contact dermatitis, allergy to an additive can be identified, and few patients show isolated positive patch tests to NRL gloves in the absence of rubber chemical allergy.

We did not observe any strong allergic reactions ($\geq ++$) to the latex patches in our study. Most patients tested failed to react to this series, and in those who did, the majority of reactions were weak or doubtful. These reactions tended to clear by R2, which would be in keeping with mild irritant responses. None of the patients showed allergic reactions to all 4 latex patches, and the only patients with allergic reactions on both readings were thiuram sensitive. It is therefore likely that these reactions were caused by the additives rather than by NRL itself. A few patients showed isolated positive reactions to 1 or 2 latex patches at R1, which were of undetermined relevance, and we suspect that these were false-positive reactions.

NRL, as sold commercially, is a colloidal dispersion of rubber hydrocarbon (polyisoprene) in water, and it is concentrated so that the proportion of rubber is about 60%. By using this preparation in an undiluted form, we should have achieved an adequate concentration of allergens to elicit allergic reactions. Poor penetration of allergens would be an unlikely explanation for the weak nature of the reactions we observed, as contact urticaria can easily and rapidly be elicited by NRL on direct contact with intact skin. Preservatives and anticoagulants such as ammonia are added to fresh latex to prevent its otherwise rapid autocoagulation, degradation and bacterial contamination. Ammoniated latex (HA latex) contains up to 0.7% ammonia by weight. Additional preservatives are added to low-ammonia lattices, such as zinc oxide plus tetramethylthiuram disulfide (LATZ latex). Other chemicals may also be added in the country of origin, and this makes it difficult to ensure that even the high-ammonia preparation is additive

free, unless a specially prepared sample is obtained from the supplier (personal communication, Malaysian Rubber Research Association).

We observed more doubtful reactions to the wet preparations of HA latex and LATZ latex than to their dry counterparts, and suspect that the ammonia and alkalinity of liquid NRL evoke irritant reactions under occlusive patch test conditions, even though all patches subsequently solidify. Natural latex contains a complex mixture of organic substances, including tannins, alkaloids, acids, carotenoids enzymes and proteins, and irritant and caustic reactions to the latex from other species of plant have been described (12).

Our results do not agree with the findings of Wilkinson & Beck (11), who noted allergic patch test reactions in 10 (1.2%) out of 822 patients patch tested to HA latex. 5 of these patients had additional positive prick tests to latex, whilst the remainder were prick-test-negative. On further testing to a dilution series, 1 patient was reported to show strong ($++$) allergic reactions even to a 1:30 dilution of HA latex. In a subsequent study of 117 patients with hand dermatitis by Wilkinson & Burd (13), 7 patients (6%) had positive patch tests to HA latex, and 5 of these had no other positive reaction to a series of rubber additives. Neither of these studies report the number of doubtful or irritant reactions.

It is possible that our results reflect differences in the case mix of these study populations, the latex formulations used for patch testing or the methodology, i.e., interpretation of patch test reactions. Our population was subject to selection bias by the exclusion of many individuals with immediate-type latex allergy, as well as some members of the department having a poor rate of recruitment. (We thought that patch testing to latex conferred no added benefit for a patient with a positive prick test, but did carry a potential risk of anaphylaxis.) It is of interest that 2 of our 4 prick-test-positive patients who were patch tested showed weak reactions to the latex patches on R1 in the absence of thiuram sensitivity. These could have represented a mild protein contact dermatitis, but the reactions were transient and had cleared by R2. Patients in our study were prick tested to latex only if they had a symptoms suggestive of contact urticaria, and this investigation was not carried out in most patients who reacted to the latex patches. Therefore the prick test status of these patients remains unknown, although it would be unlikely for many cases of immediate-type latex allergy to have been missed. It is possible that some of our doubtful reactions represented weak allergic reactions, and the sub-population showing these responses did

have a higher frequency of hand dermatitis (76%) than the overall population (34%). However, interpretation of these reactions was difficult in the absence of a more concentrated patch-test formulation.

We conclude that allergic contact reactions to NRL are not sufficiently frequent to justify its routine use in patch testing at present. Patch-test reactions to latex are difficult to interpret, and further studies are needed to explain the difference in frequency of positive patch tests amongst different populations.

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