

Sensitivity to some rubber additives

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The frequency of positive patch tests to 13 rubber accelerators in Poland was recorded. Of particular interest was the relatively large group of patients positive to several, mostly chemically unrelated, accelerators. The mechanism of this multiple sensitivity is discussed. Positive tests to N-isopropyl-N-phenyl-p-phenylenediamine were observed in more than half of the patients reacting to several aromatic amines. Anamnesis indicated that in the case of cross-reactions to many aromatic amines, none of the patients positive to N-isopropyl-N-phenyl-p-phenylenediamine had complained of a reaction to rubber products.

Key words: accelerators – antioxidant – aromatic amines – rubber additives.

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Rubber additives are among the most frequent causes of contact dermatitis. The purpose of our work was to study the relationship between positive patch tests to thirteen rubber accelerators and one antioxidant.

Material and Methods

A total of 2,075 consecutive patients were tested with two to six accelerators: mercaptobenzothiazole, tetramethylthiuram disulphide, dibenzothiazole disulphide, diphenyl thiourea, zinc ethylphenyl-dithiocarbamate and N-cyclohexyl-2-benzothiazyl sulphenamide. Of these 2,075 patients, 1,570 were tested with N-isopropyl-N-phenyl-p-phenylenediamine and 200 patients with seven additional accelerators: o-tolyldiguandine, diethylthiourea, ethylene thiourea, dipentamethylene-thiuram tetrasulphide, zinc diethyl-dithiocarbamate, tetramethylthiuram monosulphide and N-oxydiethylene-2-benzothiazole. Tests with N-isopropyl-N-phenyl-p-phenylenediamine were performed on 31 patients positive to p-phenylenediamine,

who had previously been tested with 25 other aromatic amines: o-toluidine, m-toluidine, p-toluidine, o-nitroaniline, m-nitroaniline, p-nitroaniline, o-aminophenol, m-aminophenol, p-aminophenol, o-toluenediamine, m-toluenediamine, p-toluenediamine sulphate, o-phenylenediamine, p-aminobenzoic acid diethylaminoethyl ester (novocaine), N-phenyl-2-naphthylamine, p-nitro-o-aminophenyl, p-nitro-o-phenylenediamine, o-nitro-p-phenylenediamine, o-chloro-p-phenylenediamine sulphate, N,N-diethyl-p-phenylenediamine sulphate and N-ethyl-N-hydroxyethyl-p-phenylenediamine sulphate.

All the allergens were diluted in yellow soft paraffin, with the exception of novocaine which was dissolved in water. Apart from 1 % p-phenylenediamine, all the remaining contactants were applied in 2 % concentrations.

Results

The percentage of patients with positive reactions to the additives is shown in Table 1. It is clear that patch tests in Poland are

Table 1. Patch tests to individual rubber additives.

Allergen	Number tested	Positive reactions %		
		All	Men	Women
Tetramethylthiuram disulphide	2074	3.27	2.76	3.77
Mercaptobenzothiazole	2075	3.25	2.46	4.05
Tetramethylthiuram monosulphide	200	2.50	—	—
N-oxydiethylene-2-benzothiazole	200	2.50	—	—
N-cyclohexyl-2-benzothiazyl sulphenamide	1538	2.27	1.76	2.76
Zinc diethyl dithiocarbamate	200	1.50	—	—
Dibenzothiazole disulphide	1698	1.46	1.11	1.80
o-tolyldiguanidine	200	0.50	—	—
Diethyl thiourea	200	0.50	—	—
Ethylene thiourea	200	0.50	—	—
Diphenyl thiourea	1191	0.25	0.30	0.16
Zinc ethylphenyl dithiocarbamate	1203	0.08	0	0.17
Dipentamethylenethiuram tetrasulphide	200	0	—	—
N-isopropyl-N-phenyl-p-phenylenediamine	1540	8.7	7.40	10.00

frequently positive with mercaptobenzothiazole and tetramethylthiuram disulphide and with N-cyclohexyl-2-benzothiazyl sulphenamide, tetramethylthiuram monosulphide and dibenzothiazole disulphide. The latter two compounds, however, were tested on 200 patients only. On the other hand, not one patient reacted to dipentamethylenethiuram tetrasulphide. Relatively numerous positive patch tests were obtained with diphenylguanidine (1.0 %). However, these results were not taken into account because it is believed that they were irritant reactions, at least in some of the patients. All accelerators tested on more than 1,150 patients gave positive reactions more frequently in women than in men. The frequency of sensitivity to all rubber additives, when compared in four age groups (below 20 years, 20–40 years, 40–60 years and over 60 years) increased with age.

In the group of 200 patients tested with thirteen accelerators, 16 subjects were posi-

tive to at least one accelerator. Most of them were sensitive to several (Table 2). Not one of them, however, was positive to N-isopropyl-N-phenyl-p-phenylenediamine.

Among 31 patients positive to p-phenylenediamine, 16 were also positive to N-isopropyl-N-phenyl-p-phenylenediamine. Positive tests with this antioxidant were somewhat more frequent among subjects who reacted to several amines (Table 3). Two were positive to mercaptobenzothia-

Table 2. Multiple sensitivity to 13 accelerators in 200 patients

Positive to	Number of positive patients
One accelerator	5
Two accelerators	3
Three accelerators	3
Four accelerators	2
Five accelerators	1
Six accelerators	2

Table 3. Positive reactions to N-isopropyl-N-phenyl-p-phenylenediamine (IPPD) in cross-sensitivity to aromatic amines

IPPD	Number	Patients positive to																
		2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
		aromatic amines																
Positive	16	2		1		2	1		2	1	1			1	1	2	2	
Negative	15	1	3	4		1		2		1		1		1				1

zole, and one was positive to tetramethylthiuram disulphide. With the exception of these three patients, none of the 31 had noticed sensitivity to rubber products.

Discussion

Some of the patients tested with 13 accelerators were positive to 3, 4, 5 and even 6 of these compounds. This may have been partly a cross-reaction between substances with a similar chemical structure. The main cause of these multiple reactions, however, was concomitant sensitization. This was particularly seen in the patient J.C. who was positive to mercaptobenzothiazole, tetramethylthiuram disulphide, tetramethylthiuram monosulphide, N-cyclohexyl-2-benzothiazyl sulphenamide, zinc diethyl dithiocarbamate and diphenyl thiourea. Cross-reactions in this case were probably only between the two thiuram sulphides. It would seem that sensitization to one accelerator produces an inflammation which plays the role of a *sui generis* portal of sensitization and facilitates penetration through the skin of other chemically unrelated accelerators. In patients tested with 4 accelerators, positive reactions were frequently found to 2 or 3 of them; reactions to zinc diethyl dithiocarbamate were positive only in patients who reacted to the thiuram accelerators as well (Wilson 1969).

Multiple sensitivity to rubber additives probably concerns mainly accelerators, since none of the 16 patients (Table 2) posi-

tive to one or many accelerators reacted to N-isopropyl-N-phenyl-p-phenylenediamine. On the other hand, reactions to this substance are frequent in patients with cross-sensitization to many aromatic amines (Table 3). The diagnostic value of such tests is doubtful, as none of our patients positive to many aromatic amines including N-isopropyl-N-phenyl-p-phenylenediamine but negative to accelerators, had noticed any exacerbation from rubber contacts, although aromatic amines are among the most commonly used antioxidants in Poland. But the lack of such observations by persons with frequent recurrences of dermatitis who have not been warned that they may be sensitive to rubber does not rule out their sensitization to para group antioxidants. Patients have been repeatedly described with relevant sensitivity to N-isopropyl-N-phenyl-p-phenylenediamine (Volum & Marten 1968, Calnan 1971, Cronin 1973, Lintum & Nater 1973). The reactions to accelerators in our patients, however, were always either relevant or showed sensitivity with past relevance, according to the terminology introduced by the ICDRG (Wilkinson et al. 1970); this is in contrast with our findings in the case of N-isopropyl-N-phenyl-p-phenylenediamine.

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