

Accelerator-free gloves as alternatives in cases of glove allergy in healthcare workers

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Summary

Background. Accelerators in rubber gloves constitute an important group of contact allergens, particularly in healthcare workers.

Objectives. To assess the efficacy of accelerator-free medical gloves in the secondary prevention of allergic contact dermatitis caused by rubber accelerators in healthcare workers.

Methods. Nine healthcare workers with hand eczema were advised to use accelerator-free rubber gloves after a diagnosis of allergic contact dermatitis caused by rubber accelerators.

Results. Switching from conventional medical single-use gloves containing accelerators to accelerator-free medical gloves led to improvement in all cases, and more than two-thirds of the patients were completely free of symptoms.

Conclusion. The use of accelerator-free medical gloves can be an effective alternative in healthcare workers who are allergic to rubber accelerators.

Key words: accelerator-free gloves; allergic contact dermatitis; glove allergy; healthcare workers; prevention; rubber accelerators; thiurams.

Rubber accelerators constitute an important group of contact allergens, particularly in healthcare workers. Gloves are the main sources of exposure to these chemicals. Accelerators speed up the process of rubber vulcanization; very fast accelerators include thiurams, dithiocarbamates, and thiophosphates, moderately fast accelerators include 1,3-diphenylguanide, mercaptobenzothiazoles, and sulfonamides, and

slow accelerators include thiourea derivatives and amines (1).

The allergens most frequently yielding positive patch test results are mainly thiurams, dithiocarbamates, 1,3-diphenylguanidine, mercaptobenzothiazole and/or its derivatives, and, more rarely, thioureas. In recent epidemiological studies, healthcare workers have been found to show a high prevalence of positive patch test reactions to rubber accelerators. For instance, delayed-type hypersensitivity to thiuram mix is significantly associated with healthcare work [OR 1.60 (95%CI: 1.10–2.30); (2)], and affects 5–12% of healthcare workers (3–5). Although the ingredients lists for medical gloves suggest that most international rubber glove companies have replaced thiurams with dithiocarbamates (6, 7), thiurams still remain the rubber allergens that most frequently yield positive patch test results (8, 9). This is probably because

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thiuram disulfides and dithiocarbamates constitute a redox pair; that is, during oxidation of a dithiocarbamate, the corresponding thiuram disulfide is formed, and during reduction of a thiuram disulfide, a dithiocarbamate is formed (6). The higher frequency of positive patch test reactions to thiurams than to dithiocarbamates is consistent with studies showing that thiurams are better markers for sensitization to the dithiocarbamate/thiuram redox pair (6, 9).

To address this issue, new glove manufacturing processes have been developed to produce accelerator-free medical gloves. However, there are no data regarding the efficacy of these new gloves in the secondary prevention of allergic contact dermatitis (ACD) caused by rubber accelerators in sensitized patients. The impact of replacing conventional gloves with accelerator-free gloves was evaluated in a small series of healthcare workers with ACD caused by rubber accelerators diagnosed in our department.

Methods

Our study is based on a small series of 9 patients with hand eczema, all of them healthcare workers, who were advised to use accelerator-free rubber gloves after a diagnosis of ACD caused by rubber accelerators confirmed by positive and relevant patch test reactions from 2015 to 2016 (Table 1). These patients were patch tested with the European baseline series, a rubber series, a cosmetics series, additional allergens from other series, glutaraldehyde, limonene hydroperoxide, and linalool hydroperoxide (Chemotechnique Diagnostics, Vellinge, Sweden). Seven patients were tested with pieces of their medical gloves (internal and external faces) 'as is'. Semi-open tests were performed with the soaps and antiseptics used. Standardized patch testing was performed according to international recommendations of the ESCD (10). Patch testing was performed with IQ Ultra chambers® (Chemotechnique) fixed on the back with Mefix® (Mölnlycke, Göteborg, Sweden), and read on day (D) 2, D3 or D4, and D10. Reactions with grades of either +, ++ or +++ were considered to be positive. Irritant, doubtful and negative test reactions were interpreted as negative. All 9 patients were advised to change gloves and use only accelerator-free gloves. The choice of brand was left to the respective patient's hospital pharmacy. During this study, gloves used by patients were obtained from two glove producers, namely, Ansell (Gammex Non-Latex Sensitive, Dermaprene, MICRO-TOUCH® accelerator-free) and Sempermed (Syntegra UV). At that time, thermoplastic elastomer Finessis® surgical gloves were not available on the French market.

Results

The severity of the disease was assessed with the Osnabrueck Hand Eczema Severity Index (OHSI) (11, 12). The efficacy of advising the patient to substitute accelerator-free gloves (Table 2) was evaluated by comparing the OHSI before accelerator-free gloves had been recommended with the OHSI at least 2 months after regular use of accelerator-free gloves and avoidance of the offending ones. At the second assessment, all of the patients had a lower OHSI, and more than two-thirds of them were completely healed (OHSI = 0) (Figs. 1 and 2). The results are summarized in Table 2.

Discussion

This small series of nine healthcare workers with occupational ACD caused by rubber accelerators showed that switching from conventional medical single-use gloves containing accelerators to accelerator-free medical gloves led to improvement in all cases, with more than two-thirds of the patients completely recovering. The two patients with less favourable course of disease were co-diagnosed with atopic dermatitis or pompholyx.

The first-line treatment for ACD is allergen avoidance. In cases of contact allergy to thiurams, prevention is based on avoidance of contact with the dithiocarbamate/thiuram redox pair by use of accelerator-free medical gloves available on the European market. The possibility of making accelerator-free gloves depends on the type of crosslinks created between the polymer molecules. Conventional rubbers should be 'chemically crosslinked' to provide adequate mechanical and physical properties. The crosslinking is traditionally provided by creating covalent bridges with molecular sulfur between rubber chains in a process called vulcanization. As vulcanization with sulfur alone entails reactions that are too long and that would require very high temperatures, chemical additives termed accelerators are added. It is a common practice to use a mix composed of different accelerators that are selected from different families to optimize the vulcanization speed and performance. However, whereas sulfur is integrated into the polymer network by covalent bonding, accelerators are not. Also, they can 'bloom' at the surface of the glove during storage, owing to their limited compatibility with the rubber. To manufacture rubber accelerator-free gloves, particularly medical single-use gloves, different base materials can be used, such as polychloroprene, nitrile, polyisoprene, and styrenic block copolymers (SBCs).

Although the traditional vulcanization of polychloroprene rubber is carried out with sulfur crosslinks and accelerators, it is also possible to use zinc oxide (ZnO)

Table 1. Patch test results and glove patch test results (gloves used at work and suspected to be responsible for hand eczema)

Patients	Age (years)		Diagnosis	Occupation	Positive patch test reactions to rubber allergens	Glove patch test results	Positive patch test reactions to other allergens	Prick test results with latex
	Sex							
1	56 M		ACD	Surgeon	Thiuram mix ++ TMTM + IPPD + CPPD +	Negative	Colophonium	Negative
2	62 M		ACD	Surgeon	1,3-Diphenylguanidine ++	NT	<i>Myroxylon pereirae</i> (balsam of Peru), fragrance mix I	NT
3	49 F		ACD Pompholyx	Assistant nurse	Thiuram mix +++ TMTM +++ TETD +++ DPTD ++	Negative	Formaldehyde, quaternium-15, benzylhemiformal, <i>p</i> -phenylenediamine, chromium	Negative
4	61 M		ACD Atopic dermatitis	Surgeon	1,3-Diphenylguanidine +++	Negative	Chromium, cobalt, fragrance mix I, fragrance mix II, cocamide DEA	Negative
5	34 F		ACD Atopic dermatitis	Nurse	Thiuram mix +++ TMTM +++	NT	Methylisothiazolinone, methylisothiazolinone/methylchloroisothiazolinone, linalool, limonene	Negative
6	50 F		ACD	Operating room nurse	1,3-Diphenylguanidine +++	++		NT
7			ACD Atopic dermatitis	Podiatrist	Thiuram mix +++ TMTD + TMTM +++ TETD +++ 1,3-Diphenylguanidine ++	++	Methylisothiazolinone, methylchloroisothiazolinone, glutaronitrile	Negative
8	62 F		ACD	Nurse	Thiuram mix ++ TETD +++ 1,3-Diphenylguanidine +++	Negative	Fragrance mix I, methylchloroisothiazolinone, glutaronitrile, glutaraldehyde	Negative
9	60 M		ACD	Surgeon	Thiuram mix +++ ZDEC ++ ZDMC ++ MBT +	++	Fragrance mix I, fragrance mix II, linalool, limonene	NT

ACD, allergic contact dermatitis; CPPD, *N*-cyclohexyl-*N*-phenyl-*p*-phenylenediamine; DPTD, dipentamethylenethiuram disulfide; IPPD, *N*-isopropyl-*N*-phenyl-*p*-phenylenediamine; MBT, 2-mercaptobenzothiazole; NT, non tested; TETD, tetraethylthiuram disulfide; TMTD, tetramethylthiuram disulfide; TMTM, tetramethylthiuram monosulfide; ZDEC, zinc diethyldithiocarbamate; ZDMC, zinc dimethyldithiocarbamate.

as a vulcanization agent. The crosslink is then made via an ether bond (–O–), and a sulfur–accelerator complex is not needed. Several manufacturers have developed accelerator-free polychloroprene gloves, including Ansell (Gammex® Non-Latex Sensitive; Ansell PF Dermaprene®) and Mölnlycke Health Care (Biogel® NeoDerm).

In the case of nitrile, the traditional vulcanization process is carried out with sulfur crosslinks. However, it is also possible to use an improved material called carboxylated nitrile rubber (XNBR). XNBR is polymerized with three monomers: butadiene, acrylonitrile,

and methacrylic acid. This nitrile polymer has carboxyl groups (R–COO) attached to the butadiene units of the polymer. ZnO is again used as the vulcanization agent. The crosslink is then made via an ionic bond involving a zinc cation (Zn²⁺) provided by ZnO. This new process avoids the use of a sulfur–accelerator complex. Such a crosslinking mechanism is only possible for XNBR, and not for ordinary nitrile rubber and synthetic polyisoprene rubber. Several manufacturers have developed accelerator-free nitrile gloves, including Ansell (MICRO-TOUCH® Nitrile accelerator-free) and Sempermed (SemperSure® accelerator-free gloves).

Table 2. Evolution of the Osnabrück Hand Eczema Severity Index (OHSI) before and at least 2 months after the use of accelerator-free gloves

Patients	Accelerator-free gloves	OHSI before and at least 2 months after the use of accelerator-free gloves	
		Before intervention	After at least 2 months of prevention
1	Sempermed® Syntegra UV	14	0
2	Ansell Gammex® Non-Latex Sensitive	18	0
3	Ansell Dermaprene®	18	8
4	Ansell Gammex® Non-Latex Sensitive and Sempermed® Syntegra UV	18	4
5	Ansell Gammex® Non-Latex Sensitive	18	0
6	Ansell Gammex® Non-Latex Sensitive	18	0
7	Ansell MICRO-TOUCH® Nitrile accelerator-free	12	0
8	Ansell Gammex® Non-Latex Sensitive	13	0
9	Sempermed® Syntegra UV	18	0

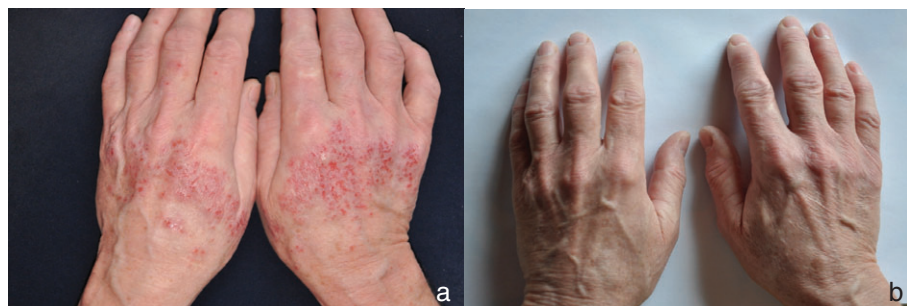
**Fig. 1.** Hand eczema of patient 5 before (a) and 6 months after the use of accelerator-free gloves (b).

A new rubber manufacturing process involving photocrosslinking has been developed and patented by Semperit (Vienna, Austria). This complicated production process is quite different from vulcanization, because it does not require elementary sulfur and rubber accelerators. Gloves based on this technology are marketed under the brand name Sempermed® Syntegra UV surgical gloves. The raw materials for this glove include synthetic isoprene, a photoinitiator, a crosslinker, and an antioxidant. They are mixed and irradiated with ultraviolet (UV) light. During the irradiation, the polymer chains (polyisoprene) are crosslinked. This reaction is very fast. Therefore, no accelerators are needed. Gloves are dipped from this

irradiated compound in the usual dipping process. The final curing of the gloves is also performed with UV irradiation. In the patents describing the process for making a crosslinked elastomer, different types of photoinitiator are used, such as 2-hydroxy-2-methyl-1-phenylpropanone. As the crosslinking aid is preferably at least one thiol, and/or a selenol, different crosslinkers may be used, such as trimethylolpropane tris(3-mercaptopropionate).

Other specific synthetic rubbers, namely, SBCs, can organize themselves in the form of elastic films with adequate physical and mechanical properties without the use of any 'chemical crosslinking', and therefore without the use of any accelerators. Usually, SBCs consist of

Fig. 2. Hand eczema of patient 8 before (a) and 6 months after the use of accelerator-free gloves (b).



three blocks: generally, two hard polystyrene end blocks, and one soft, elastomeric (polybutadiene, polyisoprene, hydrogenated or not hydrogenated) midblock. The hard and soft blocks are immiscible, so that, on a microscopic scale, the polystyrene blocks form separate domains in the rubber matrix. As both ends of each rubbery block are terminated by polystyrene segments, these rigid domains act as multifunctional junction points to give a 'physically' crosslinked elastomer network similar, in many respects, of that of a conventional vulcanized rubber ('chemical crosslinking'). Flexylon™ is a specific composition based on SBCs, and is used as a core component for Finessis® surgical gloves developed and patented by Advanta Health. At the time of the study, accelerator-free Finessis® surgical gloves were not yet available in France.

Recently, EN 455-3 was updated, and the following passage was added to subclause 4.2 'chemicals': 'Manufacturers may only declare the absence of a substance if the substance is not used in any part of the manufacturing process'. This implies that accelerator-free gloves may

only be labelled as such if accelerators are not used in any part of the manufacturing process.

Conclusion

In secondary prevention, accelerator-free medical gloves seem to constitute an effective alternative for healthcare workers who are allergic to rubber accelerators. However, these results should be confirmed by a larger intervention study. Furthermore, efficacy in primary prevention should be evaluated by monitoring the frequency of sensitization to rubber accelerators after the introduction of allergen-free gloves on a large scale for healthcare workers.

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