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Successful inhibition of allergic contact dermatitis caused by methylchloroisothiazolinone/methylisothiazolinone with topical glutathione

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The preservative methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) is a well-known sensitizer, and many cases of allergic contact dermatitis have been published over the past 30 years. MI alone has been used as a preservative in occupational and household products, and in cosmetics for <10 years. In the last few years, an epidemic of contact allergy to, and allergic contact dermatitis caused by, MI has been seen in Europe and the United States (1). Numerous articles have been published on facial dermatitis in women caused by cosmetics and skin care products, and hand eczema caused by occupational products such as water-based paints, coolants, and fillers, and cosmetic products such as wet wipes for intimate hygiene or baby-care (2–5).

Case Report

A 56-year-old non-atopic male worked for 18 years as a process operator in a plant where water-based chemicals such as flocculants, defoamers and tank detergents for the paper pulp industry were manufactured. He had previously worked with defoamer chemicals containing MCI/MI, and for 1 year prior to presentation he had worked in the manufacture of a glue, to which a preservative, Acticide® LA 0614 [Thor Specialities (UK) Limited, Wincham, Northwich Cheshire, UK] was added. Following this, the glue mix was heated to 40°C. Production took place in a closed system, with chemicals being mixed in a tank. Subsequently, the glue was passed through a

tube with a valve, which was handled by the patient, who suspected inhalation 'of something in the glue'.

Ten years prior to presentation, the patient had spilled some liquid at work on his right thigh, thinking it was water, but in the evening erythema developed, and on the following morning bullous lesions, which took 1 month to resolve. No investigation including a patch test with MCI/MI was performed, but in the referral note from the company physician there was a suspicion of a chemical burn caused by MCI/MI at the time (6). The current problem and reason for consultation was erythema and pruritus on the face, eyelids, and neck, with papules on the neck, each time that the patient had been exposed to steam containing MCI/MI (Fig. 1) in the last 2 years. The erythema and papules took a week to heal after cessation of exposure. Such exposure would only occur when there was a mishap in the production and the glue had to be heated up to 80°C, exposing the patient to steam. At weekends, when the patient was off work, the facial erythema was much less evident, and during holidays the patient was completely free of symptoms.

At presentation, the patient had no skin lesions and he had not worked for 3 days. He was patch tested with the Swedish baseline series (Chemotechnique Diagnostics, Vellinge, Sweden), our paint series, and two samples of preservatives brought from the workplace by him: Acticide® LA 0614 (containing <1% MCI/MI) and Kathon™ WT (containing 13.9% MCI/MI) (formerly Rohm and Haas, now Dow Chemical Company, Midland, MI, USA). Patch testing was performed with Finn Chambers® (diameter 8 mm) (Epitest Oy, Tuusula, Finland) covered with Scanpor® tape (Norgesplaster A/S, Vennesla, Norway). Readings were performed on day (D)3 and D7, according to ICDRG criteria (Table 1; Figs. 2

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Fig. 1. The patient suffered from erythema and pruritus on his face, eyelids and neck, with papules on the neck, each time that he was exposed to steam containing MCI/MI.

Table 1. Test results in the patient: D3 and D7 readings

Test substance	Concentration/vehicle	D3	D7
MCI/MI	200 ppm aq.	+++*	NR
MCI/MI	100 ppm aq.	+++	NR
MCI/MI	50 ppm aq.	+++	NR
MCI/MI	25 ppm aq.	—	NR
MDBGN	1.0% pet.	++	+
MDBGN	0.5% pet.	++	+
Acticide® LA 0614	1.0% aq.	+++*	NR
Kathon® WT	0.1% aq.	+++*	NR
Bronidox® L	2.5% pet.	+++	+
MI	1000 ppm aq.	+	NR
MI	500 ppm aq.	+	NR
MI	250 ppm aq.	—	NR
MCI	75 ppm aq.	+++	NR
MCI	37.5 ppm aq.	+++	NR
MCI	18.8 ppm aq.	—	—
OIT	0.22% ethanol	—	—

Bronidox® L, 5-bromo-5-nitro-1,3-dioxane; MCI, methylchloroisothiazolinone; MDBGN, methyldibromo glutaronitrile; MI, methylisothiazolinone; NR, not read; OIT, 2-n-octyl-4-isothiazolin-3-one.

*Bullae, treated with potent corticosteroids after the first patch test reading.

and 3). To further investigate the reactivity to MCI/MI and possible cross-reactivity with other isothiazolinones, the patient was patch tested with serial dilutions of such substances (Table 1), as were all of our MCI/MI-allergic patients at the time (7).

Intervention

Owing to previous exposure to high concentrations of MCI/MI when he had the chemical burn, the patient was primarily sensitized to the MCI moiety of MCI/MI, as



Fig. 2. Bullous patch test reaction to methylchloroisothiazolinone/methylisothiazolinone 200 ppm aq.



Fig. 3. Bullous patch test reactions to Acticide® LA 0614 1.0% aq. and Kathon® WT 0.1% aq.

shown by his positive test reactions to lower concentrations of MCI than of MI (7). As the patient had to expose himself occasionally to the steam containing MCI/MI because of mishaps in production, we tried to inhibit the advent of allergic contact dermatitis caused by MCI/MI by offering him a cream containing the reducing agent glutathione (GSH) 2.0% (ICN Biomedicals Inc., Aurora, OH, USA) (8). Deactivation of MCI is considered to be achieved via the ring opening initiated by simple hydrolytic cleavage of the S–N bond in the presence of GSH. We mixed 2.0% GSH in Essex® cream (Merck Sharp & Dohme Sweden AB, Stockholm, Sweden) in our laboratory. Each time the patient knew he would risk such exposure, he rubbed the emollient onto his face and neck, thereby inhibiting allergic contact dermatitis caused by MCI/MI. The duration of exposure to MCI/MI-containing steam could be up to 3 hr at each exposure. Earlier investigations had shown that the GSH concentration in the emollient was of crucial

importance for the inactivation of MCI/MI, and that emollients containing 2% GSH were capable of inactivating up to 2400 ppm MCI/MI (8). If such an emollient is placed

in a suitable tube in which there is no free air between the GSH-containing emollient and the lid, malodorous mercapto compounds will not be generated (8).

References

- 1 Urwin R, Wilkinson M. Methylchloroisothiazolinone and methylisothiazolinone contact allergy: a new 'epidemic'. *Contact Dermatitis* 2013; **68**: 253–255.
- 2 García-Gavín J, Vansina S, Kerre S, Naert A, Goossens A. Methylisothiazolinone, an emerging allergen in cosmetics? *Contact Dermatitis* 2010; **63**: 96–101.
- 3 Murad A, Marren P. Prevalence of methylchloroisothiazolinone and methylisothiazolinone contact allergy in facial dermatitis: a single centre Irish study. *J Eur Acad Dermatol Venereol* 2015; doi:10.1111/jdv.12956 (e-pub ahead of print).
- 4 Schwensen J F, Lundov M D, Bossi R et al. Methylisothiazolinone and benzisothiazolinone are widely used in paint: a multicentre study of paints from five European countries. *Contact Dermatitis* 2015; **72**: 127–138.
- 5 Schwensen J F, Menné T, Andersen K E, Sommerlund M, Johansen J D. Occupations at risk of developing contact allergy to isothiazolinones in Danish contact dermatitis patients: results from a Danish multicentre study (2009–2012). *Contact Dermatitis* 2014; **71**: 295–302.
- 6 Gruvberger B, Bruze M. Can chemical burns and allergic contact dermatitis from higher concentrations of methylchloroisothiazolinone/methylisothiazolinone be prevented? *Am J Contact Dermat* 1998; **9**: 11–14.
- 7 Isaksson M, Gruvberger B, Bruze M. Patch testing with serial dilutions of various isothiazolinones in patients hypersensitive to methylchloroisothiazolinone/methylisothiazolinone. *Contact Dermatitis* 2014; **70**: 270–275.
- 8 Gruvberger B, Bruze M. Can glutathione-containing emollients inactivate methylchloroisothiazolinone/methylisothiazolinone? *Contact Dermatitis* 1998; **38**: 261–265.