

Airborne contact dermatitis from methylchloroisothiazolinone in wall paint. Abolition of symptoms by chemical allergen inactivation

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Preservatives such as isothiazolinones in paints have been reported to cause airborne contact dermatitis. The patients whom we report experienced acute dermatitis on air-exposed skin and respiratory symptoms after staying in recently painted rooms. Kathon[®] (methylchloroisothiazolinone/methylisothiazolinone) added as preservative to the wall paint was identified as causative agent. In one individual symptoms rapidly disappeared after treatment of the painted walls with inorganic sulfur salt, which leads to inactivation of the allergenic properties of methylchloroisothiazolinone/methylisothiazolinone. We describe the patients, the clinical course and review the literature pertinent to such cases. In addition we report on the chemical analyses of the decorating paints used, and on experiments on emission and air concentration of methylchloroisothiazolinone/methylisothiazolinone from a painted surface before and after inactivation by sodium bisulfite.

Key words: airborne contact dermatitis; mucosal symptoms; methylisothiazolinone; methylchloroisothiazolinone; Kathon[®]; chemical allergen inactivation; prevention. © Munksgaard, 2000.

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In the last decade the paint industry has developed new types of paints. Mainly for ecological reasons the use of solvent-based paint has noticeably decreased, the majority of paints now being water-soluble. Water-based paints require the addition of biocides to prevent microbial contamination which may cause physical and chemical degradation of the product. At present the mixture of methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) is the most commonly used preservative in water-based paints (1, 2).

Exposure to isothiazolinones may provoke irritation of skin and mucous membranes. Moreover isothiazolinones have a high sensitizing potency and are a frequent cause of contact allergy. In the literature there have been several reports of airborne dermatitis due to isothiazolinones from paints.

We report 5 female patients with airborne contact dermatitis due to MCI/MI from wall paints, confirmed by positive patch tests to MCI/MI and in some to the paints used. In addition, the experimental demonstration of emission of MCI from dried wall paint and the abolition of MCI emission by chemical inactivation of MCI by application of sodium bisulfite are presented.

Patients and Methods

Case no. 1

A 46-year-old woman presented with a 7-week history of dermatitis with pruritic, scaling erythema of the face, neck, forearms and lower legs. In addition, she later suffered from cough with expectoration, mild dyspnoea, nasal and conjunctival irritation. Her GP diagnosed atopic dermatitis and infectious asthma. Symptomatic therapy with topical and systemic corticosteroids and antibiotics resulted in temporary relief, but all symptoms relapsed upon tapering the corticosteroids.

On clinical examination, eczematous macules on the face, neck and distal extremities were present. Inspection of nose and pharynx, pulmonary auscultation and a lung function test, including methacholine provocation, were normal. She took no other medications and worked as a housewife. She had no history of atopy or contact allergy to cosmetics or jewellery. 1 day before the onset of symptoms she had returned to her completely renovated apartment, renovation included painting the ceiling and walls and varnishing the wooden floors. Upon hospitalization, symptoms resolved spontaneously within a few days; when spending one

night at home, they relapsed. According to the declaration obtained from the manufacturers, the wall paint, the ceiling paint and the parquet varnish all contained MI and MCI.

Case no. 2

A 47-year-old woman presented with a 4-week-history of a pruritic dermatitis which had started on her forearms and later spread to her chest and thighs. 4 days before the onset her husband, a former painter, had painted the walls and ceilings of their apartment. She had no history of atopy or contact allergy and took no medication. She had a part time job as a medical secretary outside her home.

Case no. 3

After moving into a newly painted apartment, a 25-year-old woman developed an eczematous, disseminated exanthema on the face and trunk, conjunctival irritation and cough. The walls had been painted with a paint containing isothiazolinones. She had negative prick tests to common respiratory allergens, and there was no history of contact allergy.

Case no. 4

After her husband painted the walls of their apartment with a biologic paint without solvents, a 52-year-old woman developed 2 days later a disseminated airborne contact dermatitis involving the face, neck, arms and hands. 3 years before she had had contact dermatitis from a cosmetic cream containing Kathon® CG.

Case no. 5

A 46-year-old woman suffered a few days after her apartment was painted by her husband from a contact dermatitis of the face and the neck. She had no history of contact allergy.

Analyses of MCI/MI

Determinations of MCI/MI were performed as previously described (2). Samples (5 g fresh weight each) of paints and varnish were mixed with 1% formic acid and extracted in an ultrasonic bath. MCI/MI in formaldehyde is stable for at least 1 week at 5°C. After centrifugation the upper phase was filtered and analyzed by HPLC. For the measurement of the emission of MCI/MI samples (20 g fresh weight) were painted on glass plates (400 cm²) and stored in an exsiccator. For 4 weeks air

was continuously pumped through at a rate of ~300 ml/min and the waste air was lead through 2 serially connected impingers with 15 ml formic acid (1% v/v) for the absorption of MCI/MI. Starting after ≥2 h 100 µl aliquots were taken from the impingers for analyses by HPLC. Calibration for HPLC was in a linear array for MI (2.8 to 56 ng) and for MCI (8.5 to 170 ng), the determination threshold being 0.6 mg/kg for MI and 1.7 mg/kg for MCI. Inactivation of MCI was attempted by applying an aqueous solution of sodium bisulfite (10% v/v) on the dried painted glass plates and was left overnight at room temperature for drying.

Results

In the wall and ceiling paint and in the varnish from patient no. 1, MCI/MI was measured at total concentrations ranging from 5 to 28.4 mg/kg (Table 1). Emission of MCI/MI from paint was found from wet as well as from dried glass surfaces. Air concentrations of MCI released from paint at the beginning were 80 µg/m³ and still 5 µg/m³ after 4 weeks (Fig. 1). After application of sodium bisulfite on dried painted surfaces no emission of MCI/MI was detectable (2).

In patient no. 1, patch tests with the European standard series were positive at day (D) 2 and D 3 for nickel sulfate (++/++), cobalt chloride (+/+), para-mix (includes p-phenylenediamine, p-toluylenediamine, p-aminodiphenylamine hydrochloride, +/+), and MCI/MI (++/+++). Patch testing with the undiluted paints and varnish used resulted in a positive reaction to the wall paint (++/++) but negative reactions with the 2 other agents (Table 1). Because of repeated relapses of cutaneous and respiratory symptoms upon staying in her apartment, the surfaces painted with wall paint were treated by the manufacturer with an inorganic sulfur salt solution 16 weeks after the renovation. After this intervention no further relapse occurred.

In patient no. 2, patch tests with the European standard series and other preservatives were positive at D 2 and D 3 for colophonium (+/+), methylidibromo glutaronitrile/phenoxyethanol (+/

Table 1. Concentrations of MI and MCI in paints^{a)} and patch test results

	MI (mg/kg)	MCI (mg/kg)	Total (mg/kg)	Patch tests day 2/3
wall paint	12.9	15.5	28.4	++/++
ceiling paint	5.9	<0.6	5.9	-/-
parquet varnish	5.0	<0.6	5.0	-/-

^{a)} 4 other paints did not contain MCI/MI and gave negative patch test results.

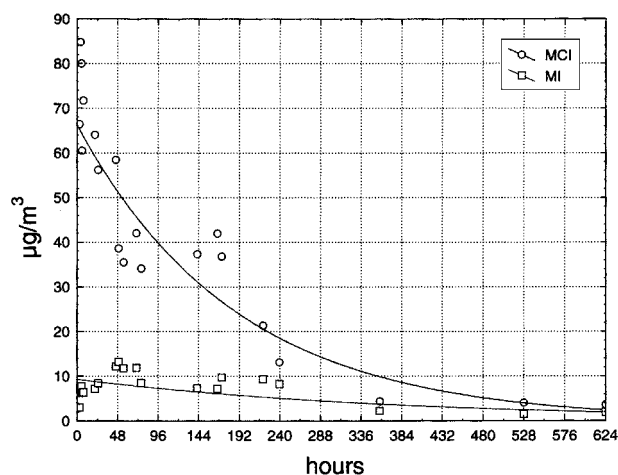


Fig. 1. Temporal evolution of emission and air concentration of methylchloroisothiazolinone/methylisothiazolinone under experimental conditions.

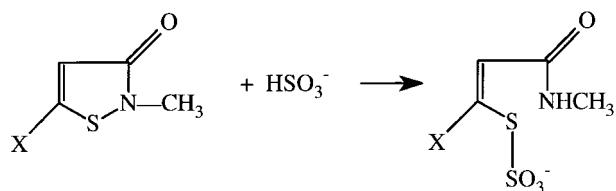


Fig. 2. Inactivation of methylchloroisothiazolinone/methylisothiazolinone by adding sodium bisulfite (according to 11, 22).

++), and MCI/MI (+++/+++). Patch test with ceiling paint was negative, with the wall paint strongly positive (+++/+++). 7 weeks after the onset and after treatment with topical corticosteroids she was free of symptoms.

In patient no. 3, patch tests with the European standard series were positive to MCI/MI (exact grading not available) only. The symptoms slowly regressed over time, but were still present after 4 months. Information on her drug treatment was not available.

In patient no. 4, patch tests with the European standard series showed only MCI/MI to be positive (+++/+++). The symptoms slowly cleared with topical corticosteroids but lasted 5 weeks.

Patient no. 5 had patch tests with the European standard series and cosmetics and had positive patch tests to MCI/MI (-/++) and methyldibromoglutaronitrile/phenoxyethanol (-/++). Her symptoms lasted for 3 weeks and cleared with topical corticosteroids. After stopping this treatment she had a relapse of her facial dermatitis.

Discussion

Preservatives are required especially in water-based products to prevent growth of micro-organisms.

The isothiazolinone derivatives are frequently used for this purpose and are now marketed under more than 30 trade names. Active ingredients constitute 5-chloro-2-methyl-4-isothiazolin-3-one (MCI) and 2-methyl-4-isothiazolin-3-one (MI) in a 3-to-1 weight ratio. MCI/MI is effective against gram+ and gram-bacteria as well as against moulds and yeasts. Kathon® is one of the proprietary names of the mixture of MCI/MI. It consists of 1.5% active ingredients in water stabilized by 23% of magnesium and calcium salts. Several formulations are commercially available. Kathon CG® (cosmetic grade), Kathon WT® (water treatment) and others were introduced in the early 1980s and since then have been widely used in cosmetics and body care products, such as shampoos, toiletries, skin creams and lotions, as well as in industrial products such as water-cooling systems, cutting oils, paints, glues, latex emulsions and papermills. In the European Community the maximal concentration of MCI/MI in cosmetic products has been limited to 15 ppm and labelling is mandatory. Despite that effort MCI/MI is still among the most common contact allergens, the rate of sensitization in Europe ranging from about 0.7 to 8.4% (3–10). MCI is a more potent sensitizer than MI (11). 100 ppm (0.01% w/v) in water is its currently recommended test concentration in the European standard series. At higher concentrations MCI/MI is highly irritant (12–14).

We have observed 5 female patients sensitized to MCI/MI who had cutaneous signs, and 2 also had rhinitis and cough after staying in newly painted rooms. In our 1st case, chemical analyses of the paints revealed MCI/MI, though not in the concentrations given on the material safety data sheets. Interestingly, the chlorinated compound (MCI) with the higher sensitizing capacity was contained only in the wall paint, in the ceiling paint and the floor varnish only the non-chlorinated compound (MI) being found (Table 1). The distribution of the exanthema mainly on air-exposed areas and the mucosal signs indicate that airborne MCI likely provoked the symptoms. Moreover, we could show the emission of significant quantities of MCI as well from wet as from dried wall paint over a considerable time period (Fig. 1), and that inactivation of MCI in the wall paint by applying inorganic sulfur salts solved her problem without any further relapse of cutaneous or respiratory symptoms.

So far, 11 patients with airborne dermatitis and in 3 also mucosal symptoms elicited by MCI/MI from paints have been reported (15–20). As in our cases, most such patients were females without occupational exposure to MCI/MI and who did not paint themselves. Symptoms occurred after a short

Table 2. Cases of non-occupational airborne contact dermatitis to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) from paints

Nr	Age (years)	Sex	Exposure to paint	Sensitization by	Positive patch tests	Clinical presentation	Onset of symptoms, duration of relapses at reexposure	Ref.
1	58	F	nm	day cream body lotion	MCI/MI day cream, body lotion	airborne dermatitis	nm	15
2	42	F	painted self	day cream	MCI/MI white "environment paint"	airborne dermatitis	1 day, >2 months	16
3	47	F	worked in a newly painted office	cosmetics	MCI/MI paint furniture wax	disseminated dermatitis conjunctival and nasal symptoms, pyrexia	2 days, >1 year	17
4	33	F	worked in a newly painted restaurant	moisturizing cream	MCI/MI	airborne dermatitis conjunctivitis	1 day, 6 months	18
5	46	M	painted self	not known	MCI/MI	airborne dermatitis	4 hours, healed after 3 weeks	19
6	40	F	husband painted kitchen	massage cream	MCI/MI formaldehyde, fragrances	airborne dermatitis	2 days, healed after removal of paints	20
7	44	F	husband painted apartment	occupation (nurse)	MCI/MI fragrances, formaldehyde methyltribromo glutaronitrile	airborne dermatitis	3 days evolution nm	20
8	31	F	husband painted bedroom	occupation (dairy work)	MCI/MI nickel, tetramethylthiuram	airborne dermatitis conjunctival symptoms	1 day >6 months	20
9	11	M	father painted apartment	shower gel	MCI/MI, formaldehyde methyltribromo glutaronitrile ammoniated mercury, thimerosal	airborne dermatitis	4 exposures/relapses evolution complicated by other contact allergens	20
10	50	F	husband painted apartment	cosmetics	MCI/MI dexpanthenol	airborne dermatitis	2 days, nm, resolved after inorganic sulfur salt	20
11	31	F	painted self	cosmetics	MCI/MI 3 paints	airborne dermatitis	few days, nm, resolved after inorganic sulfur salt	20
12	46	F	painter painted apartment	not known	MCI/MI nickel, cobalt, para-mix, wall paint	airborne dermatitis rhinitis, cough	few days 4 months, resolved after inorganic sulfur salt	case no. 1
13	47	F	husband painted apartment	not known	MCI/MI methyltribromo glutaronitrile colophony, wall paint	airborne dermatitis	4 days 7 weeks	case no. 2
14	25	F	painter painted apartment	not known	MCI/MI	dermatitis rhinitis, cough	few days >4 months	case no. 3
15	52	F	husband painted apartment	cosmetics	MCI/MI	disseminated airborne dermatitis	2 days 5 weeks	case no. 4
16	46	F	husband painted apartment	not known	MCI/MI methyltribromo glutaronitrile/ phenoxethanol	dermatitis face and neck	few days 3 weeks	case no. 5

nm=not mentioned.

exposure time without direct contact (Table 2). This suggests that most of these patients were already sensitized to MCI/MI, probably by the earlier use of cosmetics or body care products. In this respect, it is also of interest that professional painters have a low prevalence of sensitization to MCI/MI (1, 21), whereas male hobby painters have a sensitization rate of 11.7% to MCI/MI (21). This suggests that not inhalation but direct skin contact by negligent handling, e.g., spilling, etc., may lead to contact sensitization, since professional painters are more likely exposed to higher air concentrations for extended time periods. It has also been suspected that sometimes unnecessarily high concentrations of MCI/MI have been added to paints, which would facilitate sensitization (21). On the other hand, even low air concentrations may elicit symptoms in presensitized highly sensitive individuals, which may last for several months. It also appears that airborne MCI/MI may cause mucosal symptoms, which may have an irritant or allergic pathogenesis, but presently there is not enough information to conclude as to the pathogenesis in these cases. The clinical picture of cutaneous signs may be atypical for contact dermatitis and contact allergy to MCI/MI may manifest with unusual clinical presentations (15). Therefore, there may be a considerable number of unidentified patients in whom symptoms have been related to other allergen sources or have been misinterpreted, e.g., as infectious exanthemas, drug rashes or infections of the respiratory tract. Diagnosis may then be delayed for weeks or months, as in some of the cases reported.

Sodium bisulfite has the capacity to inactivate MCI/MI (22). The bisulfite ions react with MI and MCI molecules, resulting in an opening of the ring, thereby reducing the allergenic property (Fig. 2) (22). In our case no. 1 and 2 others (20), treatment of the painted walls with an inorganic sulfur salt resulted in rapid disappearance of allergic symptoms. Experimentally, no emission of MCI/MI after applying the sulfur salt on the painted surface could be measured. However, in highly sensitive patients even after inactivation patch tests containing 6.25 ppm MCI/MI were positive (22). In addition, sodium bisulfite is known itself as a potential contact allergen (23), and especially in chronic asthmatics sulfites may induce bronchospasm (24). For these reasons, this procedure cannot be generally recommended at present. Glutathione, an endogenous non-toxic substance also leading to degradation of MCI/MI (11), could possibly be an alternative. In less sensitive cases, heating and thorough airing of the rooms may be sufficient to reduce MCI/MI emission to tolerated levels (16).

Considering that currently up to 80% of water-based paints contain MCI/MI (1, 2), a large proportion of the general population is exposed over long time periods. MCI/MI belongs in the top 10 contact allergens in Europe, sensitization rates are high, and therefore a considerable number of sensitized patients may become exposed and are at risk. Consequently, we believe that labelling of the MCI/MI content in paints should be mandatory and regulatory action should be taken to control the concentrations of MCI/MI added to paints. Before an equally effective but clearly safer preservative is available, replacing MCI/MI with other preservatives, such as methylidibromo glutaronitrile, may just shift the problem. In the meantime, it may be desirable to have a non-toxic inactivator of MCI/MI which can be added at the time the paint is used.

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References

1. Fischer T, Bohlin S, Edling C, Rystedt I, Wieslander G. Skin disease and contact sensitivity in hose painters using water-based paints, glues and putties. *Contact Dermatitis* 1995; 32: 39–45.
2. Niederer M, Bohn S, Bircher A J. Emission von Isothiazolonen aus wässrigen Anstrichstoffen als Ursache für gesundheitliche Probleme nach Wohnungssanierungen. *Mitt Lebensm Hyg* 1999; 90: 325–332.
3. Bruckner-Tudermann L, König A, Schnyder U W. Patch test results of the Dermatology Clinic Zurich in 1989: Personal Computer-Aided Statistical Evaluation. *Dermatology* 1992; 184: 29–33.
4. De Groot A C, Weyland J W, Kathon CG: A review. *J Am Acad Dermatol* 1988; 18: 350–358.
5. De Groot A C, Herxheimer A. Isothiazolinone preservative: cause of a continuing epidemic of cosmetic dermatitis. *Lancet* 1989; 1: 314–316.
6. Hunziker N, Pasche F, Bircher A J, Bruckner-Tudermann L, Hunziker Th, Schmid P, Suard A, Suter H, Perrenoud D, Stäger J, Thürlimann W. Sensitization to the isothiazolinone biocide. Report of the Swiss Contact Dermatitis Research Group 1988–1990. *Dermatology* 1992; 184: 94–97.
7. Perrenoud D, Bircher A J, Hunziker T, Suter H, Bruckner-Tudermann L, Stäger J, Thürlimann W, Schmid P, Suard A, Hunziker N. Frequency of sensitization to 13 common preservatives in Switzerland. *Contact Dermatitis* 1994; 30: 276–279.
8. Van Ginkel C J W, Rundervoort G J. Increasing incidence of contact allergy to the new preservative 1,2-dibromo-2,4-dicyanobutane. *Br J Dermatol* 1995; 132: 918–920.
9. Jacobs M C, White I R, Rycroft R J G, Taub N. Patch testing with preservatives at St John's from 1982 to 1993. *Contact Dermatitis* 1995; 33: 247–254.
10. Schnuch A, Geier J, Uter W, Frosch P J. Patch testing with preservatives, antimicrobials and industrial biocides. Results from a multicenter study. *Br J Dermatol* 1998; 138: 467–476.

11. Gruvberger B. Methylisothiazolinones. Diagnosis and prevention of allergic contact dermatitis. *Acta Dermato-venereologica* 1997; 200 (suppl): 1–42.
12. Rietschel R L, Nethercott J R, Emmett E A, Maibach H I, Storrs F J, Larsen W G, Adams R M, Taylor J S, Marks J G, Mitchell J C, Fisher A A, Kanof N B, Clendenning W E, Schorr W F. Methylchloroisothiazolinone-methylisothiazolinone reactions in patients screened for vehicle and preservative hypersensitivity. *J Am Acad Dermatol* 1990; 22: 734–738.
13. Stejskal V D M, Forsbeck M, Nilsson R. Lymphocyte transformation test for diagnosis of isothiazolinone allergy in man. *J Invest Dermatol* 1990; 94: 798–802.
14. Fewings J, Menné T. The patch test concentration for methylchloroisothiazolinone/methylisothiazolinone. *Contact Dermatitis* 1998; 39: 320–321.
15. Morren M A, Dooms-Goossens A, Delabie J, De Wolf-Peeters Ch, Marien K, Degreef H. Contact allergy to isothiazolinone derivatives: unusual clinical presentations. *Dermatology* 1992; 184: 260–264.
16. Finkbeiner H, Kleinhans D. Airborne allergic contact dermatitis caused by preservatives in home-decorating paints. *Contact Dermatitis* 1994; 31: 275–276.
17. Fernández de Corrés L, Navarro J A, Gastaminza G, Del Pozo M D. An unusual case of sensitization to methylchloro- and methyl-isothiazolinone (MCI/MI). *Contact Dermatitis* 1995; 33: 215–216.
18. Schubert H. Airborne contact dermatitis due to methylchloro- and methylisothiazolinone (MCI/MI). *Contact Dermatitis* 1997; 36: 274.
19. Bentrop I. Aerogenes Kontaktekzem auf (Chlor)Methylisothiazolon in einer Wandfarbe. *Allergo J* 1999; 8: 39–40.
20. Hausen B M. Aerogene Kontaktdermatitis durch (Chlor)-methylisothiazolinon (Kathon CG) in Wandfarben. *Akt Dermatol* 1999; 25: 9–14.
21. Schnuch A. Untersuchungen zur Verbreitung von umweltbedingten Kontaktallergien mit Schwerpunkt im privaten Bereich. *Abschlussbericht Forschungsvorhaben 116 01 114*. Umweltbundesamt 1998.
22. Gruvberger B, Bruze M. Can chemical burns and allergic contact dermatitis from higher concentrations of methylchloroisothiazolinone/methylisothiazolinone be prevented? *Am J Contact Derm* 1998; 9: 11–14.
23. Vena G A, Foti C, Angelini G. Sulfite contact allergy. *Contact Dermatitis* 1994; 31: 172–175.
24. Gunnison A F, Jacobsen D W. Sulfite hypersensitivity. A critical review. *CRC Crit Rev Toxicol* 1987; 17: 185–214.

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