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LETTER TO THE EDITOR

Dear Editor

Occupational Airborne Contact Dermatitis by Isothiazolinones Contained in Wall Paint Products

Isothiazolinone includes 5-chloro-2-methyl-4-isothiazolin-3-one (MCI; Fig. 1a), 2-methyl-4-isothiazolin-3-one (MI; Fig. 1b), Kathon® CG (MCI/MI) and 1,2-benzisothiazolin-3-one (BIT; Fig. 1c).[1,2] Occupational contact dermatitis due to isothiazolinone has been often reported and discussed in Europe,[3] however such cases was not much reported in Japan and not yet widely recognized by Japanese tradesperson. Recently, the cases of isothiazolinone related dermatitis in Japan was reported in 2010,[4] which is about non-occupational allergic contact dermatitis from isothiazolinone preservative in a Japanese mattress gel-sheet used for cooling and it made big impact on those customers. Although mattress gel-sheet gathered attention, isothiazolinone is included in various other products and especially tradesperson should be aware that there might be a risk of contact dermatitis from it. More important point is that contact dermatitis by isothiazolinone can occur even from aerially-sprayed materials.[5] Then, here we report a case of occupational airborne contact dermatitis by isothiazolinone in wall paint products to reaffirm such an occupational problem.

A 66-year-old man, who worked as a house painter, developed painful and pruritic eczema on the eyelids, neck, hands, fingers, arms and trunk (Fig. 1d-f), two years after he started using a particular kind of paint. He also had pain in the nasal mucosa, oral mucosa and the eyes. He was wearing short sleeves and cotton gloves while spraying the above-mentioned paint on walls. His symptom improved when he stopped using the paint for a while. He had no history of atopic dermatitis or other skin diseases. Eczema appeared both on exposed and unexposed areas. He had never directly touched the paint. The patient commenced topical glucocorticosteroids and his symptom gradually improved after using goggles, protective mask and gloves. After the rash improved and he stopped using glucocorticosteroids to the trunk, patch test was planned. We did not prepare healthy controls for the patch test.

The paint consisted of more than 30 chemicals, but through information from the manufacturer, several potential sensitizers were selected, BIT (0.0385% in the product), BIT/MCI (both 0.006%), 2,2,4-trimethyl-1,3-pentadiolmonoisobutyrate (TP; 3.5%) and triazine (0.147%). We prepared two concentrations for each allergen: the component concentration and 0.1%, which was most commonly used from previous reports.[1,6] We added rosin (20% pet., Brial, Greven, Germany), formaldehyde (1% aq., Brial) and MCI/MI (0.01% aq.,

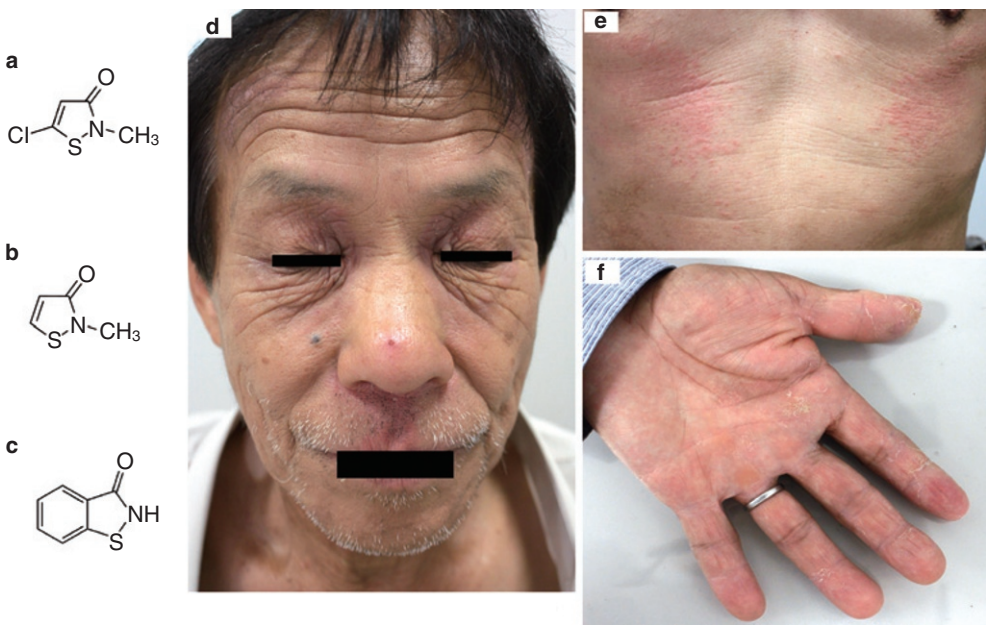

Fig. 1 Chemical structure of 5-chloro-2-methyl-4-isothiazolin-3-one (MCI, **a**), 2-methyl-4-isothiazolin-3-one (MI, **b**) and 1, 2-benzisothiazolin-3-one (BIT, **c**). Picture of the eczema that appeared on the face, which was most noticeable on the eyelids and around the nose (**d**). Eczema and papules were seen bilaterally on the trunk (**e**). His hands and fingers showed eczema with scale and desquamation (**f**).

Table 1 Patch test results

	D2	D3
BIT 0.0385% aq.	-	-
BIT 0.1% aq.	+ ?	+ ?
BIT/MCI 0.006% aq.	-	-
BIT/MCI 0.1% aq.	+	+
Kathon CG (MCI/MI) 0.01% aq.	+	+
TP 0.1% pet.	-	-
TP 3.5% pet.	-	-
Triazine 0.147% aq.	-	-
Triazine 0.1% aq.	-	-
Rosin 20% pet.	-	-
Formaldehyde 1% aq.	-	-
Purified water	-	-
White petrolatum	-	-

Brial) from the Japanese standard allergen series as potential sensitizers. Allergens were applied on Patch tester Torii® (Torii Pharmaceutical, Tokyo, Japan) and left on the upper back for 2 days and read on Day 2 and Day3. The reaction was scored according to the International Contact Dermatitis Research Group system. Patch tests showed "+?" reaction to BIT (0.1% aq.) and "+" reaction to MCI/MI (0.01%aq.) and BIT/MCI (0.1%aq.) at Day2 and Day3 (Table 1). Others were negative.

In this case, sensitization to MCI or both MCI and MI can be presumed, since MCI/MI consists of MCI and MI[2,7] and BIT alone had doubtful reaction. Another possibility was cross reaction between isothiazolinone. However, cross reaction of BIT or MI and MCI has been thought unlikely from previous reports.[1,2,6,7] While MCI has a vinyl-activated chlorine atom and is classified as a chlorinated isothiazolinone, MI and BIT are classified as non-chlorinated isothiazolinones.[2] Chlorinated isothiazolinones are the strongest sensitizers due to its allergenic chlorinated epitope and there seems to be no cross reaction between them.[2]

Furthermore, MI can also be positive at the same time. It is possible that our patient was sensitized to MI in his professional activity. As our patient complained that the symptom worsened only when he used the suspected paint and MI was not included in the paint, we suspected that MCI was likely to be the cause of the symptom, though we didn't perform patch test with MCI alone. Moreover, MCI is a more potent sensitizer than MI[7] and the threshold concentrations of MCI for skin sensitization were 0.001 - 0.002%,[2] there is a potential for skin sensitization.

As we could not find a paper mentioning dermatitis occurred by irritant reaction and our patients developed contact dermatitis 2 years after he started using the paint, we concluded that the patient's contact dermatitis was not due to irritant but due to allergic reaction.

Systemic contact dermatitis is one of the differential diagnoses. But our patient's lower body didn't show any skin symptoms. If he had systemic contact dermatitis, his lower body should have shown dermatitis. Airy sprayed paint could reach his trunk from his short sleeves thus dermatitis might appear on his trunk, and his lower body didn't have dermatitis probably because he wore trousers. We could not find previous reports that mentioned systemic contact dermatitis by isothiazolinone, but if he continued inhaling the sprayed paint, there might be a risk of systemic contact dermatitis.

Isothiazolinone can induce allergic contact dermatitis such as hand dermatitis with thick stratum corneum.[1] Insufficient protection from aerial spraying is thought to have culminated in severe airborne contact dermatitis after the repeated sensitization/elicitation events. It seemed difficult for tradespersons to recognize airborne materials could cause dermatitis even if isothiazolinones were known as strong sensitizer. This reaffirms the risk of contact dermatitis from airborne isothiazolinones materials and the importance of education and protection for those who are at risk of occupational contact dermatitis.

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