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Five cases of severe chronic dermatitis caused by isothiazolinones

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Preservatives used in both industrial and consumer products are well-known and important causes of contact allergy (1). The allergens relevant for this article are the preservatives methylchloroisothiazolinone (MCI) (CAS: 26172-55-4), methylisothiazolinone (MI) (CAS: 2682-20-4), and benzisothiazolinone (BIT) (CAS: 2634-33-5). MCI/MI (3:1) has been used as a preservative in cosmetics and household products such as cleaning agents, as well as in industrial products, since the early 1980s. Since the beginning of the millennium, MI has been available on its own for industrial products, and in 2005 its use in cosmetic products was permitted (2). In cosmetics, MCI/MI has been limited to a concentration of 15 ppm, whereas MI alone is limited to 100 ppm. BIT is used in both industrial and household products, such as cleaning and impregnating agents, paints, polishes, and printing inks (3), but was recently rejected by the Scientific Committee on Consumer Safety for use in cosmetic product, owing to the negative experiences with MI concerning contact allergy (4). From 2009 to 2011, the prevalence of MI contact allergy increased dramatically (5, 6).

In 2011, the first 2 cases of airborne allergic contact dermatitis caused by MI in paint were published (7), and it was recently shown that 3 of 4 of MI-allergic patients with relevant exposure to paint had signs of airborne allergic contact dermatitis (6). In 2012, the first case of systemic allergic dermatitis caused by airborne exposure to BIT was published (8). The entity systemic contact dermatitis can present with clinically characteristic features or be clinically indistinguishable from other types of contact dermatitis (9). The clinical features include

dermatitis in areas of previous exposure, skin symptoms in previously unaffected skin, usually flexures, and general symptoms. These features make the diagnosis difficult, but, on the basis of our clinical evaluation, the cases presented below meet the suggested criteria. All of the patients had been heavily exposed to isothiazolinones during occupational procedures, resulting, in all cases, in severe chronic contact dermatitis and substantial impairment of normal life. Two of the cases (2, 5) have been described individually in Contact Points (8, 10), but are included here to point out the severe consequences of exposure to high concentrations of isothiazolinones.

Case 1

A 47-year-old male metalsmith with no history of previous skin disease was referred to our department in 2009. Prior to referral he was patch tested, and had a positive reaction to BIT (3+). After repeat patch testing, positive reactions to MCI/MI (2+), MI (2+) and octylisothiazolinone (2+) were observed.

During a period of 17 years prior to skin manifestations in 2006, the patient was heavily exposed to Proxel™ (a microbiostat preservative), in which the active agent is BIT. As a part of his job, he had to pour Proxel™ into tanks, and, as he was not wearing proper protection, his hands and face were exposed directly to BIT. He initially presented with severe dermatitis affecting the hands, arms, and face, which today has developed into widespread chronic dermatitis, including flare-ups of previous dermatitis, flexural dermatitis, vesicular hand eczema, maculopapular rash, and general symptoms. This severe condition is being sustained by small-scale airborne exposures to isothiazolinones, constituting systemic exposure. There is a certain correlation between the exposure to BIT and the contact dermatitis that has

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developed. The sensitization to other isothiazolinones that developed later is most likely correlated with the primary exposure. He has been reallocated at work several times without successfully avoiding exposure to the allergen, and is also exposed in his spare time, which provokes flare-ups. Today, he has difficulty in maintaining his house, and his family life is being affected by his lack of energy caused by the chronic disease.

Case 2 (8)

A 35-year-old male had a positive patch test reaction to BIT on first referral in 2009; repeat patch testing in 2011 showed new allergies to sorbic acid, chlorhexidine diacetate, different perfume chemicals, and chrome, but also MI (2+) and MCI/MI (2+).

The patient had been heavily exposed to Proxel™, and has developed a severe chronic dermatitis with both occupational and spare-time flare-ups.

Case 3

In August 2012, an otherwise healthy 42-year-old female was referred to our department. Five years earlier, she had a positive patch test reaction to MCI/MI when seen by a practising dermatologist. Our repeat patch testing gave a positive reaction to MI (1+).

The patient had been working in a paint factory for the last 15 years. Her job included many different cleaning procedures for which protective gloves were used, but, when the paint was drained, work procedures did not include the use of gloves, and spillage and skin contact with the MI-containing fluids was unavoidable. Her only initial symptom was a vesicular dermatitis on the second phalanx of the right hand. The dermatitis then developed to a more severe pattern, including all of both hands, the neck, and the face. Approximately 1.5 years ago, she was reallocated at work, but rooms containing paint vapours are unavoidable at her workplace, and this has led to several flare-ups. She is currently taking maternity leave, which has eased her symptoms, but she has experienced a flare-up in relation to a paint job in her house. When her maternity leave is over, she will be forced to either be reallocated again or quit her job.

Case 4

A 32-year-old male handyman with no history of previous skin disease was referred to our department in 2012. He had positive patch test reactions to MCI/MI (1+) and MI (2+).

The patient worked for 2 years at a glue factory with various work procedures, some of which included mixing different types of glue containing a chemical product called Kathon™ LXE, which is a trade name for a mixture of MCI and MI. The patient handled Kathon™ LXE while wearing latex gloves, a face mask covering the mouth and nose, a regular T-shirt, and work trousers. The work-related exposure suggests direct contact with the allergen through vapours and from containers dripping chemicals directly onto his trousers.

The initial dermatological symptoms were local erythema and burning sensations on the hands, face, and femoral region. These manifestations later developed into a more severe flare-up of the previously affected area, now with a papular vesicular dermatitis pattern, also involving the flexural part of the knees, and general symptoms, including malaise, and respiratory and gastrointestinal symptoms. The dermatitis initially developed after 1 year of exposure, and its severity has been correlated with his work schedule. His condition does not allow him to return to his former employment.

Case 5 (10)

A 64-year-old former painter had a positive patch test reaction to MCI/MI; repeat patch testing resulted in a 2+ reaction to MI and a 2+ reaction to MCI/MI. He is now retired, with a severe chronic dermatitis that is slowly improving with careful avoidance of the allergen.

Discussion

The common denominator of the presented cases is the high level of occupational exposure to isothiazolinones, resulting in severe contact dermatitis and substantial impairment of normal life (Table 1). New cases of contact dermatitis caused by these preservatives are being observed on a daily basis, but these cases are some of the more severe. The patients have a significant disadvantage as compared with regular contact dermatitis patients, as they all react to airborne exposure, and the increase in the number of products containing MI, in particular, makes exposure very difficult to avoid. Airborne contact dermatitis caused by exposure to isothiazolinones has been known for a long time; however, the severity and number of patients affected are unprecedented, and are a reason for concern.

How exactly exposure to these allergens will affect society in the future is uncertain; however, studies have been published showing an increased prevalence of contact allergy to MCI/MI and MI (5, 6). Currently, only MCI/MI is covered by relevant legislation outside cosmetic

Table 1. Case characteristics

Case	Sensitized isothiazolinones	Primary sensitization	Systemic exposure	Clinical aspects
				(1) Flare-up of previous dermatitis (2) Skin symptoms in previously unaffected skin (3) General symptoms
1	BIT, MCI/MI, MI, octylisothiazolinone	Transcutaneously	Inhalation	(1) Hands and face (2) Flexural dermatitis, maculopapular rash (3) Malaise and sleep disorder
2	BIT, MCI/MI, MI	Transcutaneously	Inhalation	(1) Face, neck, chest, hands, and ears (2) Flexural dermatitis, vesicular foot eczema (3) Malaise
3	MI	Transcutaneously	Inhalation	(1) Hands (2) Maculopapular rash
4	MCI/MI, MI	Transcutaneously	Inhalation	(1) Hands, face, and femoral region (2) Flexural dermatitis (3) Malaise, respiratory symptoms, gastrointestinal symptoms
5	MCI/MI, MI	Transcutaneously	Inhalation	(1) Hands and lower arms (2) Flexural dermatitis (3) Malaise

BIT, benzisothiazolinone; MCI, methylchloroisothiazolinone; MI, methylisothiazolinone.

and household products, and there are no requirements for labelling on industrial products, which again makes it very difficult to avoid exposure to the isothiazolinones. These cases are yet more examples of the growing problem

of contact allergy to isothiazolinones, and especially MI. We suggest that the current safety requirements for MI and BIT are re-evaluated for all relevant product groups.

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