Allergic contact dermatitis to methylisothiazolinone in hair care products: report of a case

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Abstract
Methylisothiazolinone (MI) is commonly used as a preservative in personal care products and is a frequent cause of allergic contact dermatitis. We present a patient with allergic contact dermatitis caused by MI in hair care products and discuss this allergen to bring attention to this common cause of contact dermatitis, and to highlight its frequent use in hair care products. If allergy to MI is suspected, testing should be performed to this individual preservative, as testing solely for the combination preservative, methylisothiazolinone/methylchloroisothiazolinone (Kathon CG®), may miss many cases of MI allergy.

Keywords: methylisothiazolinone, isothiazolinones, Kathon CG®

Introduction
Contact dermatitis is a common disorder estimated to affect more than 72 million Americans each year. It causes significant burdens on health and quality of life. In 2004, the estimated direct cost of medical care for contact dermatitis was 1.6 billion dollars. Indirect costs related to lost productivity added another $560 million to the toll. Adverse impact on quality of life such as discomfort, loss of sleep, social stigma, and disruption of intimacy adds to the intangible costs of this skin disease [1, 2].

Methylisothiazolinone (MI) is a common preservative in skin and hair care products such as wipes, shampoos, conditioners, soaps, bubble baths, moisturizers, and sunscreens. These products may be marketed for babies, children, men, and women, and are a frequent cause of allergic contact dermatitis. Furthermore, these products may be described as “hypoallergenic,” “gentle,” “natural,” “organic,” “dermatologist-tested,” or “dermatologist-recommended,” implying that reactions to them are unlikely[3]. Methylone at a higher concentration replaced the combination preservative methylisothiazolinone and methylchloroisothiazolinone (Kathon CG®) in many personal care products after an epidemic of allergic contact dermatitis (ACD) to the combination product; it was assumed that the MI alone would be less allergenic. Using solely the standard patch test for the combination preservative may miss many cases of MI allergy. Therefore, if MI allergy is suspected, customized patch testing is necessary.

We present a case of a man with ACD to MI in his hair care products to increase awareness of products that may contain this allergen and thus trigger ACD.

Case Synopsis
A male patient in his 60s was referred for patch testing. His rash had been present for over 3 years and had involved multiple areas of the body, including the dorsal hands, forearms, torso, and face. He was retired and his hobbies included gardening and some landscaping work. Multiple topical steroids had been used, with partial improvement of his rash. His dermatologist had diagnosed him with contact dermatitis and referred the patient for patch testing. The differential diagnosis included allergic contact dermatitis, irritant contact dermatitis, and endogenous eczema.

On exam, red scaling patches were noted on the forehead, eyelids, forearms, dorsal hands, and posterior thighs (Figures 1 and 2).
The patient underwent patch testing with the North American Contact Dermatitis Group standard series and a preservatives series.

At the 72-hour delayed patch test reading, he had a 3+ positive reaction to methylisothiazolinone (MI) and a 2+ reaction to Kathon CG (methylchloroisothiazolinone/methylisothiazolinone) (Figures 3 and 4). Scoring was performed as per the guidelines of the International Contact Dermatitis Research Group, in which a 2+ reaction indicates a strong positive reaction, with erythema, infiltration, and papules, and a 3+ reaction indicates an extreme positive bullous reaction.

A review of his personal care products revealed that his hair gel and hair conditioner both contained MI. He reported using multiple different hand and body soaps. He was provided a list of alternative skin and hair care products to use and advised to continue use of desoximetasone 0.25% spray to areas of dermatitis.

At a 6-month phone follow-up, the patient reported that he had been compliant with all recommendations. His skin had improved and was now clear.

**Case Discussion**

Methylisothiazolinone [preferred International Union of Pure and Applied Chemistry (IUPAC) name: 2-methyl-1,2-thiazol-3(2H)-one] belongs to a group of chemically related biocides/preservatives known as isothiazolinones (Figure 5). These
preservatives are found in many skin and hair care products as well as industrial products such as paint, waxes, and oils. Other members of this group include methylchloroisothiazolinone (MCI) and benzisothiazolinone (BIT). Benzisothiazolinone is used in industry but not approved for use as a preservative in personal care products [2]. Isothiazolinones are biocidal for a broad range of microorganisms by interacting and oxidizing cellular thiols [4].

The isothiazolinones MI/MCI (in a fixed ratio of 3:1) were first registered as preservatives in the United States in 1977 under the trade name Kathon CG. They are compatible with surfactants and emulsifiers and able to maintain biocidal activity over a wide pH range; in the 1980s became extensively used in personal care products and industry [2, 4]. In 1988, de Groot and colleagues reported that preservatives were the most common cause of ACD in cosmetics and that Kathon CG (MI/MCI) caused the vast majority of reactions attributed to preservatives [5]. Shortly after, de Groot and Herxheimer reported additional cases of ACD to Kathon CG. They stated that an epidemic had begun and recommended that the use of isothiazolinones in “leave on” products be abandoned [6]. Expert panels in the United States and the European Union recommended decreasing concentrations of MI/MCI in leave-on and rinse-off products [5, 6]. Because MCI was believed to be a more potent allergen than MI, MI was approved for use as an individual preservative in cosmetics in 2005 [2, 7]. Subsequently, a dramatic increase in positive patch test reactions to MI/MCI was noted and attributed to increased use of MI, and a second epidemic of isothiazolinone allergy was declared [8, 9]. In 2013, MI was named allergen of the year by the American Contact Dermatitis Society [10].

Allergic contact dermatitis is a type IV delayed hypersensitivity reaction. Delayed onset and chronicity, as well as the large number of allergens in our environment, often obscure the triggering allergen and the condition must be distinguished from primary irritant dermatitis and other eczematous processes. Patch testing is the gold standard for diagnosis of ACD [12]. Relevance of positive tests must be confirmed by history, and ideally, elimination of the allergen from the patient’s environment should result in resolution of the dermatitis. Histologically, acute and subacute ACD causes a spongiotic dermatitis. Chronic ACD typically exhibits hyperkeratosis, psoriasiform epidermal hyperplasia, and mild papillary dermal fibrosis with little spongiosis, as one would expect to see in chronic eczematous processes [13, 14]. Skin biopsy is not required for the diagnosis of ACD and may not distinguish it from other eczematous processes. However, it may be helpful in differentiating ACD from histologically distinct conditions such as psoriasis and bullous pemphigoid.

The North American Contact Dermatitis Group (NACDG) previously recommended patch testing the combination of MI/MCI at a concentration of 100 ppm [15]. The 2013-2014 NACDG patch test screening series includes MI alone, at a concentration of 2000 ppm [2]. Some studies have shown that 33% to 60% of patients that are MI sensitive may be missed when patch testing using only the combined MI/MCI preparation [8, 10]. The T.R.U.E. Test® patch test battery, the only FDA approved patch test kit, used in many dermatologists’ offices, tests only the combined MI/MCI at the lower concentration.

Because of the ubiquitous presence of the isothiazolinones, patients sensitive to them may need extra assistance in avoidance. Table 1 lists other

Table 1

Using 2013 data from the American Contact Dermatitis Society’s (ACDS) Contact Allergen Management Program (CAMP), Scheman and Severson analyzed 4660 consumer products for MI. MI was found in dishwashing products (64%), shampoos (53%), household cleaners (47%), hair conditioners (45%), hair dyes (43%), laundry additives/softeners (30%), soaps/cleansers (29%), and surface disinfectants (27%), [11].
names for the isothiazolinones [16]. Members of the ACDS may utilize the Contact Allergen Management Program (CAMP), which will produce a list of products free of specific allergens. Additional resources for patients allergic to the isothiazolinones are listed in Lipp’s Update on Isothiazolinones [2].

**Conclusion**

Allergy to isothiazolinones should be considered in patients with recalcitrant or recurrent dermatitis with patch testing used to confirm the diagnosis. As this preservative has become more commonly used, patients and physicians must recognize the wide array of products that may potentially contain this allergen. A thorough history of personal care product use and household and industrial exposures may suggest the diagnosis and be essential in avoiding further exposure. It is worth emphasizing that patch testing with the standard combined MI/MCI allergens may miss a significant number of cases of ACD secondary to MI. Therefore, when allergy to MI is suspected, it should also be patch tested alone at the higher concentration.

**References**