Allergic contact dermatitis caused by methylisothiazolinone from different sources, including ‘mislabelled’ household wet wipes

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Case Report

A 39-year-old non-atopic nurse was referred to our contact allergy unit in November 2012 because of eczematous skin lesions on the arms, neck and trunk of 7-month duration. Initially, the diagnosis of pityriasis rosea of Gibert had been suspected, but a biopsy of a lesion on the trunk had shown a spongiotic dermatitis with eosinophils, compatible with eczema. Application of a cream containing hydrocortisone 17-butyrate had resulted in clearance of the lesions, which reappeared after this treatment had been stopped. Following the use of betamethasone dipropionate 0.05% and chlorhexidine 0.5% in a non-ionic ointment base, the dermatitis improved; however, 2 months later, the patient also developed palmar hand dermatitis.

The history revealed that the patient had never reacted to adhesive tape, jewellery, or perfume, but that she had previously developed a severe eczematous (even bullous) reaction on the hands when handling a water-soluble paint, and that she had also suffered from dermatitis on the eyelids when her house was being painted.

As a nurse in a neonatology department, the patient wore nitrile gloves and washed her hands several times a day; she also came into contact with skin cleansing products and wipes for the babies’ hygiene. She herself suspected contact with the rubber parts of the incubators to be the cause of the lesions on her arms, as the skin lesions improved when she was off work.

At home, the patient came into contact with Universal Everyday® moist household tissues (Colruyt, Halle, Belgium) and several other cleansing products. She also used several cosmetic products, among which were Nivea Pure & Natural body milk® (Beiersdorf, Hamburg, Germany) and Aderma Exomega® emollient and cleansing oil (Pierre-Fabre, Castres, France).

Patch testing was performed with IQ Ultra® patch test chambers (Chemotechnique, Vellinge, Sweden) covered with Mefix® (Mölndlycke Health Care, Göteborg, Sweden), with the European Baseline series (Trolab, Hermal, Reinbeck, Germany), with a cosmetic and rubber series (Chemotechnique, Vellinge, Sweden), and with the contacted products (and the known allergens in them). The readings were performed after 2, 4 and 7 days, according to the International Contact Dermatitis Research Group criteria. The positive results are shown in Table 1. The positive reaction to Compositae mix, which is a mix of five different plants, namely Arnica, chamomile, feverfew, yarrow, and tansy, was partly relevant for the hand dermatitis, as chamomile was present in the household wet wipes and in the bath oil used for the babies at work, as well as in a shampoo for personal use. Moreover, Calendula officinalis (also belonging to the Compositae or Asteraceae family) was also found in a hand soap.

As to the relevance of methylisothiazolinone (MI), according to the labelling it was present in the body

Table 1. Positive patch test results

<table>
<thead>
<tr>
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<th>D2</th>
<th>D4</th>
<th>D7</th>
</tr>
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<tbody>
<tr>
<td>Methylisothiazolinone 500 ppm aqua*</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Compositae mix 5% pet.†</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nivea body milk® tested ‘as is’</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Everyday® wipes tested ‘as is’</td>
<td>+</td>
<td>+</td>
<td>+</td>
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* Trolab, Hermal, Reinbeck, Germany.
† Chemotechnique, Vellinge, Sweden.
milk and the cleansing oil (which has recently been changed in composition, eliminating this preservative), as well as in several household cleansing products; however, on the packaging of the household wet wipes to which the patient reacted positively, only the presence of phenoxyethanol, benzoic acid, and dehydroacetic acid, as well as five paraben esters (besides a non-ionic surfactant <5%), was mentioned.

Inquiries to the company revealed that, at the beginning of the year, its supplier was using isothiazolinones for preservation, but had changed the preservative system to other substances, and therefore no longer used MI and methylchloroisothiazolinone, either in the lotion for the Everyday® wipes, or for the preservation of any lotion raw material used for the Everyday® lotion, and that the particular batch that the patient had reacted to was definitively free of isothiazolinones.

Thereupon, the laboratory in Malmö was contacted, and the wipes were chemically analysed with high-performance liquid chromatography (HPLC). Each wipe was extracted in 10 ml of methanol/water (70%/30% vol/vol) in an ultrasonic bath for 5 min. The resulting solution was filtered and used for the HPLC analysis. A ThermoFinnigan system was used, consisting of a P4000 quaternary pump, an ultraviolet (UV) 6000 diode array detector, an AS3000 autoinjector and an SN4000F control module. The system was software controlled by CHEOMQUEST 4.1 and UV spectra monitored with CHROMQUEST spectral analysis software (ThermoFinnigan, San José, CA, USA). The injection volume was 20 μl. The column (4.6 mm internal diameter × 250 mm) was packed with Nucleosil (100 Å, 5 μm) (Macherey-Nagel & Co., Düren, Germany). The detector scanned the eluate in the range 200–400 nm. The isocratic elution was performed with methanol (Mallinkrodt Baker B. V., Deventer, The Netherlands)/water (70%/30% vol/vol). The identity of the substances was determined from retention time and UV spectrum. A sample of Kathon CG (Rohm and Haas, Croydon, UK) was used as a reference for MI and methylchloroisothiazolinone.

In one wipe, measuring 19.5 × 18 cm and weighing, when fresh/wet, ~5 g, it was found that both methylchloroisothiazolinone and MI were present, at 34 and 26 ppm, respectively (60 ppm in total). Patch testing with the mixture of MCI and MI, diluted 100 ppm aqueous, had remained negative.

Discussion
In both cosmetics and paints, MI is creating an epidemic of allergic contact dermatitis (1). Our patient was diagnosed with allergic contact dermatitis caused by MI, to which she had most likely become primarily sensitized through a water-based wall paint, which first caused severe blistering lesions on the hands, and then airborne dermatitis, resulting from evaporation of the paint. The lesions on the neck, trunk and arms could be explained by the use of the body milk and cleansing oil (from which MI had actually been removed), whereas those on the hands also resulted from the use of household detergents and wipes, all containing MI. Moreover, the patient also had contact allergy to Compositae plant material, which was also present in some of the contacted products.

This case report shows that we should be cautious when reading (trusting) product labels, and that one can obtain misleading information from manufacturers/suppliers of products!

Reference