Title: The methylisothiazolinone contact allergy epidemic in Australia

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Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of conflicting interests

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

Author contribution

Ursula Flury collected data, wrote the first draft of the manuscript and developed the study outline with Rosemary Nixon. Amanda Palmer helped in the acquisition of data. Rosemary Nixon developed the study outline and reviewed the first draft of the manuscript.

Keywords

Allergic contact allergy • methylisothiazolinone • epidemic • occupational contact dermatitis • patch testing

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1111/cod.13025](https://doi.org/10.1111/cod.13025)

Methylisothiazolinone (MI) is a preservative released in early 2000 for occupational uses, particularly in paints, adhesives and cleaning agents. It was widely used in cosmetics and household products from 2005 (1), although it had been known to cause sensitization in humans and guinea-pigs since the mid-1980s (2,3). The first case of occupational contact dermatitis due to MI was published in 2004 (4) and MI allergic contact dermatitis (ACD) caused by cosmetic products was first reported in 2010 (5). European regulations, introduced in February 2017 have completely forbidden the use of MI in leave-on cosmetics (6). From the end of April 2018, the acceptable MI concentration in rinse-off cosmetics on the European market will be lowered to 0.0015% (7). In Australia, the MI limit of 0.01% applied to both leave-on and rinse-off cosmetics, however MI was banned in leave-on cosmetics from October 2017 (8). The aim of this study was to track the rate of MI contact allergy diagnosed at our institution and investigate the likely sources of exposure to MI at the height of the epidemic.

Method

Patients

This retrospective study included all patients who underwent patch testing for MI from 01.01.11 to 31.12.17 in our Occupational Dermatology and Contact Dermatitis Clinics, Melbourne, Australia. These are tertiary referral clinics for the investigation of patients with suspected contact dermatitis.

Patch testing

Patients were patch tested using allergens from Chemotechnique, (Vellinge, Sweden) or Allergeaze (Smart Practice, Tucson, AZ, USA) using either Finn chambers or Allergeaze test chambers (Smart Practice, Tucson, AZ, USA). MI was tested at 0.2 in aqua. The patches were removed at D2 and read at D2 and D4. Later readings were not routinely performed unless patients noted additional reactions. Readings were performed according to International Contact Dermatitis Research Group guidelines.

In the cohort who reacted to MI in 2014, details of exposure to MI were ascertained from their medical records.

Results

The number of patients tested and the positive results are summarized in Table 1. Across 7 years from 2011 to 2017 inclusive, 2787 patients were tested for MI and 14.5% (404 patients) had a positive test result. 77% had a relevant reaction with documented exposure to MI in a product used and/or a positive patch test to their product. The percentage of positive reactions to MI in those attending the clinic rose from 4.1% in 2011 to 20.3% in 2015. In 2016 the percentage decreased to 18.8% and in 2017 to 11.4%.

Table 2 summarizes the suspected sources of exposure in 2014, the year with the most reactions (n=84). The most important sources of MI were shampoo/conditioner (27 cases, 32.2% of total cases for that year), moisturiser/body lotion/face cream/hand cream (23 cases, 27.4%), wet wipes (22 cases, 26.2%,) and hand/body wash (20 cases, 23.8%). In 11 cases (13.1%), the source of MI exposure was either not identified by the attending dermatologist or recorded in the patient file. It was not usually possible to identify the source of sensitization, only the current exposure.

Table 1: Numbers of patients patch tested to MI and relevant reactions

Year	Tested	Total reactions to MI (percentage)	Relevant reactions to MI (percentage)	Old/unknown reactions
2011	419	17 (4.1%)	14 (82.4%)	3
2012	452	56 (12.4%)	41 (73.2%)	15
2013	372	58 (15.6%)	49 (84.5%)	9
2014	428	84 (19.6%)	70 (83.3%)	14
2015	389	79 (20.3%)	60 (76.0%)	19
2016	361	68 (18.8%)	45 (66.2%)	23
2017	366	42 (11.4%)	31 (73.8%)	11
Totals	2787	404 (14.5%)	310 (76.7%)	94

Table 2: Suspected sources of MI exposure in 2014 (n=84)*

Suspected source of exposure	No. of reports* (percentage)
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Shampoo/conditioner	27 (32.2%)
Moisturiser/body lotion/ face cream/hand cream	23 (27.4%)
Wet wipes	22 (26.2%)
Hand/ body wash	20 (23.8%)
Unknown	11 (13.1%)
Occupational (paint, biocide)	7 (8.3%)
Face cleanser/scrub	7 (8.3%)
Deodorants	4 (4.8%)
Hair gel	2 (2.4%)
Dishwashing detergent	2 (2.4%)
Sunscreen	1 (1.2%)
Mouth wash	1 (1.2%)
Total	127

*Some people were exposed to more than one source

Discussion

Our rates of contact allergy to MI are higher than reported elsewhere, with a peak rate of 20.3% of those patch tested in 2015. In contrast, the rate of MI allergy in the USA was 10.9% in 2013-2014 (9). In Leeds, UK, the MI allergy rate increased from approximately 1% in 2009 to around 10% in 2014, and decreased to 4% in 2015 (10). Data from 11 centres in Europe in 2015 revealed rates of 5% to 13% (11).

This study has shown that the rate of sensitization to MI has decreased since 2015, but is still high at 11.4% in 2017. The reason for the decrease may relate to the increasing removal of MI from products, especially from wet wipes. It is not known whether there has indeed been more exposure to MI in Australia or whether the high rates of MI allergy that we report have been influenced by lower rates of patch testing (12).

Finally, from approximately 2015, patients attending for patch testing were instructed to avoid MI before attending, and this may have resulted in some patients not proceeding to patch testing because their dermatitis improved. There has also been increased awareness of MI allergy, with greater understanding amongst dermatologists

as well as local publicity. This would mean that our high rates of MI allergy may actually be an underestimate.

While we can only comment on likely sources of exposure of MI, and do not know for certain how patients became sensitized, it is interesting that the most important source of exposure to MI in our study was rinse-off products (shampoo/conditioner).

As listed in Table 2, wet wipes were also a frequent source of MI. In 2013, Boyapati from our group reported contact dermatitis involving the hands in parent and carers of babies and hypothesized that it was the result of the widespread use of a particular brand of baby wipes which was widely used in Australia (13). It is unknown how many babies may have been sensitized through the use of wet wipes, as none were tested.

The use of MI in cosmetic products accounts for the majority of cases of contact allergy to MI, with it surprisingly being present in a mouthwash, but we also report 7 cases of definite occupational exposure to MI in paints and biocides. MI was also found in a number of work hand cleaners (number not specified) and shampoos used by hairdressers (number not specified). MI is volatile and may cause airborne allergic contact dermatitis, asthmatic symptoms, and even systemic allergic dermatitis in newly painted rooms (14). In contrast to the more regulated market for MI in cosmetic products, the use of MI in industrial products including paints or detergents are not restricted, but in EU by REACH decisions in February 2018 products with more than 0.0015% (15 ppm) MI must be labeled that it “may cause allergic sensitization”.

Every cloud has a silver lining, and one upside of the MI epidemic has been somewhat of a resurgence of interest in patch testing in Australia, aided by our centre proposing the first Australian Baseline Series which includes MI (15), and establishing a Contact Allergen Bank, which has facilitated patch testing, especially for remote and rural dermatologists (16).

Conclusion

Australia appears to have experienced the highest rates of MI allergy reported in the literature. Our data shows that the frequency of sensitization to MI in Australia is now decreasing. Clinicians need to be aware of the possibility of allergic contact dermatitis caused by MI, especially from shampoos/conditioners, lotions and creams, wet wipes and skin cleansers, and also from occupational sources.

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Title:

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Date:

2018-09-01

Citation:

Flury, U., Palmer, A. & Nixon, R. (2018). The methylisothiazolinone contact allergy epidemic in Australia. CONTACT DERMATITIS, 79 (3), pp.189-191. <https://doi.org/10.1111/cod.13025>.

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