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The rise in prevalence of contact allergy to methylisothiazolinone in the British Isles

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Since 2005, in the EU, the use of methylisothiazolinone (MI) as a single-agent preservative has been permitted in both leave-on and rinse-off cosmetic products at concentrations of up to 100 ppm. Like others, we have observed a recent large increase in the number of patients with contact allergy to MI.

Fourteen dermatology centres from across the British Isles (10 in England, one in Scotland, two in Wales, and one in Ireland) provided their patch test data on MI and methylchloroisothiazolinone (MCI)/MI contact allergy. Nine centres contributed data on both MI and MCI/MI, two centres [number 4 (Cork) and number 14 (Canterbury)] contributed data on MCI/MI alone, and three centres [number 12 (St John's, London), number 13 (St Mary's, London), and number 8 (Manchester)] contributed data on MI alone.

In 2010, five centres were testing with MI. This number increased over the study period to 12 centres.

Analysis was performed on data from January 2010 to June 2013. In all centres, test agents were applied in Finn Chambers® according to International Contact Dermatitis Research Group guidelines. Readings were performed on D2 and D4.

Of the 11 centres contributing data on MCI/MI, nine centres tested with MCI/MI 0.02% aq. (Chemotechnique

Diagnostics, Vellinge, Sweden). MCI/MI was tested at 0.01% aq. (Trolab, Reinbeck, Germany) by centre 11 (Sheffield) and centre 14 (Canterbury).

MI was tested at 0.05% aq. by centre 1 (Aylesham/Hillingdon) in 2010–2012 and at 0.2% aq. in 2013 (1). MI was tested at 0.02% aq. by centre 6 (Leeds) in 2010, at both 0.02% aq. and 0.2% aq. in 2011 and 2012, and at 0.2% aq. in 2013. MI was tested at 0.02% aq. by centre 11 (Sheffield) in 2010–2011 and at 0.2% aq. in 2012–2013. MI was tested at 0.05% pet. by centre 12 (St John's, London) from 2010 to 2012 (2).

One hundred and thirty of 3185 patients tested in the seven British centres that submitted data from 2010 had a positive patch test reaction to MCI/MI. One hundred and sixty-nine of 2033 patients tested in 11 centres from January to June 2013 had a positive patch test reaction to MCI/MI.

This represents an increase in prevalence from 4.3% to 8.3% (Table 1). The range of positive patch test reactions to MCI/MI in the first 6 months of 2013 was 3.2–15.8%.

Thirty-eight of 2279 patients tested in five centres in 2010 had a positive patch test reaction to MI.

Two hundred and ninety-five of 2786 patients tested in 12 centres in January to June 2013 had a positive patch test reaction to MI. This represents an increase in prevalence from 1.7% to 11.1% (Table 1). The range of positive patch test reactions to MI in the first half of 2013 was 5.7–15.3%.

Whereas the prevalence of positive patch test reactions to MCI/MI rose 2.0-fold over the 42-month study period, that of positive patch test reactions to MI rose 6.4-fold over the same period (Fig. 1).

The only centre in which the rate of contact allergy to MI has fallen in the last 2 years is centre 5 in Dundee, Scotland (Fig. 2).

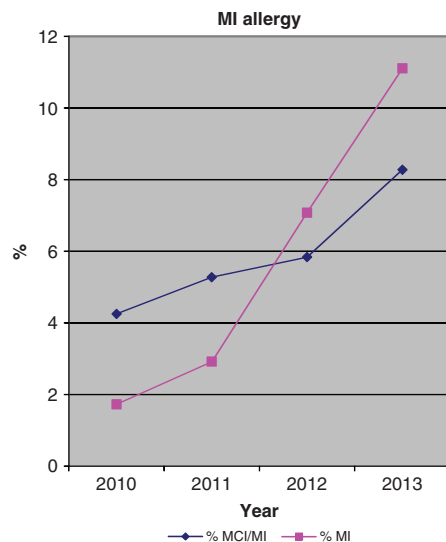
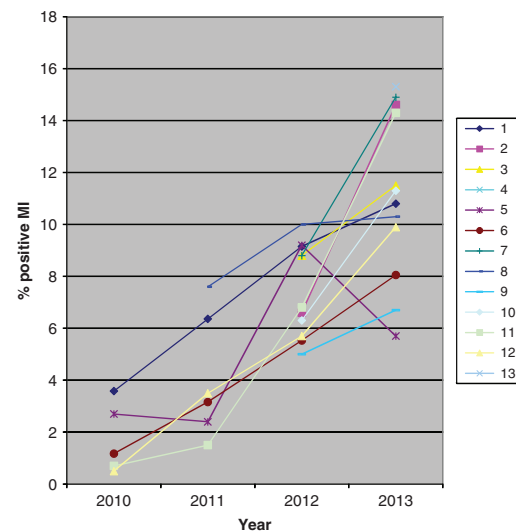
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Table 1. Number of patients tested with, and number of patients with a positive patch test reaction to, methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) and MI in participating centres from January 2010 to June 2013

	Patients tested MCI/MI	Patients positive MCI/MI	% positive	Patients tested MI	Patients positive MI	% positive
2010	3185	130	4.3	2279	38	1.7
2011	4368	220	5.3	2543	125	2.9
2012	4612	275	5.8	4984	383	7.1
2013	2033	169	8.3	2786	295	11.1

**Fig. 1.** Percentage of patients with a positive patch test reaction to methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) and MI in participating centres from January 2010 to June 2013.**Fig. 2.** Percentage of patients with a positive patch test reaction to methylisothiazolinone (MI) by year in participating centres. Line numbers refer to the centres in the text.

Discussion

Our data for 2010 and 2013 confirm the sudden and large increase in the frequency of MI contact allergy. Although different patch test concentrations of MI were used in the various centres, 2000 ppm MI is now recommended for the European baseline series (3).

Although allergic contact dermatitis to MI resulting from wall paint and household products has been reported (4, 5), the majority of our cases appear to be caused by cosmetics (Williams et al., submitted for publication). This is consistent with another recent report on MI allergy from Australia, in which the majority of cases were related to exposure to MI in cosmetics (6).

The 'safe' levels of MI permitted in rinse-off and leave-on products were determined from a safety dossier provided to the Scientific Committee on Cosmetic Products and Non-food Products of the European Commission (7). This included data from animal and human testing available at the time of assessment. In some of the human testing, patch test concentrations of MI used for elicitation were

suboptimal (e.g. 100 ppm MI aq.). In addition, a local lymph node assay study showing that MI had an EC3 of 0.4%, classifying it as a strong sensitizer (8), was not included in the dossier submitted for review.

What does a frequency of > 10% in patch test clinics mean in terms of allergy prevalence in the general population? Certain epidemiological methods have been used to estimate the prevalence of contact allergy in the general population, extrapolating from contact clinic data, namely the 'clinical epidemiology' and 'drug utilization research' (CE-DUR) data (9). This tool estimates that an allergy frequency of 6% in patch test clinics would convert to a general population allergy prevalence of over 1/100 (medium case scenario) and an epidemic category of 'generalized'. Therefore, the prevalence of allergy to MI in the general population may be over 1%.

Frequency reports from elsewhere in Europe, although showing a recent increase in MI allergy, generally show a lower frequency than in the British Isles, and a prevalence that is still below 10% (10).

Why is the frequency of allergy to MI apparently higher in the British Isles than elsewhere in Europe? It is possible that this could be related to the test concentration of MI used and the organization of patch test clinics in the British Isles. Most British clinics have been testing MI at 0.2% aq., and the British health service referral system may make patch testing more accessible to patients. It is also possible that exposure factors may have an influence, with greater use in the British Isles of cosmetic products containing MI or greater use of moist tissues containing MI.

The last general outbreak of cosmetic allergy preservative was to methyl dibromo glutaronitrile, but the increase in frequency was much slower, and the frequency did not peak above 6% (11).

One working definition of an epidemic is 'the occurrence in a community or region of cases of an illness, specified health behaviour, or other health-related events clearly in excess of normal expectancy' (12).

By this definition, the current increased frequency of MI contact allergy represents an epidemic. Urgent intervention is needed.

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