

Chloromethylisothiazolinone/Methylisothiazolinone, still a prevalent allergen causing Contact Dermatitis

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Introduction

Isothiazolinones are heterocyclic compounds used as biocides (Fig.1). Five derivatives are used in significant amounts: Methylisothiazolinone (MIT,MI), Chloromethylisothiazolinone (CMIT,CMI,MCI), Benzisothiazolinone (BIT), Octylisothiazolinone (OIT,OI), Dichlorooctylisothiazolinone (DCOIT,DCOI), Butylbenzoisothiazolinone (BBIT).

Isothiazolinones are antimicrobials used to control bacteria, fungi and algae in cooling water systems, fuel storage tanks, pulp and paper mill water systems, oil extraction systems, wood preservation and antifouling agents. They are frequently used in personal care products such as shampoos and other hair care products, as well as certain water-based paints formulations. There, often combinations of MIT and CMIT or MIT and BIT are used.¹

Kathon CG is a 3:1 mixture of MIT (1.125%) and MCI (0.375%) with magnesium nitrate and magnesium chloride as stabilizers (23%) and water (75.5%). Initially, using RIPT test no sensitization was observed at 10, 6 or 5 ppm (n=1121) or at 15 ppm (n=200).² From January 1990, cosmetics products in the EEC should not contain more than 15 ppm. MCI/MIT ratio is disturbed in the 73% of the Kathon-CG-preserved "leave on" cosmetics.³ MCI is significantly stronger sensitizer than MIT and BIT.⁴

MCI/MI (100 ppm) was included at the EECDRG and ESCD recommended standard patch test serie at the 1980s. At that time, positive MCI/MI positive patch test prevalence reported was 0.4-8.4.⁵ Recently, the European Surveillance System of Contact Dermatitis reported a prevalence of positive MCI/MI patch test of 2.22% during the 2004 year.⁶ Formaldehyde and MCI/MI had the highest positivity rates of positive patch test at 2% in UK (2004-5).⁷ MCI showed a 3.4% of positive reactions (1998-2004) in Tel Aviv.⁸

The actual MCI/MI patch test at 100 ppm shows high concordance rate of positive results among allergen providers⁹ and high persistence of positive reaction through years¹⁰. Nevertheless an increase of the MCI/MI patch test concentration to 200 ppm will be recommended by Magnus Bruze group from Sweden. MCI/MI as biocide is still widely used. The total number of chemical products preserved with MCI/MI on Swiss market, for instance, is about 6000.¹¹

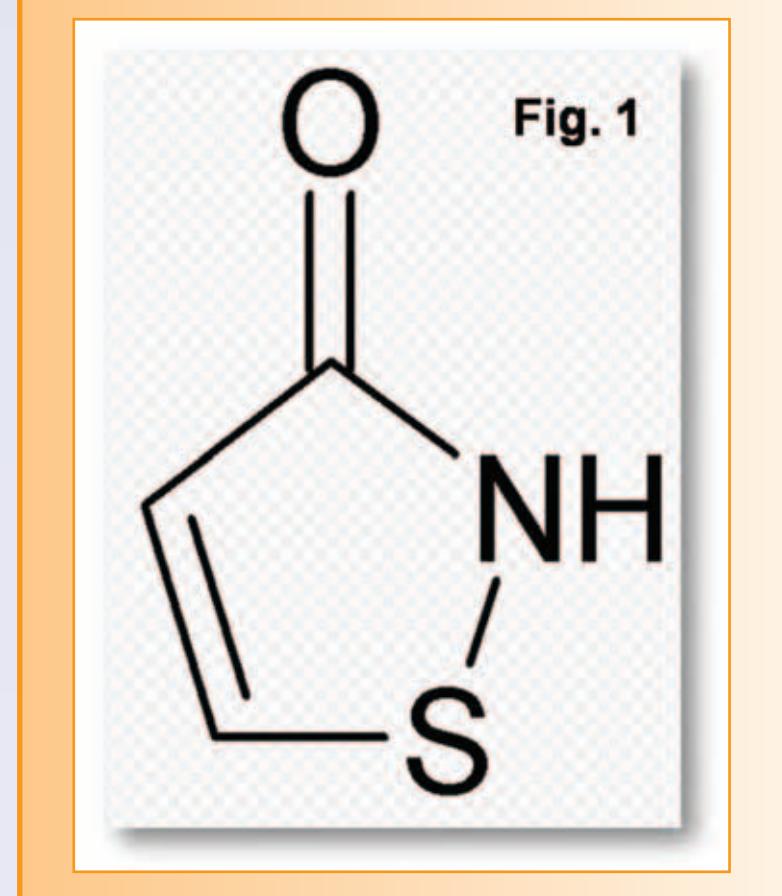


Fig. 1

Objective

The prevalence of positive patch test reaction to MCI/MI in the Dermatology Department at the Hospital del Mar, IMAS Barcelona (Spain) from 2004 to 2006 was 4.25, twice as high as the average 2004 ESSCA reported prevalence. Thus we performed an in depth analysis of our patients with MCI/MI contact dermatitis between 2004-2007, analyzing the population characteristics and trying to identify possible sources of exposure.

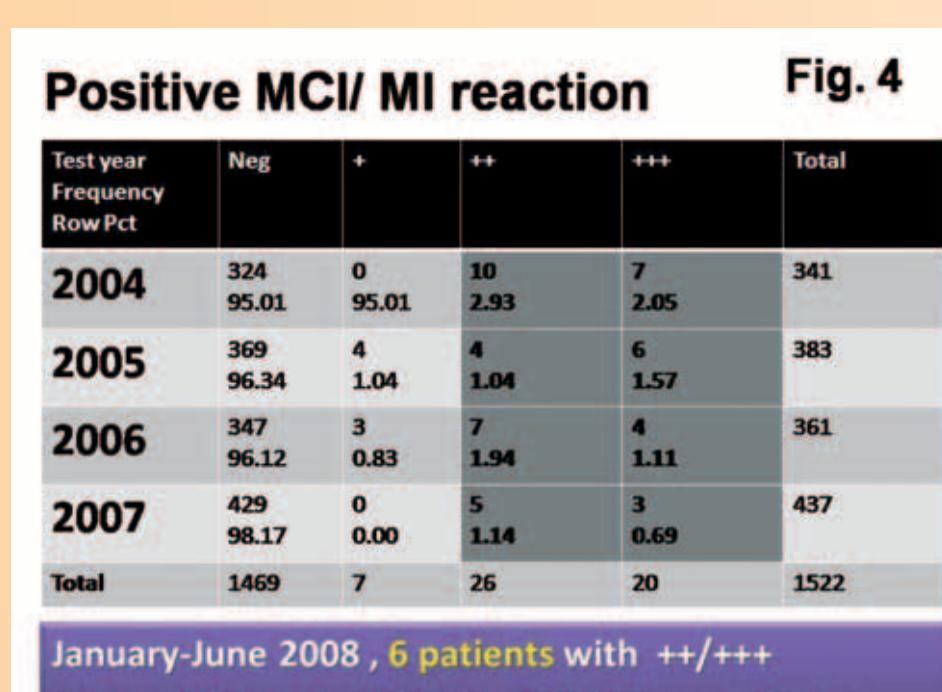
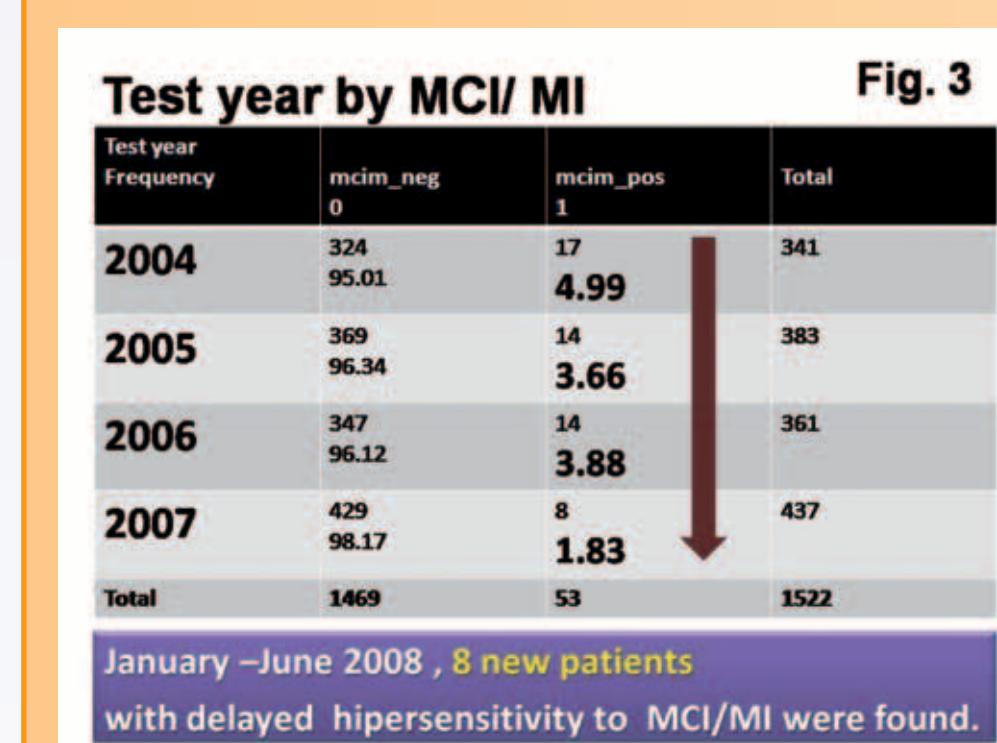
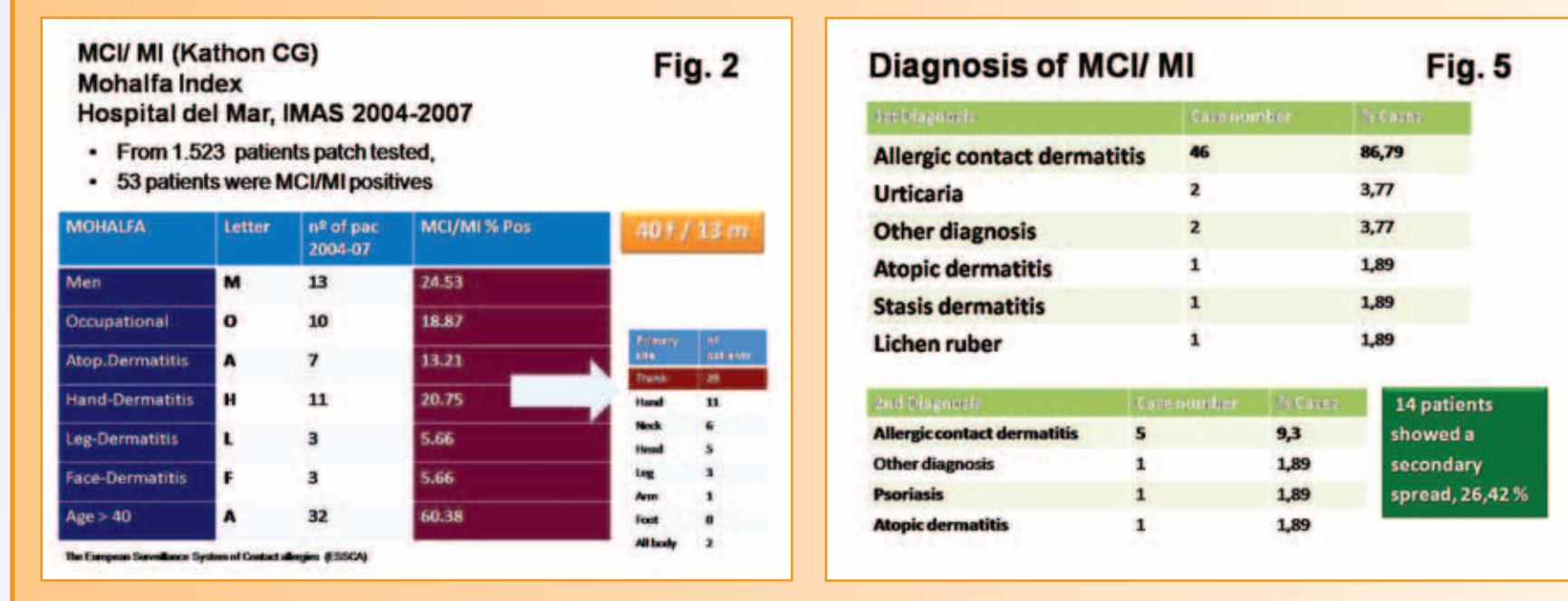
Material and methods

Patients who attended the Contact Dermatitis Clinic at the Hospital del Mar, Barcelona (Spain) from January 2004 to December 2007 were patch tested following the recommendations of the European Society of Contact Dermatitis and the Environmental Contact Dermatitis Research Group. MCI/MI allergen (100 ppm in water) was provided by Hermal-Almirall. Data were recorded in the Spanish version of the multilingual "WinAlldat/ESSCA" software (www.essca-dc.org). Data analysis followed current guidelines using SAS(tm) statistical software (ver.9.1,SAS Institute,Cary,NC).¹

Results

From 1522 tested patients 53 (3.4%) showed a positive MCI/MI patch test. The MOHALFA index (Fig.2), the prevalence of MCI/MIT positive patch tests per year (Fig.3), also subdivided for weak, moderate and severe positive reactions (Fig.4) were calculated. Gender ratio was 40 females/13 males and the most frequent primary site affected was the trunk. The percentage of atopic dermatitis did not differ from the percentage observed when we consider all the positive standard patch test reactions. While the drop of MCI/MI positive reactions in 2007 seems to indicate a downward trend, it must be noted that from January to 30 June 2008 alone, 8 new patients with delayed hypersensitivity to MC/MIT were identified in our Department and higher number in 2008 is to be expected. The most frequent primary diagnosis was allergic contact dermatitis. (Fig.5) Some unusual clinical presentation such as i.e. atypical lymphocytic infiltrate must be considered.

We had the opportunity of diagnose a MCI/MI allergy in two patients with a presumptive diagnosis of cutaneous T cell lymphoma even with clonal TCR rearrangement who were free of symptoms after allergen avoidance. (Fig.6) From the 53 patients with MCI/MI positive patch test reaction, 34 patients (10 female/9 male) showed multiple sensitization and 19 showed just one sensitization with regard to other standard series allergens. The most frequent common concomitant detected allergens were nickel sulphate, cobalt chloride, and formaldehyde. Female patients also showed fragrance mix, Balsam of Peru, p-phenylenediamine whereas male patients showed thiuram, thiomersal and carba mix as concomitant positive reactions. A 18.87% of cases disclosed past or present occupational relevance. Architecture, paint, maintenance machines, textile and nursing workers were mainly affected. The most frequent contact allergy were leave on cosmetics products, rinse of products and cleaning agents.



Conclusions

1. Sources of MCI/MI exposure continue to be broad, in the industry and also in final products exposing many consumers.
2. From 1522 tested patients, 53 (3.4%) showed a positive MCI/MI patch test.
3. Unusual clinical cutaneous presentations i.e. atypical lymphoid infiltrate must be taken into account in exceptional cases.
4. To control of isothiazolinone exposure continues to be a challenge.

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