Abstracts of references

1. Contact Dermatitis. 2015 Sep;73(3):150-6. doi: 10.1111/cod.12413.
Occupational contact allergy to methylchloroisothiazolinone/ methylisothiazolinone and methylisothiazolinone.
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BACKGROUND: Methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) and MI are common preservatives in industrial and household products and in cosmetics. Occupational contact allergy to MCI/MI or MI has been reported among painters and paint factory workers in particular.
OBJECTIVES: To retrospectively describe patients with occupational contact allergy to MCI/MI and MI at the Finnish Institute of Occupational Health (FIOH).
METHODS: Patch test files and clinical records of patients examined at the FIOH between January 2002 and February 2013 were reviewed to identify the patients.
RESULTS: Seventy-two of 1745 patients showed positive reactions to MCI/MI and/or MI. Of these, 36 were occupational cases, and 31 were diagnosed during the second half of the study period. Hairdressers and beauticians, mechanics and repairmen, and machinists were the most significant occupational groups, followed by painters and paint factory workers, and café and restaurant workers.
CONCLUSIONS: We observed a sixfold increase in the number of occupational cases in the second half of the study period as compared with the first half. Liquid soaps and industrial hand cleansers were common sources of exposure to MCI/MI or MI. A total of 33% of the patients used products without any mention of MCI/MI or MI in safety data sheets or product declarations.

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2. Contact Dermatitis. 2011 Jan;64(1):49-53. doi: 10.1111/j.1600-0536.2010.01811.x.
Contact sensitization to methylisothiazolinone in Finland--a multicentre study.
Ackermann L(1), Aalto-Korte K, Alanko K, Hasan T, Jolanki R, Lammintausta K, Lauerma A, Laukkanen A, Liippo J, Riekki R, Vuorela AM, Rantanen T.
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BACKGROUND: Antimicrobials constitute the second most common cause of contact allergy to cosmetics. Methylisothiazolinone (MI), previously always used together with methylchloroisothiazolinone (MCI), has recently been approved in the EU for use on its own in cosmetics and also various industrial products. MCI has been classified as an extreme-strong and MI as a strong-moderate sensitizer.
OBJECTIVES: To study the frequency of positive patch test reactions to MI, and its relevance and relation to MCI/MI sensitivity, in Finland.
METHODS: Over a period of 3 years (2006-2008), MI 0.1% (1000 ppm) and 0.03% (300 ppm) were patch tested in 10,821 patients at eight Finnish

dermatological clinics. During 2008, patients with positive reactions to MI were asked to take part in a repeated open application test (ROAT).
RESULTS: Of the patients tested, 1.4% and 0.6% showed positive patch test reactions to 0.1% and 0.03% MI, respectively. Sixty-six per cent of those who were MI-positive were also positive to 100 ppm MCI/MI. Thirty-three agreed to undergo the use test, and 10 of these gave positive results (30%).
CONCLUSIONS: Our data show that MI used alone also potentially induces contact allergy. Careful monitoring is needed to determine whether or not this antimicrobial is safe to use in cosmetics.

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3. Br J Dermatol. 2015 Jul;173(1):115-22. doi: 10.1111/bjd.13751.
Methylisothiazolinone in rinse-off products causes allergic contact dermatitis: a repeated open-application study.
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BACKGROUND: In recent years, the prevalence of contact allergy to the preservative methylisothiazolinone (MI) has increased dramatically. Cosmetic products are one of the major sources of exposure.
OBJECTIVES: To examine whether allowed concentrations of MI in cosmetic rinse-off products have the potential to cause allergic contact dermatitis.
METHODS: Nineteen MI-allergic subjects and 19 controls without MI allergy applied,two liquid hand soaps five times per day on areas of 5 × 10 cm(2) on the ventral side of their forearms. One soap contained 100 ppm MI, the maximum allowed concentration in cosmetics, and was used by 10 allergic subjects and all controls. Another liquid soap with 50 ppm MI was used by nine allergic subjects. As the negative control, all subjects used a similar soap that did not contain MI. The repeated open applications proceeded until a positive reaction occurred or up to 21 days. The study was conducted in a randomized and blinded fashion.
RESULTS: Ten out of 10 MI-allergic subjects developed positive reactions to the soap with 100 ppm and seven out of nine reacted to the 50 ppm soap, while none of the 19 controls had a positive reaction during 21 days of application. No reactivity was seen to the soap without MI. The difference in reactivity to MI between MI-allergic subjects and controls was statistically significant (Fisher's exact test, $P < 0{\cdot}0001$).
CONCLUSIONS: Rinse-off products preserved with 50 ppm MI or more are not safe for consumers. No safe level has yet been identified.

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5. Contact Dermatitis. **2015** Mar;72(3):127-38. doi: 10.1111/cod.12322.
Methylisothiazolinone and benzisothiazolinone are widely used in paint: a multicentre study of paints from five European countries.

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BACKGROUND: In view of the current epidemic of contact allergy to methylisothiazolinone (MI), it is important to clarify the extent of use of MI and related isothiazolinones in paints currently available for the consumer and worker in Europe.
OBJECTIVES: To elucidate the use and concentrations of MI, methylchloroisothiazolinone (MCI) and benzisothiazolinone (BIT) in paints on the European retail market.
METHODS: Wall paints (n = 71) were randomly purchased in retail outlets in five European countries. The paints were quantitatively analysed for their contents of MI, MCI and BIT by high-performance liquid chromatography coupled to tandem mass spectrometry.
RESULTS: MI was found in 93.0% (n = 66) of the paints, with concentrations ranging from 0.7 to 180.9 ppm, MCI in 23.9% (n = 17), ranging from 0.26 to 11.4 ppm, and BIT in 95.8% (n = 68), ranging from 0.1 to 462.5 ppm. High concentrations of MI were found in paints from all five countries. Paints purchased in Denmark and Sweden contained especially high concentrations of BIT.
CONCLUSION: The use of MI across European countries is extensive. In view of the ongoing epidemic of MI contact allergy, an evaluation of the safety of MI in paints is needed.

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6. Contact Dermatitis. 2012 Nov;67(5):293-7. doi: 10.1111/j.1600-0536.2012.02074.x.
Occupational contact dermatitis in painters: an analysis of patch test data from the Danish Contact Dermatitis Group.
Mose AP(1), Lundov MD, Zachariae C, Menné T, Veien NK, Laurberg G, Kaaber K, Avnstorp C, Andersen KE, Paulsen E, Mørtz CG, Sommerlund M, Danielsen A, Thormann J, Kristensen O, Kristensen B, Andersen BL, Vissing S, Nielsen NH, Johansen JD.
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BACKGROUND: Painters are among the occupational groups that most commonly experience occupational contact dermatitis, but few investigations exist concerning this occupation.
OBJECTIVES: To characterize painters with contact dermatitis and identify the most common allergens associated with the occupation. Materials and methods. All patch test results of 219 painters and 1095 matched controls registered by the Danish Contact Dermatitis Group between 2001 and 2010 were analysed.
RESULTS: Hand eczema ($p < 0.0001$) and occupational contact dermatitis ($p < 0.0001$) were observed significantly more often in the painters than in the group of controls. Sensitizations to the following allergens from the European baseline series were associated with the occupation and were statistically significant:
methylchloroisothiazolinone/methylisothiazolinone, epoxy resin, formaldehyde, and quaternium-15. Three different isothiazolinones emerged as the most frequent sensitizers of the allergens tested in addition to the baseline series.

CONCLUSIONS: The results indicate that painters have an increased risk of developing occupational hand eczema. Isothiazolinones and epoxy resin proved to be the two most frequent sensitizers in painters.

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7. Contact Dermatitis. **2011** Jun;64(6):330-6. doi: 10.1111/j.1600-0536.2011.01901.x.
Methylisothiazolinone contact allergy and dose-response relationships.
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BACKGROUND: Methylisothiazolinone (MI) used alone is a new preservative causing a high prevalence of contact allergy. The eliciting threshold of MI is unknown. The combination of MI and phenoxyethanol enhances the antimicrobial efficacy of MI.
OBJECTIVES: The eliciting doses of MI contact allergy in a patch test and a repeated open application test (ROAT) were investigated. In the patch test, it was determined whether phenoxyethanol influenced the reactivity to MI.
METHODS: Eleven MI-allergic individuals were patch tested with two dilution series of 12 doses of MI and the same 12 doses with phenoxyethanol. The ROAT mimicked the use of a cream preserved with 100, 50 and 5 ppm MI (corresponding to 0.21, 0.105 and 0.0105 µg MI/cm(2)).
RESULTS: Phenoxyethanol had no influence on the reactions to MI. The lowest eliciting dose in the patch test was 1.47 µg MI/cm(2). In the ROAT, 7 patients (64%) reacted to 0.21 and 0.105 µg MI/cm(2) and 2 patients (18%) reacted to
0.0105 µg MI/cm(2), corresponding to a cream preserved with 5 ppm MI.
CONCLUSIONS: A maximum of 100 ppm MI is permitted in cosmetic products. Eighteen per cent of MI-allergic patients reacted to a concentration 20 times lower in a
ROAT. The amounts used in cosmetics should be reduced, and the development of MI contact allergy should be monitored closely.

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8. Contact Dermatitis. **2010** Sep;63(3):164-7. doi: 10.1111/j.1600-0536.2010.01774.x.
Prevalence and cause of methylisothiazolinone contact allergy.
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BACKGROUND: Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) has been one of the most frequent sensitizers since the 1980s. In 2005, the use of MI alone was approved for the preservation of cosmetic and household products in the EU. Before that, MI was used in industrial products, and the first cases of isolated MI contact allergy were published.
OBJECTIVES: To present the prevalence and causes of MI contact allergy.
MATERIALS AND METHODS: Patch test results from 2536 dermatitis patients tested with MI at Gentofte University Hospital between May 2006 and February 2010 were analysed. A retrospective investigation of medical

records from MI-allergic patients was performed to reveal the causes of their MI contact allergy.
RESULTS: Of patch-tested patients, 1.5% had MI contact allergy. It was associated with occupational dermatitis, hand eczema and age above 40 years. Exposure to MI in cosmetic products was found in 12 (32%) cases, and exposure to MI in occupational products was found in 11 (30%) cases; 5 of the 11 were painters.
CONCLUSIONS: The prevalence of MI contact allergy is already at the same level as that of other sensitizing preservatives, which have been on the market for several years, but no rising trend was identified. MI contact allergy was associated with both occupational and consumer products.

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9. Contact Dermatitis. 2014 Dec;71(6):348-55. doi: 10.1111/cod.12277.
Occupational contact dermatitis in blue-collar workers: results from a multicentre study from the Danish Contact Dermatitis Group (2003-2012).
Schwensen JF(1), **Menné** T, Veien NK, Funding AT, Avnstorp C, Østerballe M, Andersen KE, Paulsen E, Mørtz CG, Sommerlund M, Danielsen A, Andersen BL, Thormann J, Kristensen O, Kristensen B, Vissing S, Nielsen NH, Thyssen JP, Johansen JD.
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BACKGROUND: Blue-collar workers have a high risk of occupational contact dermatitis, but epidemiological studies are scarce.
OBJECTIVES: To investigate allergic contact dermatitis in blue-collar workers with dermatitis registered by the Danish Contact Dermatitis Group.
METHODS: A retrospective analysis of patch test data from 1471 blue-collar workers and 1471 matched controls tested between 2003 and 2012 was performed. A logistic regression was used to test for associations.
RESULTS: The blue-collar workers often had occupational hand dermatitis ($p < 0.001$). Atopic dermatitis was less commonly observed among blue-collar workers (19.6%) than among controls (23.9%) ($p = 0.005$). Allergens with a statistically significant association with the occupational group of blue-collar workers were epoxy resins, methyldibromo glutaronitrile, 2-bromo-2-nitro-1,3-propanediol, potassium dichromate, and methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI). The following occupations were additionally identified as risk factors for contact sensitization to MCI/MI and MI, epoxy resins, and potassium dichromate, respectively: painting, construction work, and tile setting/terrazzo work.
CONCLUSION: Contact allergy is a major problem among blue-collar workers. The data indicate a healthy worker effect among blue-collar workers diagnosed with dermatitis, as blue-collar workers were diagnosed significantly less often with atopic dermatitis than were controls.

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10. Contact Dermatitis. 2013 Oct;69(4):231-8. doi: 10.1111/cod.12123. Epub 2013 Jul 27.
Risk factors associated with methylisothiazolinone contact sensitization.
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BACKGROUND: The preservative methylisothiazolinone (MI) has become an important allergen, with a dramatic increase in sensitization prevalence being seen over the last few years.
OBJECTIVE: To examine risk factors associated with MI sensitization, in order to identify targets of prevention aimed at curtailing the present epidemic.
METHODS: On the basis of contact allergy surveillance data collected by the Information Network of Departments of Dermatology (www.ivkd.org), 2009-2012, in the course of 28,922 patch tests with MI, 500 ppm in water, included in a series of cosmetic preservatives, logistic regression analysis was employed to quantify the risk associated with a number of putative risk factors.
RESULTS: The prevalence of MI sensitization increased from 1.94% in 2009 to 6.02% in 2012, the increase being mainly driven by female patients aged≥40 years,
patients with face dermatitis, and the use of cosmetics. Adjusted multifactorial analysis additionally identified several occupations (e.g. painters and beauticians) and ano-genital dermatitis as risk factors for MI sensitization.
CONCLUSIONS: The present use concentrations of MI, both cosmetic and industrial, are too high; (self-)regulatory action is urgently needed. MI should be added to the baseline series.

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