

CASE REPORT

Polysensitisation in a laboratory scientist associated with allergic contact dermatitis from methylisothiazolinone in skin cleansers

Matthew J Palmer and Rosemary Nixon

Occupational Dermatology Research and Education Centre, Skin and Cancer Foundation, Melbourne, Victoria, Australia

ABSTRACT

Polysensitisation refers to reactivity to three or more allergens on epicutaneous patch testing, and is likely to affect a distinct subgroup of individuals with allergic contact dermatitis (ACD). Methylisothiazolinone (MIT) is an increasingly prevalent allergen, recently having been described as occurring in epidemic proportions. We report a patient with ACD to 12 allergens, including MIT, and discuss the implications of polysensitisation and the likely need for repeat patch testing in such patients if they subsequently re-present with dermatitis.

Key words: allergy, hand eczema, moisturising cream, patch testing, preservative.

INTRODUCTION

Polysensitisation refers to reactivity to three or more allergens on epicutaneous patch testing, and is likely to affect a distinct subgroup of individuals with allergic contact dermatitis (ACD).¹ Methylisothiazolinone (MIT) is an increasingly prevalent allergen, which has recently been described as occurring in epidemic proportions.² We report a patient with ACD to 12 allergens, including MIT, and discuss the implications of polysensitisation and the likely need for repeat patch testing in these patients if they subsequently re-present with dermatitis.

CASE REPORT

A 52-year-old laboratory scientist was referred for patch testing with a 5-year history of hand dermatitis that started on her palms and then spread to involve the dorsal aspects of both hands. She described swelling of her hands and itchy blisters on her fingers. Several months preceding this she had also developed a facial rash, which had resolved. The patient worked for a mining company and in particular was involved in testing limestone pyrites. She regularly wore powder-free latex gloves, often with cotton gloves underneath to reduce associated pruritus, and used disposable nitrile or rubber gloves for domestic chores.

There was no significant improvement in her condition during her time off work. Treatment with betamethasone dipropionate cream led to an initial improvement, but her condition soon recurred. She applied a moisturising cream to her hands and used skin cleansers at home and at work.

She had no definite history of eczema, though she did describe an undiagnosed widespread rash for a 6-month period in 2005. She had a history of seasonal allergic rhinitis and thought she might be allergic to nickel and perfume. An initial examination revealed mild erythema and scaling on the palms, with a discoid eczematous patch on her right lateral calf and eczematous patches on her right lateral back and the left side of her face. Epicutaneous patch testing was performed and elicited a surprising number of positive reactions (Table 1). A radioallergosorbent test to latex was negative.

MIT was found to be present in the Soft Care Dermawash Aloe Vera Hand Wash (Diversey, Sydney, New South Wales, Australia) she used at work, as well as in the Cetaphil Restoraderm Skin Restoring Body Wash (Galderma, Sydney, New South Wales, Australia) she used at home.

Abbreviations:

ACD	allergic contact dermatitis
AD	atopic dermatitis
IOBC	iodopropynyl butylcarbamate
MCI	methylchloroisothiazolinone
MIT	methylisothiazolinone

Correspondence: Dr Matthew J Palmer, Skin and Cancer Foundation, Level 1, 80 Drummond Street, Carlton, Vic 3053, Australia. Email: matthewpalmer@hotmail.com
Matthew J Palmer, MBBS. Rosemary Nixon, FACD.
Conflict of interest: none.
Submitted 11 January 2014; accepted 15 February 2014.

Table 1 Patch testing results showing 12 positive reactions. Methylisothiazolinone was subsequently identified as the most relevant allergen

Allergen	Result
Nickel sulphate	+++
Iodopropynyl butylcarbamate	++
Methylisothiazolinone	+
Methylchloroisothiazolinone	++
Methyldibromo glutaronitrile	+
Fragrance mix 1	+
Fragrance mix 2	+
Lyrall	+
<i>Myroxylon pereirae</i> (formerly Balsam of Peru)	+
Potassium dichromate	+
Cobalt chloride	+
Formaldehyde	Doubtful reaction
Olay cleanser	Doubtful reaction
Redwin Sorbolene cream	Doubtful reaction
Sorbolene hand wash	Doubtful reaction

+++ extreme reaction; ++ strong positive; + weak positive.

Iodopropynyl butylcarbamate (IOBC) was present in her Olay Foaming Face Wash Combination/Oily Skin (Procter & Gamble, Cincinnati, OH) and formaldehyde releaser imidazolidinyl urea in her Redwin Sorbolene moisturiser (PharmaCare Laboratories, Sydney, New South Wales). Unspecified fragrances were present in a number of the products she used. No definite current exposures to nickel, Lyrall (International Flavors & Fragrances, New York, USA) or *Myroxylon pereirae* were identified, while reactions to potassium dichromate, cobalt and methyldibromo glutaronitrile were of unknown relevance.

The following diagnoses made were:

- 1 ACD to MIT present in the hand wash used at work and in the body wash used at home
- 2 ACD to IOBC in facial cleanser
- 3 ACD to fragrance in several perfumed products, including a hair care product
- 4 ACD to formaldehyde (although a doubtful reaction) from the formalin-releaser imidazolidinyl urea in the Redwin Sorbolene cream (which also caused a doubtful reaction)
- 5 Contact allergy to nickel, of past relevance from exposure to cheap jewellery
- 6 Contact allergy to *M. pereirae*; which often cross-reacts with fragrance and was probably of old relevance
- 7 Contact allergy to chromate, methyldibromo glutaronitrile and cobalt, all of unknown relevance

Some 6 months after attending the clinic, the patient reported that her skin condition was much improved.

DISCUSSION

Polysensitisation refers to the phenomenon where patients demonstrate multiple contact allergies on patch testing, and it has been defined as an allergy to three or more allergens.¹ Approximately 5% of patients with ACD demonstrate

polysensitisation.¹ This must be distinguished from the angry back syndrome in which hyper-reactive skin or a strongly positive patch test nearby causes false-positive results.⁵

The development of contact allergy is dependent on two main factors: individual susceptibility and exposure to sensitising allergens.¹ Exposure to multiple allergens, such as may occur in an occupational setting, increases the risk of developing polysensitisation. The reason that individuals develop polysensitisation is not yet well established, although they can be divided into two groups: those who are more susceptible, and those who have high-risk exposures with or without pre-existing increased susceptibility.¹ Susceptibility is probably associated with as-yet unidentified genetic factors and, therefore, polysensitisation should be considered to be a phenotype of ACD. An association has been found between polysensitisation and contact allergy to a weak sensitiser, with approximately twofold to fourfold the risk of polysensitisation compared with sensitisation to a strong sensitiser.⁴

In the European Standard series, nickel sulphate, fragrance mix and *M. pereirae* have the highest incidence of duplet allergen association,¹ and in one European study of patients with polysensitisation 49% were allergic to fragrance mix I, 44% were allergic to nickel sulphate, and 35% were allergic to *M. pereirae*.⁴ These allergies were all present in our patient. The association between nickel allergy and polysensitisation seemingly exists because nickel allergy is so common: 40% of *M. pereirae*-allergic patients and 31% of fragrance mix I-allergic patients exhibited polysensitisation, compared to only 18% of nickel-allergic patients.⁴ There are no identified individual allergens that predict the risk of polysensitisation. However, seven allergens have been shown to have a statistically significant association with polysensitisation: sesquiterpene lactone mix, parabens mix, isopropylaminodiphenylamine, wool alcohols, *M. pereirae*, potassium dichromate and cobalt chloride. Mercapto-mix allergy has also been shown to occur more frequently in association with other allergens than as a single allergen.⁴

Five allergens have been shown to have significant negative association with polysensitisation: neomycin sulphate, p-phenylenediamine, epoxy resin, primin and nickel sulphate.⁴

Risk factors associated with development of polysensitisation include cumulative environmental exposure to sensitising allergens, increasing age, pre-existing venous stasis dermatitis or leg ulcers, and atopic dermatitis (AD), particularly in women.¹ Carlsen and colleagues demonstrated in 2009 that of polysensitised individuals, 45% were women with AD, compared to 31% of single or dual sensitised patients, 40% of patients with polysensitisation suffered persistent AD, compared to 25% of single or dual sensitised patients and 88% of polysensitised patients have suffered AD at some point, compared to 86% of single or dual sensitised patients.⁵ This fits with a recent study suggesting AD is associated with contact allergy, particularly to metals,⁶ and highlights the importance of patch testing in patients with persistent and severe AD.

Polysensitisation also has important implications for people diagnosed with ACD who then experience a new presentation of dermatitis. Repeat patch testing is likely to be of value, as those with previous or existing ACD are more susceptible to the development of additional allergies. One study showed that additional relevant allergens were identified in 63% of patients referred for repeat patch testing.⁷ It may thus be considered that individuals with contact allergy have a proven ability to acquire contact allergy, and therefore have an increased risk of developing polysensitisation. Repetitive occupational exposure to sensitising allergens, as seen in tradespeople, labourers, health-care workers, hairdressers and beauty therapists, increases the risk of ACD: this probably confers a higher risk of developing polysensitisation.

We have recently reported on our experience with ACD to the preservative MIT, particularly from exposures to baby wipes, skin cleansers and deodorants.⁸ MIT and methylchloroisothiazolinone (MCI) were developed in the 1960s and first used in cosmetics in Europe in the 1970s, with the first contact allergy cases associated with cosmetics having been reported in 1985.⁹ MIT is the non-halogenated derivative of isothiazolinone and was used as a sole agent in industrial products prior to its approval for domestic use. The first cases of occupational ACD from paint exposure were reported in 2004.¹⁰ In 2005 MIT was approved for use as a preservative in cosmetics and household products.¹¹ The first non-occupational cases were published in August 2010 and consisted of seven patients sensitised to cosmetic products including make-up remover and sanitary wipes.¹² It would appear that MIT was initially considered to be a weaker sensitizer than MCI, however, that information may be incorrect.¹⁵ Allergy to MIT is dramatically increasing worldwide, from under 1–2% between 2006 and 2009 to 4% in 2011.¹⁴ The American Contact Dermatitis Society named MIT as their allergen of the year in 2013.¹⁵ Approximately 10% of patients tested in our clinic in 2013 have shown positive reactions to MIT (R Nixon, unpublished data 2013). There has been great concern worldwide about the increasing prevalence of allergy to MIT.²

ACD to MIT is associated with occupational dermatitis, hand dermatitis, age >40 years and female sex,¹⁶ all of which were relevant in this case.

In conclusion, polysensitisation is an important condition to recognise. Polysensitisation is associated with persistent AD, especially in women, and patch testing should be considered in such patients. Repeat patch testing should be considered if patients have a history of ACD and then

present with new clinical symptoms suggestive of contact dermatitis. MIT is currently a significant cause of ACD in our clinic as well as in Europe, and practitioners should be alert for exposure to this important allergen.

REFERENCES

1. Carlsen BC, Andersen KE, Menne T *et al.* Patients with multiple contact allergies: a review. *Contact Dermat.* 2008; **58**: 1–8.
2. Lundov MD, Opstrup MS, Johansen JD. Methylisothiazolinone contact allergy – a growing epidemic. *Contact Dermat.* 2013; **69**: 271–5.
3. Mitchell JC. The angry back syndrome: eczema creates eczema. *Contact Dermat.* 1975; **1**: 193–4.
4. Carlsen BC, Menne T, Johansen JD. Associations between baseline allergens and polysensitization. *Contact Dermat.* 2008; **59**: 96–102.
5. Carlsen BC, Andersen KE, Menne T *et al.* Characterization of the polysensitized patient: a matched case-control study. *Contact Dermat.* 2009; **61**: 22–30.
6. Malajian D, Belsito DV. Cutaneous delayed-type hypersensitivity in patients with atopic dermatitis. *J. Am. Acad. Dermatol.* 2013; **69**: 232–7.
7. Soni BP, Sherertz EF. Evaluation of previously patch-tested patients referred to a contact dermatitis clinic. *Am. J. Contact Dermat.* 1997; **8**: 10–4.
8. Boyapati A, Tam M, Tate B *et al.* Allergic contact dermatitis to methylisothiazolinone: exposure from baby wipes causing hand dermatitis. *Australas. J. Dermatol.* 2015; **54**: 264–7.
9. de Groot AC, Herxheimer A. Isothiazolinone preservative: cause of a continuing epidemic of cosmetic dermatitis. *Lancet* 1989; **1**: 314–6.
10. Isaksson M, Gruvberger B, Bruze M. Occupational contact allergy and dermatitis from methylisothiazolinone after contact with wallcovering glue and after a chemical burn from a biocide. *Dermatitis* 2004; **15**: 201–5.
11. Commission Directive 2005/42/EC of 20 June 2005. *Official Journal of the European Union.* 2005.
12. Garcia-Gavin J, Vansina S, Kerre S *et al.* Methylisothiazolinone, an emerging allergen in cosmetics? *Contact Dermat.* 2010; **65**: 96–101.
13. Roberts DW. Methylisothiazolinone is categorised as a strong sensitizer in the murine local lymph node assay. *Contact Dermat.* 2013; **69**: 261–2.
14. Geier J, Lessmann H, Schnuch A *et al.* Recent increase in allergic reactions to methylchloroisothiazolinone/methylisothiazolinone: is methylisothiazolinone the culprit? *Contact Dermat.* 2012; **67**: 334–41.
15. Castaneda-Tardana MP, Zug KA. Methylisothiazolinone. *Dermatitis* 2013; **24**: 2–6.
16. Uter W, Geier J, Bauer A *et al.* Risk factors associated with methylisothiazolinone contact sensitization. *Contact Dermat.* 2013; **69**: 251–8.