

CONTACT POINTS

Contact urticaria with anaphylaxis caused by chlorocresol, chloroxylenol, and thiourea

Sarah H. Mehrtens | Christine Reckling

Department of Dermatology, Kent and Canterbury Hospital, East Kent Hospitals University NHS Foundation Trust, Canterbury, UK

Correspondence

Dr Sarah H. Mehrtens, Department of Dermatology, Kent and Canterbury Hospital, Ethelbert Road, Canterbury, Kent, CT1 3NG, UK.

Email: smehrtens@doctors.org.uk

KEYWORDS: anaphylaxis, CAS no. 59-50-7, CAS no. 62-56-6, CAS no. 88-04-0 / 1321-23-9, case report, chlorocresol, chloroxylenol, contact urticaria, thiourea

Contact urticaria (CU) is defined as an immediate wheal-and-flare skin reaction following direct contact with a protein or chemical agent.^{1,2} CU has been described in association with numerous chemicals, including preservatives, antiseptics, fragrances, and medicaments.^{3–6} CU syndrome ranges from localized urticaria (stage 1) to anaphylactoid reactions with shock (stage 4).⁷ The exact mechanism of CU caused by chemicals is unknown, although it is thought most likely to be IgE-mediated. Prick tests have been shown to be useful for diagnosing CU caused by some chemicals, including chlorhexidine, chloramine-T, and isocyanates.⁸ We present a unique case of CU with anaphylaxis caused by chlorocresol (*p*-chloro-*m*-cresol, CAS no. 59-50-7), chloroxylenol (CAS no. 88-04-0/1321-23-9), and thiourea (CAS no. 62-56-6).

CASE REPORT

A 41-year-old woman presented with a 6-month history of recurrent urticaria, occasionally associated with angioedema, after using cleaning spray or washing-up liquid, and when unloading the dishwasher. Other triggers included mouthwash, tea-tree shampoo, and body spray. Additionally, the patient reported a persistent eczematous eruption on her left foot, with intermittent oedema affecting both feet after contact with rubber shoes. Treatment with topical creams, including Dermovate cream (clobetasol propionate 0.05%; Glaxo-SmithKline, Uxbridge, UK; excipients: cetostearyl alcohol, chlorocresol, and propylene glycol), Diprobace cream (Bayer, Reading, UK; excipients: chlorocresol, cetomacrogol, and cetostearyl alcohol), and Trimovate cream (clobetasone 17-butyrate 0.05%, calcium oxytetracycline 3.0%, and nystatin 100 000 units/g; Ennogen Healthcare, Dartford, UK; excipients: chlorocresol, cetostearyl alcohol, sodium metabisulfite), made things worse. The patient worked as a carer, and her only regular medication was omeprazole for hiatus hernia.

Histopathological examination of a biopsy from the left foot showed spongiosis and a mild perivascular lymphocytic infiltrate with eosinophils (Figure 1), in line with a hypersensitivity reaction as seen in allergic contact dermatitis (ACD).

The patient was patch tested with the British Society for Cutaneous Allergy (BSCA) baseline series, our extension to this, the BSCA medicament series, the BSCA footwear series, extended fragrances, and thiourea. Ultra IQ chambers (Chemotechnique Diagnostics, Vellinge, Sweden) were used with allergens also from Chemotechnique Diagnostics. The patient was observed within our department for 20 minutes, with no immediate reactions. However, on travelling home, she noticed widespread irritation and urticarial eruptions on the upper and lower back, requiring removal of all of the patches, with resultant relief in her symptoms. The patch tests were read on day 4, and were all negative.

The patient was retested, under observation, with haptens at these sites. The arms were used for rechallenge to separate the allergens widely, in view of the previous widespread reaction, to make interpretation more accurate, and also to make it easier for the patient to remove the patches at home if needed. Within 30 minutes, she became extremely distressed and unwell, developing wheals at three sites, namely, the chlorocresol, chloroxylenol and thiourea sites (Figure 2), with widespread urticaria and oedema. She complained of shortness of breath, and her pulse became weak, thready, and tachycardic. Her blood pressure then dropped, and her extremities became cold, clammy, and peripherally shut down, with reduced consciousness, indicating stage 4 CU syndrome.⁷ She was safely resuscitated with emergency anaphylaxis treatment including oxygen, two doses of adrenaline, and other intravenous medications, including fluids, chlorphenamine, and hydrocortisone. She was not brought back for readings, as the patch tests had been removed, but patient photographs on day 4 showed erythema at the chlorocresol and chloroxylenol sites. A diagnosis of

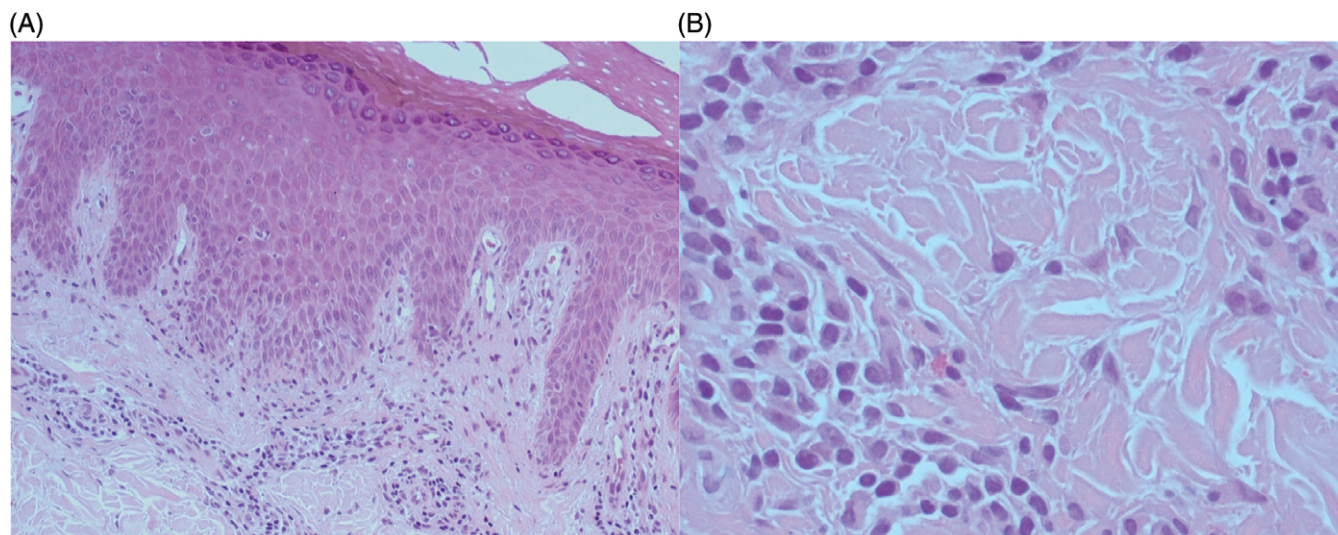


FIGURE 1 Histological examination of a biopsy taken from the left foot. (A), Medium magnification showing spongiosis and a mild perivascular lymphocytic infiltrate. (B), At high magnification, an eosinophil is visible. Haematoxylin and eosin, original magnification $\times 200$ (A) and $\times 400$ (B)

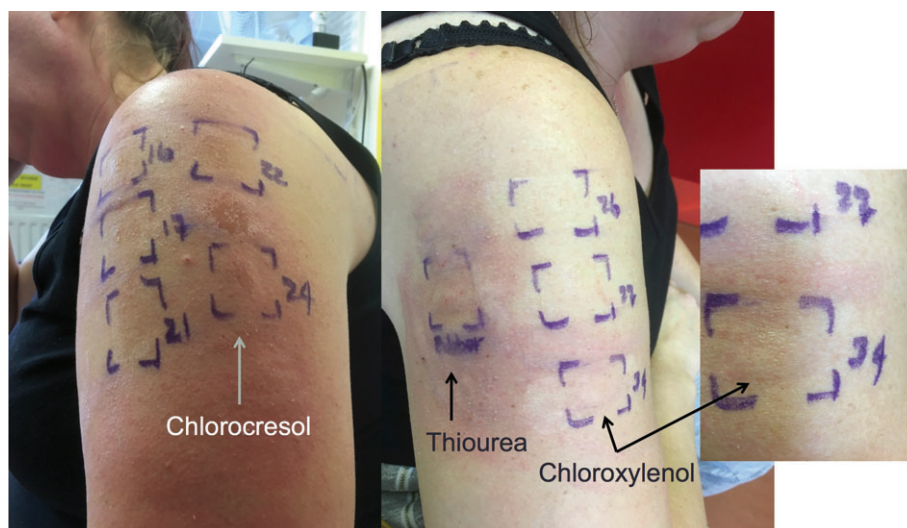


FIGURE 2 Photographs taken 30 minutes after the second series of patch testing. Wheals developed at three sites: chlorocresol, chloroxylenol, and thiourea. Erythema and oedema of the neck and face is also visible in these images

immediate hypersensitivity to chlorocresol, chloroxylenol and thiourea was made, with concomitant delayed hypersensitivity to chlorocresol and chloroxylenol. Blood tests showed normal immunoglobulins, including total IgE, nuclear antibodies, tryptase, and complement. The patient was given education on these allergens, regular antihistamines, and an adrenaline autoinjector. She finds this diagnosis extremely restrictive, as these allergens are present in many everyday products.

DISCUSSION

Chlorocresol is a well-recognized rare cause of ACD. CU caused by chlorocresol has been previously described in three case reports, but none of these cases developed severe reactions or anaphylaxis. The first reported case was of a woman working in an aviary, who complained of red swollen eyelids every time that she had to wash the chicken incubators.⁹ The second case reported was of a woman working in a pathology

laboratory who developed progressive eyelid oedema and conjunctivitis after entering the laboratory.¹⁰ The third case was of a woman presenting with severe pruritus and erythema after applying several emollients, steroid creams, perfumes, and cosmetics.¹¹

Chloroxylenol and thiourea are also well-recognized causes of ACD, but not of immediate hypersensitivity reactions. On reviewing the literature, we could not identify any previously reported cases of CU caused by chloroxylenol (although it can cross-react with chlorocresol) or thiourea.

In our case, chlorocresol and chloroxylenol were present in cleaning products, household antiseptics, and dishwashing cleaning fluid, and additionally in mouthwashes, a shampoo, and body sprays, explaining the patient's immediate symptoms after she used these products. Chlorocresol is found in Dermovate, Diprobate and Trimovate creams, explaining the localized dermatitis following application on the foot. As thiourea is a rubber accelerator, we speculate that her intermittent pedal oedema is caused by CU resulting from her wearing rubber shoes.

In conclusion, we report a unique case of life-threatening immediate hypersensitivity with anaphylaxis caused by chlorocresol, chloroxylenol, and thiourea, with concomitant delayed hypersensitivity to chlorocresol and chloroxylenol. Although this is a rare presentation and the exact mechanism is uncertain, the rapid development of anaphylactic shock and the immediate response to adrenaline suggest IgE-mediated immunological processes. Identification of these allergens has life-saving implications for our patient, and requires active avoidance measures in many aspects and activities of her daily life.

ACKNOWLEDGEMENTS

We thank Dr Brigid Maguire, Consultant Histopathologist at East Kent Hospitals NHS Foundation Trust, for providing the histology slides.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

ORCID

Sarah H. Mehrtens  <https://orcid.org/0000-0002-7335-6505>

Christine Reckling  <https://orcid.org/0000-0002-7487-3563>

REFERENCES

1. McFadden J. Immunologic contact urticaria. *Immunol Allergy Clin North Am*. 2014;34:157-167.
2. Wakelin SH. Contact urticaria. *Clin Exp Dermatol*. 2001;26:132-136.
3. Temesvári E, Németh I, Baló-Banga MJ, et al. Multicentre study of fragrance allergy in Hungary. *Contact Dermatitis*. 2002;46:325-330.
4. Verhulst L, Goossens A. Cosmetic components causing contact urticaria: a review and update. *Contact Dermatitis*. 2016;75:333-344.
5. Saito M, Nakada T. Contact urticaria syndrome from eye drops: levofloxacin hydrate ophthalmic solution. *J Dermatol*. 2013;40:130-131.
6. Özkaya E, Bozkurt PK. An unusual case of triclosan-induced immunological contact urticaria. *Contact Dermatitis*. 2013;68:121-123.
7. von Krogh G, Maibach HI. The contact urticaria syndrome—an updated review. *J Am Acad Dermatol*. 1981;5:328-342.
8. Helaskoski E, Suojalehto H, Kuuliala O, Aalto-Korte K. Prick testing with chemicals in the diagnosis of occupational contact urticaria and respiratory diseases. *Contact Dermatitis*. 2015;72:20-32.
9. Freitas JP, Brandão FM. Contact urticaria to chlorocresol. *Contact Dermatitis*. 1986;15:252.
10. Gonçalves M, Gonçalves S, Moreno A. Immediate and delayed sensitivity to chlorocresol. *Contact Dermatitis*. 1987;17:46-47.
11. Walker SL, Chalmers RJ, Beck MH. Contact urticaria to p-chloro-m-cresol. *Br J Dermatol*. 2004;151:936-937.

How to cite this article: Mehrtens SH, Reckling C. Contact urticaria with anaphylaxis caused by chlorocresol, chloroxylenol, and thiourea. *Contact Dermatitis*. 2019;80:311-313. <https://doi.org/10.1111/cod.13194>