

Allergic Contact Dermatitis to Chloroxylenol

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Chloroxylenol, also known as p-chloro-m-xyleneol (PCMX), is a compound that has been used as a preservative in cosmetics and as an active agent in antimicrobial soaps. We present two patients with allergic contact dermatitis from PCMX, confirmed by positive (+++) patch-test reactions at 48 and 72 hours, identification of PCMX in a soap and in a hand cream used by the patients, and improvement following withdrawal of the incriminating products. The mechanism of action, structure, antimicrobial activity, and dangers of PCMX are reviewed.

CHLOROXYLENOL, also known as p-chloro-m-xyleneol (PCMX), is a compound widely used as a preservative in cosmetics, as an active agent in antimicrobial soaps, and in electrocardiograph paste (Fig 1). It is increasingly found in liquid soaps, particularly those found in the health care environment. In 1933, because of its broad antimicrobial activity, PCMX was used to reduce maternal childbirth deaths from *Streptococcus pyogenes* infection.¹ During this time, it was also recommended as a cleaning agent for the hands, and solutions containing different concentrations of PCMX were used for disinfection during surgery.¹ Because PCMX is absorbed by the skin and excreted by the kidneys, it has also been used as a topical agent to treat urinary tract infections.¹ Allergic contact dermatitis has previously been reported after the use of soaps, electrocardiography electrodes, and cutting fluids containing PCMX.²⁻⁴ We report two cases of allergic contact dermatitis caused by PCMX. One patient was exposed to PCMX via a liquid soap in a fast-food restaurant restroom, the other patient via a moisturizer. Both patients improved after the removal of the offending agent.

Case Report 1

A 39-year-old male restaurant manager was referred for evaluation of hand dermatitis. The dermatitis had been present for approximately 9 years, involved both hands, and was extremely pruritic. The severity waxed and waned

over time, but neither the patient nor his wife were able to identify any factors affecting the severity of the dermatitis.

The patient had been managing a fast-food restaurant for 16 years. He changed restaurants for a brief period, during which time his hands partially improved. For economic reasons, he returned to his original place of employment, and his hands returned to their baseline state. His daily activities included handling foodstuffs, cleaning with various solutions, counting money, and paperwork. He wore latex-free unpowdered gloves for hand protection whenever possible. He reported that he washed his hands seven to eight times daily, and each washing was followed by the application of a bland moisturizer. There were no unusual exposures outside of the workplace.

Previous investigations included patch-testing with the TRUE Test system (Mekos Laboratories A/S, Hillerød, Denmark), which revealed no positive reactions. Prior treatments included high-potency topical steroids (under occlusion), tar, topical and systemic antibiotics, ultraviolet light, and systemic steroids. Only systemic steroids had been effective.

Examination revealed intense erythema, scaling, and fissuring of both hands. Both the dorsal and palmar surfaces were involved, and the severity was greater on the palmar surfaces (Fig 2). There was a sharp cutoff at the wrists bilaterally.

Patch testing was carried out with the following panels: a modified North American Contact Dermatitis Group (NACDG) standard panel, a food additive panel, a topical steroid panel, an extended topical ingredient panel, an extended fragrance and botanical panel, and a textile screening panel. Readings performed at 48 and 72 hours revealed a +++ reaction to PCMX and + reactions to Disperse Blue 85 and Disperse Brown 1.

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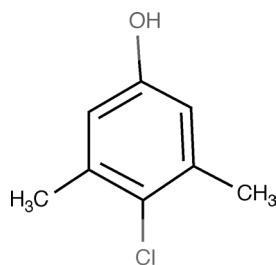


Figure 1. Structure of chloroxylenol.

The manufacturers of all cleaning products used at the patient's place of employment were contacted, and ingredient lists were obtained. The hand soap used in the kitchen and bathroom was the only product that contained PCMX. The reactions to the disperse dyes were of unknown relevance.

The patient was instructed to obtain and use an alternative soap at work. In addition, he was counseled to discontinue the use of dyed cotton gloves. At 1 month of follow-up, the patient reported an improvement of 80 to 90%.

Case Report 2

A 50-year-old female presented with chronic hand dermatitis that had severely worsened approximately 8 months earlier. The dermatitis was quite pruritic and was primarily localized to the palms. There was no foot involvement. Numerous treatments with various topical steroids had been completely ineffective.

On examination, both palms and the palmar aspects of the fingers were noted to be hyperkeratotic and fissured,

with background erythema (Fig 3). The dorsal aspects of the hands were relatively spared.

The patient reported working in a janitorial field, and there had been no changes in her job or in the products used in the previous several years. No other unusual exposures were noted. The patient did not have an atopic history.

Patch testing was performed with a modified NACDG standard panel, an extended topical and cosmetics panel, and an extended steroid panel. Readings performed at 48 and 72 hours revealed +++ reactions to PCMX at both time points.

A review of the products used by the patient found that PCMX was an ingredient in a hand cream (Miracle Hand Repair Cream, Miracle of Aloe, Dallas, TX) that the patient had purchased (after learning of it from a television infomercial) to treat her hand dermatitis. She did not recall exactly how long she had been using it, but on further consideration, she thought that her hand dermatitis had started to worsen sometime after she began using this product. After discontinuing the use of this cream, she noted significant improvement in her hand dermatitis over the ensuing 8 weeks. A mild dermatitis remained and was thought to be most consistent with low-grade irritant dermatitis.

Discussion

We present two cases of allergic contact dermatitis arising on patients' hands after exposure to PCMX. Both patients had a marked improvement of their dermatitis after cessation of the offending agent.

PCMX was introduced in Germany in 1927 and has been well recognized since the 1960s as a cause of allergic



Figure 2. Intense erythema, scaling, and fissuring of both hands. There is greater severity on the palmar surfaces and a sharp cutoff at the wrists bilaterally.



Figure 3. Bilateral palms and the palmar aspects of the fingers are hyperkeratotic and fissured. There is background erythema and sparing of the dorsal aspects of the hands.

contact dermatitis.^{2,5} PCMX is a halogenated phenolic bacteriostatic preservative, and the antigenic component is likely the chloride atom in the para position of the phenol ring.⁶ This agent is widely used in topical medications, cosmetics, and electrocardiograph paste and is tested at 1% in petrolatum.^{3,5} According to correspondence with a US manufacturer of PCMX, one of its major uses in the United States is as an ingredient in antimicrobial soaps used in the health care and food service industries. Overall use of PCMX in recent years in the United States has been slowly increasing.

The antimicrobial activity of PCMX is likely attributable to the inactivation of bacterial enzymes and the alteration of bacterial cell walls. It has a broad spectrum of antibacterial activity, with good in vitro activity against gram-positive organisms and moderate activity against gram-negative organisms and mycobacteria.¹ In one study of topical antimicrobial susceptibility of various isolates from burn wounds, all gram-positive and gram-negative isolates, with the exception of *Pseudomonas aeruginosa*, were susceptible to PCMX.¹ *Pseudomonas aeruginosa* coverage is enhanced when ethylenediaminetetraacetic acid is added.⁵ Although antimicrobial biocides (including PCMX) are usually regarded as an important defense against the spread of infection, concern has been expressed about their overuse leading to the selection of resistant organisms. One study that analyzed the minimum inhibitory concentration data from *Staphylococcus aureus* and *Pseudomonas aeruginosa*⁷ showed that the acquisition of biocide resistance is most likely of no consequence, given that the use of biocides is totally different from the administration of antibiotics.

There has been an increasing tendency to use the antimicrobial properties of PCMX in products that are designed to be used several times a day. Thus, the risk involved with numerous exposures to PCMX has been evaluated by pharmacodynamic studies. A percutaneous study in shaved rats showed that approximately one-half of a PCMX dose was absorbed from an occluded patch in 6 hours.⁸ In addition, excretion via urine was complete by 24 hours. Plasma levels of labeled PCMX reached a peak concentration of 7.8 ± 0.9 $\mu\text{g/mL}$ in 2 hours after percutaneous administration.

Although PCMX is not a common sensitizer, there is a high rate of relevance when a positive patch-test reaction to PCMX is detected.⁵ In recently released data drawn from using the British standard series, PCMX had the lowest rate of positive patch-test results of any agent.⁹ Despite the low yield of reactions to PCMX, Britton and colleagues concluded that because of extensive exposure to PCMX in the health care industry and the high relevance of positive

reactions, PCMX remains a valuable test allergen.⁹ The most recently released data from the NACDG show 0.6% of patients having positive reactions, 71.4% of which are deemed relevant.¹⁰ In another study, 17 of 951 patients (1.8%) had positive patch-test reactions to PCMX¹¹; of these 17 patients, 15 (88%) had allergic contact dermatitis of the hands.

Various studies have examined the positive response rate to PCMX, and sensitivity ranges from 0.2 to 3.2%.⁵ There have been several reports of allergic contact dermatitis after exposure to PCMX.^{2,3} In one case series, seven individuals developed allergic contact dermatitis after sensitization to PCMX contained in medicated petroleum jelly or electrocardiograph paste.¹² In addition, there have been reports that PCMX-sensitive patients may cross-react to chlorocresol.¹² Chlorocresol has a narrower antimicrobial range and is found in corticosteroid creams, cosmetics, antiseptics, and metalworking fluids.⁵

In addition to allergic contact dermatitis, several other adverse effects are associated with chloroxylenol use, especially at relatively high concentrations. One report described postinflammatory hypopigmentation following allergic contact dermatitis from PCMX.¹³

Dettol (Reckitt Benckiser, Slough, UK) is a common European household disinfectant with a very high concentration of PCMX (4.8% PCMX, 9% pine oil, and 12% isopropyl alcohol) but is generally unavailable in the United States. There have been several reports of Dettol's having caused delayed upper-airway obstruction when ingested.¹⁴ The major risks of Dettol ingestion are pulmonary aspiration leading to adult respiratory distress syndrome, pneumonia, and cardiopulmonary arrest. Dettol ingestion can also cause depression of the central nervous system and corrosion of the oral mucosa, larynx, and gastrointestinal tract. In a study of 121 patients, 3 patients (2.5%) developed renal impairment and transient hypotension after ingesting 200 to 500 mL of Dettol.^{14,15} The authors hypothesized that the renal impairment was a direct toxic effect of PCMX; however, this was a problem only with ingestion of large amounts of Dettol.

These two cases show that allergic contact dermatitis may arise from exposure to PCMX, especially with the widespread use of PCMX in antimicrobials and in cosmetic products. It is an effective antimicrobial agent with a broad spectrum of action and low toxicity when used at low concentrations. Given its widespread use, the frequency of allergic reactions to it is quite low. Because one of its major uses in the United States is in hand soaps and because exposure via soap can elicit contact dermatitis (as in the patient described in case report 1), PCMX sensitivity should be considered in anyone who presents with persistent hand

dermatitis, especially if they work in the health care or food service industries. A careful history, recognition of this condition, and patch testing are essential in making an accurate diagnosis.

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