

IMAGES

## Contact dermatitis caused by dimethylfumarate in Argentina

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For the first time in Argentina, we describe an outbreak of contact dermatitis. New pairs of shoes caused intense pruritus, pain, and eruption, followed by edema, blisters, and a severe negative impact on the epidermal barrier of the feet. We identify dimethylfumarate as the causal agent and suggest an analytical method for its fast identification.

**Keywords** Skin; Dimethylfumarate; Contact dermatitis

The antimicrobial activity of the dimethyl ester of the fumaric acid, dimethylfumarate (DMF), has been known for 70 years. DMF was applied as a fungicide to leather components of industrial products, such as furniture and shoes, mainly those manufactured in Asia. The identification of DMF as responsible for severe contact dermatitis was made recently in Finland, after a small epidemic of severe dermatitis related to chairs and sofas manufactured in China.<sup>1</sup> Then, other similar episodes were reported in other countries, mainly in the European Community, which were caused not only by furniture but also by shoes.<sup>2</sup> These events led to the European Union (EU) to prohibit its use and to ensure adequate measures in order to avoid the trade market of imported products containing this compound.<sup>3</sup>

Five adult female patients with contact dermatitis in their feet had consulted at the Center for Toxicological Research, Buenos Aires, Argentina. All the patients exhibited defined erythematous lesions in the soles of both feet with pruritus, scaling, and fissuring (Figs. 1 and 2). As there was a close similarity in symptoms and their evolution among all five patients, only one of the patients (patient A) is described here as a case report. A 25-year-old female patient previously in good health (patient A) had bought a new pair of shoes in Buenos Aires, and wore them only once for approximately 8 hours (day 1), with no socks and in direct contact with the skin. After 8 hours, her soles had become red, accompanied by intense pruritus, pain, and eruption of lesions, forcing her to report to the emergency services department in the hospital, where topical application of clobetasol 17-propionate (0.05%) was prescribed. On day 2, the lesions got worse, with the appearance of

many small blisters. Her general practitioner prescribed topical miconazole (2%) after disinfection with hydrogen peroxide (10 vol). However, over days 3 and 4, there was no improvement and the blisters had increased in number and size. Her general practitioner then prescribed calamine (8%), diphenhydramine (1%) spray, and piercing of the blisters, which were of a size of 0.5 cm approximately. However, over days 5 to 7, the symptoms did not get better as the blisters extended to the interdigital area, although the patient was treated with oral diphenhydramine (25mg/4h) and intravenous betamethasone (3mg). Over this period, they continued with the piercing of the blisters, topical treatment, and bandaging. Meanwhile, the patient was still unable to walk due to the profusion of blisters, edema, and pain. After day 10, the main symptoms seemed to improve and the general practitioner prescribed a topical treatment combined with miconazole (2%) and gentamycin (0.1%). Only a month after wearing those shoes, the symptoms



**Fig. 1.** The clinical photo showing the foot sole of patient A at the time of the first consultation.

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**Fig. 2.** The clinical photo showing the foot sole of patient B at the time of the first consultation.

faded, while maintaining the same treatment and hydrogen peroxide washing. When the blisters turned dry, the area suffered from changes in several layers of the skin and the patient remained with increased sensitivity to pressure in the soles for several months.

After the epidemic event, leather samples from the shoes suspected to be responsible for the contact dermatitis were used for the standard patch test to confirm the presence of dermal sensitizers<sup>4</sup>. Six albino rabbits were used for testing each leather sample. One square-inch of the analyzed material was fixed on a trichotomized area of the skin with adhesive tape. The rabbits were kept in cages. After 24 hours of exposure, the patches were removed and the reaction of the skin was recorded. A second reading was made at 72 hours. Severe erythema (beet redness) and severe edema were observed after 24 and 72 hours in the rabbits that were

in contact with the shoe pieces. The leather samples proved to have high sensitizing potential and were revealed as the likely cause of the current footwear dermatitis epidemic. An analytical method was developed to make a simple and fast identification of the chemical sensitizers. For this purpose, small portions of the shoes material were heated in gas-tight ampoules (20 ml) at 80°C for 30 minutes. Using a static headspace technique, the gaseous phase was extracted in a 75µm Carboxen™ Polydimethylsiloxane fiber and then analyzed by gas chromatography–mass spectrometry (GCMS). It clearly detected the presence of dimethylfumarate in amounts ranging from 18 to 37 mg/kg.

As far as we know, the present report of persistent contact dermatitis caused by shoes treated with DMF is the first one in Argentina. We considered that a new and strict legislation is needed in the country to avoid the importation of products treated with DMF.

### Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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