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Thiurams in shoe contact dermatitis – a case series

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Case Report

We present four patients who developed allergic contact dermatitis on their feet after wearing Keds® Canvas sneakers. All patients underwent patch testing

with the North American Contact Dermatitis Group (NACDG) Baseline series (Chemotechnique Diagnostics AB, Vellinge, Sweden), and various other allergen trays, depending on the clinical scenario, including a glues and adhesives series (Chemotechnique Diagnostics AB), a shoe series (Chemotechnique Diagnostics AB), and a textile tray (Chemotechnique Diagnostics AB). All 4 patients developed positive reactions to the thiuram mix, as well as to pieces of their shoes (Fig. 1). We initially believed that thiuram accelerators were used in this

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Table 1. Summary of patient characteristics and patch test results

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	15	15	25	29
Gender	Female	Female	Female	Female
Site of the dermatitis	Lateral foot, sole	Dorsal and lateral feet, sparing of sole	Dorsal feet, toes, sparing of soles	Dorsal and lateral feet
Patch testing series	NACDG Baseline series, glues and adhesives series, piece of inner portion of Keds® canvas shoe	NACDG Baseline series, glues and adhesive series, shoe series, inner portion and sole of shoe	NACDG Baseline series, glues and adhesive series, shoe series, textile series, inner portion and sole of shoe, piece of support stocking fabric	NACDG Baseline series, shoe series, dimethyl fumarate 0.01% and 0.1% pet., dibutyl maleate 5% pet., shoe inner canvas fabric
Patch test results	Day 4 Thiuram mix (+), own shoe (+)	Day 2 Inner shoe fabric (+) Day 4 Thiuram mix (+), inner shoe (+)	Days 2 and 4 Colophonium (+), thiuram mix (++), PTBFR (+), fragrance mix II (+), inner shoe (++)	Day 2 Thiuram mix (++), cobalt chloride (+), dibutyl maleate 5% pet. (+) Day 4 Thiuram mix (++), shoe fabric (++)
Outcomes	Avoided thiurams, dermatitis resolved	Avoided rubber shoes, dermatitis resolved	Avoided above allergens, dermatitis resolved	Avoided thiurams, dermatitis resolved

NACDG, North American Contact Dermatitis Group; PTBFR, 4-*tert*-butylphenol formaldehyde resin.



Fig. 1. Patient 1: positive reaction to fabric from Keds® Canvas sneaker at D4.

type of rubber-based canvas shoe. However, subsequent chemical analysis failed to identify thiurams in two different pairs of shoes. Table 1 summarizes the individual characteristics and patch test results of each patient.

Shoe canvas and supporting material were cut into small pieces, extracted with acetonitrile and dichloromethane, concentrated, and assayed by high-performance liquid chromatography with a photodiode array detector for the presence of zinc dithiocarbamates, thiurams, and 2-mercaptopbenzothiazole (MBT). Zinc dibutylthiocarbamate, zinc diethylthiocarbamate, zinc pentamethylenedithiocarbamate, zinc dimethylthiocarbamate, MBT, dipentamethylene thiuram tetrasulfide, tetramethyl thiuram monosulfide,

tetramethyl thiuram disulfide and tetraethyl thiuram disulfide standards were run in parallel with the samples. The presence of MBT was confirmed by gas chromatography–electron impact mass spectrometric analyses.

Discussion

Freeman reported that rubber was the most common cause of allergic shoe dermatitis (44%) in her cohort, followed by potassium dichromate (24%), 4-*tert*-butylphenol formaldehyde resin (PTBFR) (20%), and colophonium (9%) (1). Another retrospective study, conducted by Warshaw et al., evaluated 109 patients with allergic shoe dermatitis from the NACDG between 2001 and 2004, and analysed the frequency of causative allergens. Rubber compounds accounted for the highest percentage of allergies (40%), followed by adhesives (33%) and leather chemicals (20%). PTBFR was the commonest allergen (25%) (2).

At first, we believed that our patients had become sensitized to thiurams in the rubber parts of the Keds® Canvas shoes. Information on the manufacturing process was difficult to obtain. The company's website mentions that the shoe is manufactured from an unvulcanized rubber sole attached to a canvas fabric, which is subsequently vulcanized in order to attach the top and bottom of the shoe. The chemical analyses of the Keds® shoes did not confirm our initial hypothesis, as the shoes did not contain detectable thiurams or thiocarbamates.

However, MBT, especially concentrated in the canvas parts, was found in both shoes. This discrepancy could have been explained by the presence of 2-benzothiazolyl-*N,N'*-diethylthiocarbamylsulfide (BT-DEC), which is structurally similar to both thiurams and MBT. One case report showed positive patch test reactions to thiuram mix and BT-DEC, whereas only MBT and BT-DEC were detected in the chemical analysis of a rubber diving mask (3). However, our analysis failed to show any BT-DEC in the shoes. The allergen could be a different thiuram

species-MBT reaction product; however, this is difficult to assess without information concerning chemicals added during production. It is clear that there is a discrepancy between the patch test reactions in these patients and the chemical analyses of the shoes, implying that other factors may be involved. We thus recommend avoidance of canvas-type shoes by any patient allergic to rubber additives, regardless of the chemical composition of the shoe.

References

- 1 Freeman S. Shoe dermatitis. *Contact Dermatitis* 1997; **36**: 247–251.
- 2 Warshaw EM, Schram S E, Belsito D V et al. Shoe allergens: retrospective analysis of cross-sectional data from the North American Contact Dermatitis Group, 2001–2004. *Dermatitis* 2007; **18**: 191–202.
- 3 Bergendorff O, Hansson C. Contact dermatitis to a rubber allergen with both dithiocarbamate and benzothiazole structure. *Contact Dermatitis* 2007; **56**: 278–280.