

ORIGINAL ARTICLE

Contact allergy in Indonesian patients with foot eczema attributed to shoes

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Abstract

Background Shoe dermatitis is a form of contact dermatitis resulting from exposure to shoes. Allergens and types of shoes responsible may vary depending on manufacturing techniques, climatic conditions and indigenous traditions. This study focuses primarily on as yet unexplored shoe dermatitis cases in Indonesia.

Objective To determine the prevalence of shoe dermatitis in the Dermatology outpatient clinic, Sardjito University Hospital, Yogyakarta, Indonesia over a period of 3 years and to identify the responsible allergens.

Methods All patients meeting screening criteria for possible shoe contact dermatitis were patch tested with the European baseline series, shoe series and additional series based on earlier studies of Indonesian leather and shoe manufacturers; some were also patch tested with their own shoe materials and shoe extracts.

Results Sixty-four (7.1%) of 903 patients with foot skin disorders were diagnosed with shoe dermatitis. Twenty-five (52.1%) of 48 patch-tested patients showed positive reactions to one or more allergens related to footwear. Sixteen patients were patch tested with their own shoe materials; 11 showed positive reactions. The most frequent relevant sensitizers were rubber allergens followed by preservatives, shoe adhesives and leather materials.

Conclusion Shoe dermatitis is common in Indonesia. Using three series of patch tests, we identified responsible allergens and patterns of sensitization in Indonesian shoe dermatitis patients.

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Conflict of Interest

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Introduction

Shoe dermatitis is a form of allergic or irritant contact dermatitis resulting from exposure to shoes.¹ A patient is diagnosed with allergic shoe dermatitis based on his history, the presence of skin lesions and positive patch test reactions to one or more allergens in shoes; another indication is the absence of dermatitis when the patient wears proper substitute shoes.² Data on the prevalence of allergic shoe dermatitis are available from patch test clinics and various proportions of positive patch tests to allergens in shoes were reported.^{1,3–6} The highest prevalence has been recorded in warm climates^{1,5,6} where heat, humidity and conditions inside the shoe like friction, sweating, pressure and occlusion in conjunction with various chemicals in shoe materials contribute to the prevalence of shoe dermatitis.^{1,6–8} Recently, leather, rubber and adhesives are reported to be the most common sources of shoe

allergens.^{1,5,9–11} However, the chemicals causing shoe dermatitis may vary depending on manufacturing techniques.^{9,12} The types of shoes responsible will also differ depending on climatic conditions, socio-economic factors and indigenous traditions.^{5,7,9,10} Our current study focuses primarily on shoe dermatitis in Indonesia, where several of the above-mentioned factors contribute to its prevalence.

Materials and methods

Patients

Over 3 years (January 2008–December 2010), we studied 903 patients with foot skin disorders who came to the Dermatology outpatient clinic, of the University hospital in Yogyakarta, Indonesia. Patients fulfilling screening criteria for possible shoe dermatitis were eligible for further examination.

Screening criteria for shoe dermatitis

The screening criteria for shoe dermatitis were as follows: (i) presence of eczema on the area in contact with suspected footwear; (ii) bilateral, symmetrical eruption, corresponding to the design of the shoes such as the contact site of the shoe tips, uppers and sides, soles, heels and sandal straps and (iii) no evidence of fungal infection or of other skin diseases.^{9,12–14}

Patch test examination

After providing informed consent, patients meeting screening criteria were patch tested with the European baseline series and shoe series and 12 additional allergens, based on a literature review and our own earlier studies in Indonesian leather and shoe factories.^{15–17} Test preparations were supplied by Chemo-techniques Diagnostics®, Vellinge, Sweden and by the laboratory of the Dermatology Department, Faculty of Medicine, Gadjah Mada University, Indonesia.

A number of patients consented to patch tests with their own shoe materials. These were cut into parts, at least 1 square cm wide and ≤ 2 mm thick and were moistened with saline before being applied.^{12,14} Patients with negative patch test reactions to shoe allergens but with positive patch test reactions to their own shoe materials were patch tested with an extract from their suspected shoes. The shoe materials were separated into layers, then each cut into a 0.5×0.5 cm piece and moistened with saline. An alcohol extract was made from different parts (i.e. rubber, leather/imitation leather and cloth) of the suspected shoes by adding 100% ethanol at a ratio of 10 : 1. The material and ethanol were put into an ultrasonic bath for 2 h and centrifuged for 5 min at 500 r.p.m. The supernatant was concentrated using a Buchi vacuum evaporator. Shoe extracts were prepared at the Organic Chemistry Laboratory, Faculty of Mathematics and Natural Sciences, Gadjah Mada University, Indonesia.

Patch test materials were applied to the patient's upper back using Finn chambers® (Epitest Ltd., Helsinki, Finland) mounted on acrylate-based adhesive tape (Scanpor Alpha AS, Norges-plaster Facility, Vennesla, Norway). The patches were reinforced with extra tape at the edges and over the chamber area. After 48-h occlusion, we removed the Finn chambers and read on days 2, 3 and 4 as recommended by the ICDRG.¹⁸

The clinical relevance of positive patch test reactions to the shoe allergens was determined according to the following criteria: the probable presence of the allergen in the footwear; a clear relation between exposure to the allergen and the location of skin lesions and improvement of skin lesions after elimination of exposure. In patients tested with their own shoe material, the clinical relevance to positively tested allergens from the series was strengthened by a positive patch test with their own shoe materials.

Results

Characteristics of patients

Of the 903 patients (445 males and 458 females) visiting the Dermatology Clinic at Sardjito University Hospital for foot skin disorders, 64 (7.1%) were suspected of shoe dermatitis (Fig. 1). A total of 213 (23.6%) were diagnosed with other forms of eczematous dermatitis; the rest showed other foot skin disorders (Table 1).

Of the 64 patients suspected with shoe dermatitis, 44 (68.8%) were females and 20 (31.3%) males. The main complaint was pruritus, 58 patients (85.3%); only a minority had a history of atopy (Table 2). The dorsum of the foot was the most frequent location (47.6%) and rubber slippers/sandals the most suspected footwear (50.7%) (Table 3).

Patch test results

Forty-eight patients were patch tested with the European baseline series, shoe series and additional series. For various reasons, patch tests were not performed in 16 patients: some thought they had already identified the footwear that had triggered the allergy; the rest could not be tracked down by telephone or by the use of their registered addresses.

A total of 32 (66.7%) patients showed one or more positive patch test reactions and 25 (52.1%) patients had clinically relevant reactions, based on the probable presence of the allergen in the footwear and the relationship between the lesions and exposure to the allergens (Table 4). The most frequent positively tested shoe allergen was 2-mercaptobenzothiazole (11 patients). The most frequent relevant sensitizers were allergens from rubber materials followed by preservatives, shoe adhesives and leather materials.

Sixteen patients were patch tested with their own shoe materials: 11 showed positive reactions, five showed irritant or doubtful reactions. Of these 11 patients with positive reactions to their own shoe materials, nine also had positive reactions to allergens from the three series described above, and two did not. These two were subsequently patch tested with an extract from their own shoe materials: one showed a positive reaction to the shoe extract and one did not (Fig. 1).

Twelve patients with relevant positive patch tests to substances from the three series could not be tested with their own shoe material for several reasons: five patients showed severe eczematous skin lesions in the area of contact with rubber footwear. In these patients, we did not patch test with pieces of rubber materials since patients were not motivated because they had noted that it was very likely that rubber footwear was the cause of their shoe dermatitis. Moreover, we expected a strong positive patch test when we would test with own shoe material. Seven patients with positive reactions to rubber allergens experiencing eczema in the area of contact

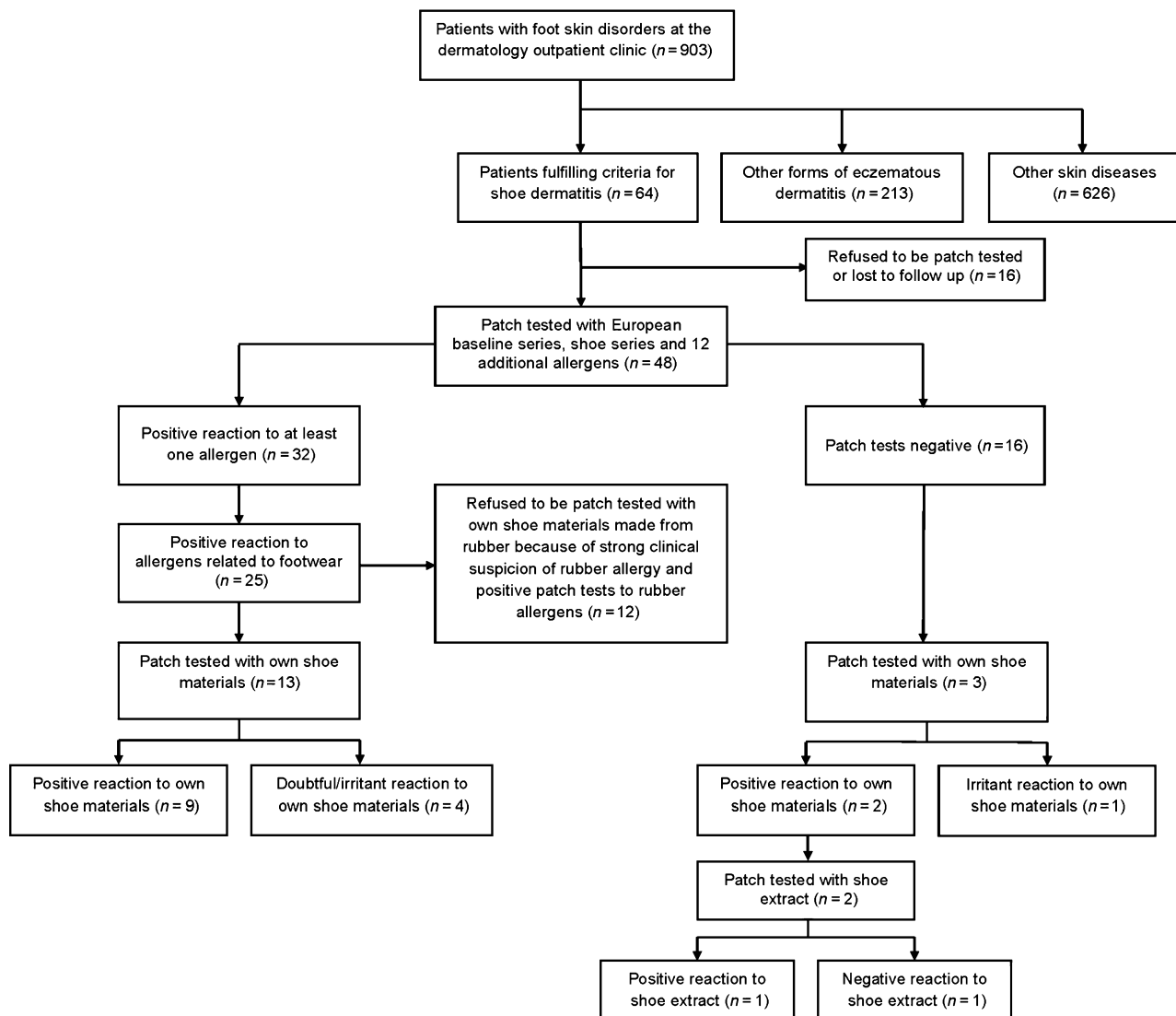


Figure 1 Research flow of patients with eczematous skin lesions on their feet.

with their rubber footwear were found to have no more lesions when they stopped wearing the footwear. We asked them to use their rubber footwear again, and their skin lesions reappeared. They were unwilling to have further patch testing with their own shoe materials.

Table 5 includes 16 patients that were patch tested with their own shoe materials. In a separate column, we recorded the allergens related to the positively tested shoe material.

Discussion

Patterns of shoe dermatitis have changed over the years, reflecting changes in fashion and shoe manufacturing technology as well as variations between countries. For this study, we accurately selected patients with shoe dermatitis from a group with

skin disorders on their feet. We patch tested patients with an extensive, carefully selected range of allergens and critically assessed the relevance of the positively tested allergens to the exposure to the shoe material. This explains our high percentage (52.1%) of patients with clinically relevant positive patch test reactions. Our results approach a study by Angelini *et al.* (65.4%).¹⁹ In this Italian study, shoe dermatitis patients were well characterized. However, positive reactions probably not all relevant for shoe dermatitis were included in the percentage. They showed 49 positive reactions to p-phenylenediamine in 108 tested patients. All positive reactions to p-phenylenediamine were included in the reported prevalence of positive reactions, although probably not relevant to shoe allergy. Reported prevalences are difficult to compare due to differences in study design,

Table 1 Characteristics of 903 patients with foot skin disorders

Condition	Number of subjects	Percentage	Sex	
			Male	Female
Shoe dermatitis	64	7.1	20	44
Other forms of eczematous dermatitis	213	23.6	109	104
Psoriasis	115	12.7	58	57
Plantar keratoderma	152	16.8	44	108
Bacterial infection	25	2.8	18	7
Warts/Viral infection	140	15.5	78	62
Fungal infection	100	11.1	57	43
Corns and Calluses	30	3.3	18	12
Ulcers	17	1.9	13	4
Other	47	5.2	31	16
Total	903	100	445	458

Table 2 Characteristics of 64 patients screened for shoe dermatitis

	Number of patients (%)
Gender	
Male	20 (31.3)
Female	44 (68.8)
Occupation	
Housewife	11 (17.2)
Office worker	17 (29.3)
Student	11 (17.2)
Farmer	2 (3.1)
Unemployed	2 (3.1)
Other	15 (23)
No information	6 (9.4)
Chief complaint*	
Pruritus	58 (85.2)
Pain	7 (10.3)
Other	3 (4.4)
History of atopy	
Yes	19 (29.7)
No	33 (51.6)
No information	12 (18.8)
Age range (years)	
0–10	2 (3.1)
11–20	5 (7.8)
21–30	13 (20.3)
31–40	8 (12.5)
41–50	16 (25.0)
51–60	9 (14.1)
61–70	6 (9.4)
71–80	5 (7.8)

*Some patients had more than one main complaint.

types of allergens/shoe materials tested, and the investigator's critical assessment of clinical relevance. Also, as high temperatures and humidity in tropical countries like Indonesia create an

Table 3 Location of skin lesions and type of footwear suspected as cause of shoe dermatitis in 64 patients

	Number of patients (%)
Location of skin lesions*	
Dorsum	50 (47.6)
Dorsum of toes	24 (23.5)
Plantar area of foot	17 (10.8)
Plantar area of toes	3 (2.9)
Lateral area of foot	3 (2.9)
Heel	2 (1.9)
Interdigital spaces	2 (1.9)
Ankle	1 (0.98)
Type of footwear†	
Rubber slipper	31 (43.7)
Imitation leather sandals	11 (15.5)
Imitation leather shoes	10 (14.1)
Leather sandals	5 (7.0)
Rubber sandals	5 (7.0)
Plastic sandals	4 (5.6)
Sneakers	2 (2.8)
Leather shoes	2 (2.8)
Leather slippers	1 (1.4)

*Some patients had lesions on more than one site.

†Some patients had contact dermatitis related to more than one type of footwear.

ideal environment for the development of shoe dermatitis, it is understandable that the highest prevalence of shoe dermatitis has been recorded in such locations.^{7,8,20–22}

Shoe dermatitis may affect all parts of the foot but the most typical location is the dorsa of the foot and toes, sparing the interdigital spaces^{5,12,14,19,23,24}; our study confirms the dorsum to be most frequently affected (47.6%). This area, with its large surface area and thin stratum corneum, is especially vulnerable to shoe allergy.⁹ Our patients most commonly wore slippers or sandals (89.1%). The majority of our patients with rubber allergy

Table 4 Relevant results of patch testing in 48 patients screened for shoe dermatitis

Allergens related to shoe dermatitis (% vehicle)	Number of patients with positive reactions to allergens relevant to shoe dermatitis	Description
Mercapto mix	13	Rubber accelerator
2-Mercaptobenzothiazole (2.0 pet)‡	11	Rubber accelerator
1,3-Diphenylguanidine (1.0 pet)‡	5	Rubber accelerator
Methylchloroisothiazoline/methylisothiazolinone (0.02 aq)‡	4	Preservatives
Diphenylthiourea (1.0 pet)‡	3	Accelerator and activator for neoprene rubber
4,4'-Dithiodimorpholine (1.0 pet)‡	3	Rubber vulcanizer
Formaldehyde (1.0 aq)‡	3	Leather tanning agent, used in finishing process
Dodecyl mercaptan (0.1 pet)‡	3	Neoprene adhesives; polymerization inhibitor added to polyurethane materials
Potassium dichromate (0.5 pet)‡	2	Leather tanning agent
2-Thiocyanomethyl-thiobenzothiazole (0.2% pet)†	2	Leather (biocide in leather processing)
Colophony (20.0 pet)‡	2	Shoe adhesive (resin extract in glue and finishing); tackifier in heel stiffener
4-tert-Buthylphenolformaldehyde resin (1.0 pet)‡	2	Resin in shoe adhesive in shoe linings and insoles
2-n-Octyl-4-isothiazolin-3-one (0.1 pet)‡	2	Preservatives
4-Aminoazobenzene (0.25 pet)‡	2	Polyurethane dye in inner soles and shoe linings
Nickel sulphate (5.0 pet)‡	2	Shoe buckles and eyelet
Thiuram mix	2	Rubber accelerator
N-Isopropyl-N-phenyl-p-phenylenediamine (0.1 pet)‡	1	Rubber antioxidant
Hydroquinone monobenzylether (1.0 pet)‡	1	Rubber antidegradant
Epoxy resin (1.0 pet)‡	1	Shoe adhesive
Glutaraldehyde (0.2 pet)‡	1	Leather tanning agent
Disperse orange 3 (1.0 pet)‡	1	Dye

In some patients more than one relevant allergen as cause of shoe dermatitis.

†Additional allergens.

‡Shoe series.

had skin lesions on the dorsum area in contact with the sandal/slipper strap. In Indonesia, sandal/slipper straps are usually made of natural rubber latex, and insoles made from neoprene rubber covered with fabric.

The female-to-male ratio in our study was 3 : 1. Female predominance also reported in other studies.^{5,12,25} Current exposure of women to an increasing variety in footwear increases their risk of shoe allergy. Moreover, Indonesian housewives are more prone to irritant dermatitis of the feet because of regular exposure to water, household detergents and cleansing agents when doing housecleaning with bare feet in slippers. This condition can result in impaired epidermal function and eventually lead to greater penetration by shoe allergens. In our study, most shoe contact dermatitis occurs between the ages of 21 and 50 years (57.8%); this agrees with earlier reports.^{1,26} At these ages individuals are most active, likely to be regularly exposed to various allergens and thus more vulnerable to shoe allergy.

Our study found rubber, the most common material in Indonesian footwear, to be the most common cause of allergic shoe dermatitis; the same was reported in many other coun-

tries.^{9,13,19,24,27–29} 2-Mercaptobenzothiazole and 1,3-diphenylguanidine caused the most frequent relevant sensitization in our patients; this corroborates results from other studies.^{1,5,10,12,30} Other rubber allergens showing relevant sensitization in our study were 4,4'-dithiodimorpholine, N-isopropyl-N'-phenyl-p-phenylenediamine and hydroquinone monobenzylether. According to a study by Shackelford and Belsito⁹ the rubber vulcanizer 4,4'-dithiodimorpholine causes the most frequent relevant positive reactions in shoe dermatitis patients. Our study showed three patients with relevant sensitization to 4,4'-dithiodimorpholine, one of which was possibly a cross reaction with 1,3-diphenylguanidine. The majority of our patients with rubber allergy showed hyperkeratotic skin lesions associated typically with rubber.⁹ Interestingly, five patients with rubber allergy had an extensive bilateral dorsal eczematous reaction on their feet, and the feet of four were covered with crusts, possibly caused by secondary infections. Moreover, the dispigmentary action of a phenolic compound used in footwear manufacture is known to cause leucodermic lesions.³¹ Our study included a patient with hypopigmented lesions who had a contact allergy to hydroquinone monobenzylether (Fig. 2).

Table 5 Sixteen patients patch tested with own shoe materials

Gender (M/F)/ age (years)	Skin location of the foot	Suspected footwear/shoe materials	Patch test results – own shoe materials	Positive patch test reactions related to suspected footwear/shoe materials
M/79	Dorsum and side	Leather sandals, shoe upper	Positive reaction to inner side of leather sandals straps	Formaldehyde Methylchloroisothiazoline/methylisothiazolinone 2-Thiocyanomethyl-thiobenzothiazole
F/71	Dorsum	Leather sandals	Positive reaction to upper side of sandal straps	Formaldehyde 2-Thiocyanomethyl-thiobenzothiazole
F/47	Plantar pedis Heels and side foot	Imitation leather shoes (polyurethane) Rubber insole	Positive reaction to polyurethane shoes	4-tert-Butylphenolformaldehyde resin 4-Aminoazobenzene Diphenylthiourea Mercapto mix
M/35	Plantar pedis Side foot (contact with shoe lining)	Polyurethane shoe Rubber insole Glues with rubber component, in shoe lining	Positive reaction to lateral part of shoe upper	4-Aminobenzene 1,3-Diphenylguanidine 4,4'-Dithiodimorpholine
F/19	Dorsum foot and toes	Shoe adhesives in imitation leather shoes Rubber insole	Positive reaction to inner side of shoe upper	Colophony 1,3-Diphenylguanidine Thiuram mix
F/22	Dorsum foot (sandal strap) Dorsal toes	Leather sandal	Positive reaction to shoe upper, shoe straps and inner sole made from leather	Methylchloroisothiazoline/methylisothiazolinone
F/58	Dorsum foot Interdigital 1 Plantar pedis	Rubber sandals Leather sandals	Positive reaction to rubber inner sole and straps Positive reaction to inside of leather sandals	4,4'-Dithiodimorpholine 2-Mercaptobenzothiazole Mercapto mix Potassium dichromate Methylchloroisothiazoline/methylisothiazolinone 2-n-Octyl-4-isothiazolin-3-one
F/68	Dorsum foot	Leather sandals	Positive reaction to outer and inner parts of leather shoe uppers	Glutaraldehyde Potassium dichromate Formaldehyde
M/34	Dorsum toes Plantar toes	Shoe adhesive Rubber sandals	Positive reaction to inner part of shoe and upper (toe cap)	Epoxy resin 1,3-Diphenylguanidine
F/66	Dorsum foot Dorsum toes	Imitation leather sandals	Positive reaction to inner part of sandal strap	Negative patch tests
M/50	Dorsum toes Plantar pedis	Imitation leather sandals	Positive reaction to inner part of sandal strap	Negative patch tests
M/20	Dorsum foot (sandal strap) Dorsum toes Plantar foot	Leather shoes	Doubtful reaction to inner sole	Disperse orange 3 Methylchloroisothiazoline/methylisothiazolinone
F/54	Dorsum foot	Imitation leather sandal (polyurethane)	Doubtful reaction to lateral area of polyurethane shoes	Dodecyl mercaptan
M/9	Plantar foot Plantar toes	Rubber insole in sneakers made of neoprene	Irritant reaction to inner sole of sport shoes	Diphenylthiourea
F/38	Side foot Heels	Imitation leather shoes	Irritant reaction to inner side of polyurethane shoes	4-tert-Butylphenolformaldehyde resin Colophony
F/31	Dorsum foot Plantar foot Dorsum toes	Imitation leather shoes	Irritant reaction to inner and outer part of imitation leather shoes	Negative patch tests



Figure 2 Patient with hypopigmented lesions had contact allergy to hydroquinone monobenzylether.

Our study showed four patients with skin lesions on the plantar area, which were sensitized to the rubber insole, and one patient sensitized to his shoe linings showed a positive reaction to rubber allergens. This could be due to an adhesive-containing rubber component. Heel and toe counters exposed patients to a number of potential allergens containing rubber resin, such as mercaptobenzothiazole and thiuram.^{32,33} This could explain why a patient with skin lesions of the heel showed sensitization to rubber allergens. Diphenylthiourea, another sensitizer, is present in various synthetic rubber and plastic products due to its use as a stabilizer in the manufacture of PVC and as an accelerator in the production of neoprene.³⁴ Allergic contact dermatitis caused by diphenylthiourea was found in patients allergic to orthopaedic braces and suits made from neoprene, but almost never to neoprene shoes.^{35–38} Liipo *et al.*³⁹ studied sensitization to thiourea derivatives among patients suspected with contact dermatitis, five showed sensitization to diphenylthiourea; one had foot dermatitis and was also sensitized to diaminodiphenylmethane. Friis *et al.*⁴⁰ noted contact allergy to neoprene shoes, but reported positive patch test reactions to diethylthiourea instead of to diphenylthiourea.

Interestingly, our study suggests that relevant sensitization to leather allergens is probably caused by leather preservatives (methylchloroisothiazoline/methylisothiazolinone; 2-n-octyl-4-isothiazoline-3-one and 2-thiocyanomethyl-thiobenzothiazole) rather than by leather tanning agents (formaldehyde, potassium dichromate and glutaraldehyde). Other studies in tropical countries like India and Pakistan,^{1,5,41} pointed to chromium as the allergen most responsible for causing leather shoe dermatitis^{9,19,32} a finding contradictory to our study, in which positive relevant sensitization to potassium dichromate showed in only two patients. This could be the result of a newer fixation method in leather processing whereby chrome allergy manifests less fre-

quently as shoe dermatitis.⁹ However, Thyssen *et al.*⁴² recently reported that most leather footwear contained chromium, which was extracted from shoes and examined with X-ray fluorescence spectroscopy. We patch tested the patients with 2-thiocyanomethyl-thiobenzothiazole from our additional allergen series because it is used as a preservative in leather tanning in Indonesia¹⁶ and two patients were sensitized to this allergen. We would therefore consider this allergen when patch-testing patients with suspected shoe allergy. We did not patch test with dimethylfumurate⁴³ because, based on our study in shoe factories¹⁵ and our consultations with the Centre of Leather and Rubber as well as the Indonesian Footwear Association, this chemical was not used as a preservative in Indonesian footwear manufacturing.

Although many parts of shoes are sewn with nylon, polyester and linen thread, shoe adhesives are still used throughout. 4-tert-Buthylphenolformaldehyde resin is used as a rubber latex or neoprene adhesive for gluing insoles and shoe linings and is occasionally present in heel and toe stiffeners as a tackifier.^{1,33} Dodecyl mercaptan is a neoprene adhesive and used as a polymerization inhibitor in polyurethane materials. Epoxy resin is present in some adhesives used for gluing toecaps and quarters.⁴⁴ Patients sensitive to colophony and 4-tert-buthylphenol-formaldehyde resin should wear shoes without linings, or with leather linings or stitched linings without heel and toe support.³²

Nickel sensitivity plays a minor role in shoe dermatitis. Fisher²; nevertheless found several cases caused by metallic nickel sulphate in shoe buckles, eyelets or other accessories. In this study, six patients had nickel sensitivity, but only two had a history of eczema related to shoe buckles.

One patient with leather shoe dermatitis was sensitized to disperse orange. However, in this case, it is not certain that the allergy was caused by the leather dye since the result after patch testing with suspected shoe material was doubtful. According to the literature, primary dye dermatitis caused by leather shoes is rare.^{2,45} This could be due to the firm fixation of dye in leather products. Allergies to shoe dye appear in patients who have redyed their shoes,⁴⁵ patients allergic to dye in fabric or plastic shoes¹² or patients allergic to stocking dye.¹⁹

The limitation of this study is that not all patients agreed to be patch tested with the three series or their own shoe materials. Despite this limitation, we have many advantages not found in similar studies in shoe dermatitis patients. Our study is a prospective study, following patients with skin problems in their feet. Most other studies are retrospective, taking their data from past results of a patch test clinic. The number of allergens tested in our study (51 allergens) was also higher compared to similar studies^{1,5,12,19} and we evaluated positive patch test results very precise for clinical relevance. We also patch tested 16 patients with pieces of suspected shoe, a procedure followed only in one other study¹² in which patch testing with shoe extract was performed on two patients. Moreover, we provided detailed descriptions of patients who agreed to be patch tested with their own shoe materials.

Conclusion

In this study, we prospectively screened patients with shoe dermatitis, which were patch tested with a wide range of clearly identified allergens. We showed in a high percentage of positive patch test reactions in which we precisely described the relation to footwear. Positive patch test reactions to their own shoe materials/shoe extract tests supported our patch test results. The most frequent clinical relevant sensitizers were rubber allergens followed by preservatives, shoe adhesives and leather materials. This correlates well with the preference of Indonesian people for shoes like rubber slippers or sandals.

Author contributions

All authors have participated sufficiently to take public responsibility for appropriate portions of the work.

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