

A case of contact urticaria syndrome due to di(2-ethylhexyl) phthalate (DOP) in work clothes

KEIJI SUGIURA^{1,2}, MARIKO SUGIURA¹, RITSUKO HAYAKAWA¹, MIKIHIRO SHAMOTO² AND KAZUMI SASAKI³

¹Department of Environmental Dermatology, Nagoya University School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550 Japan

²Division of Pathological Cytology, Institute for Comprehensive Medical Science, Fujita Health University, 1-98 Dengakugakubo, Kutsukake-cho, Toyoake 470-1192, Japan

³Textile and Chemical Technology Division, Technology Department, National Institute of Technology and Evaluation (NITE), Ministry of International Trade and Industry (MITI), 2-49-10, Nishihara, Shibuya-ku, Tokyo 151-0066, Japan

We previously reported a case of contact urticaria syndrome (CUS) due to di(2-ethylhexyl) phthalate (DOP) in a polyvinyl chloride (PVC) grip on cotton gloves. The patient reported in this previous paper was careful not to have any contact with PVC products in his daily life or in his working environment. He discontinued the use of protective gloves with a PVC grip that was the cause of CUS. When working, he used cotton gloves without a PVC grip. We prescribed antihistamines which slightly improved his condition. However, when he wore work clothes while on duty, CUS relapsed. This condition was severe and made him feel anxious. When we advised him to wear a cotton shirt under his work clothes, the contact urticaria did not develop. We suspected that some component of the work clothes was the cause of his symptoms. A prick test with the extract solution of his work clothes showed a wheal and flare at the 15 min reading. The common component of the grip and the work clothes was found by analysis to be DOP.

Key words: contact urticaria syndrome (CUS); work clothes; di(2-ethylhexyl) phthalate (DOP); plasticizers; polyvinyl chloride (PVC); occupational. © Munksgaard, 2002.

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Skin hazards due to polyvinyl chloride (PVC) are likely to increase because PVC products are widely used in products used in daily life and in the working environment. PVC is made by polymerization of vinyl chloride monomer. It is a plastic material softened by a heating process. When a small amount (<5%) of plasticizers is added, it hardens the PVC. When the amount of plasticizers is 30%–50%, it softens the PVC. Softened PVC is used in making film, sheets, chemically-resistant shoes, plastic gloves, etc. Di(2-ethylhexyl) phthalate (DOP, from its alternative chemical name, dioctyl phthalate) has been used in PVC as a plasticizer because of its superior compatibility, volatility, low temperature flexibility, insulation and heat/light stability. Besides DOP, other plasticizers for softening PVC include di(2-n-butyl) phthalate (DBP), butyl benzyl phthalate (BBP) and di-n-butyl maleate (DBM).

We experienced a case with contact urticaria syndrome due to DOP from wearing work clothes.

Case Report

A 50-year-old automobile tire wholesaler developed contact urticaria syndrome (CUS) when he wore work clothes. He had previously experienced contact urticaria syndrome (generalized urticaria, diarrhea and abdominal pain) due to the grip on cotton gloves, made of PVC containing DOP (1). Along with prescribed antihistamines, he wore cotton gloves without a PVC grip. His condition somewhat improved. However, he developed CUS again when he wore his work clothes. We suspected his condition to be due to CUS not only from the cotton gloves but also from his work clothes. We suggested that he should wear a cotton shirt under his work clothes. When he did this, he did not develop contact urticaria or gastrointestinal symptoms. We suspected that the CUS might be from his work clothes. We conducted skin testing with extracts of his work clothes. After 15 min, wheals and flares developed on the area where the extracts of his work clothes were tested.

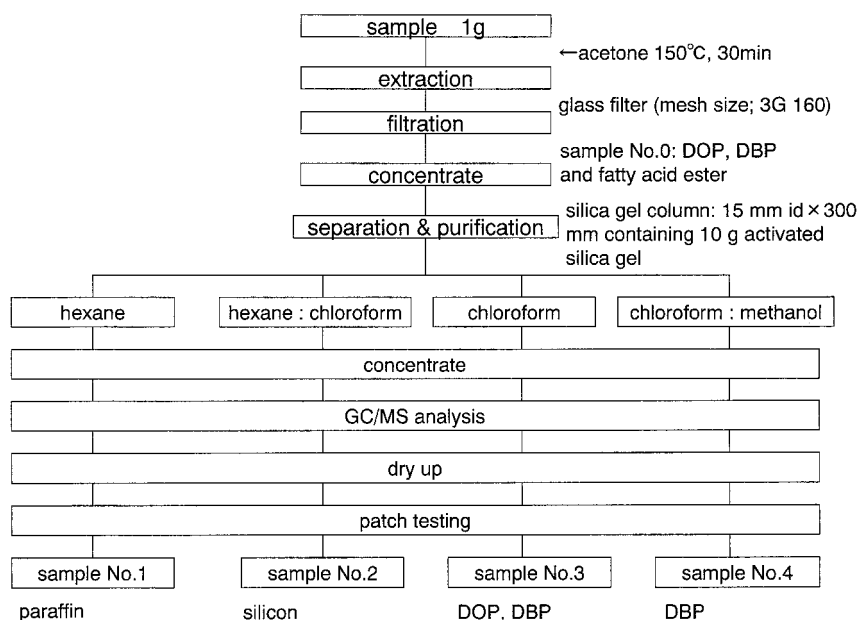


Fig. 1. Analyzing and detecting procedure for PVC.

Materials and Methods

Extraction of the components of work clothes

We suspected his condition to be CUS due to a component in his summer and winter work clothes that were made of cotton and chemical fibers. We extracted the components of his work clothes with acetone and methanol. The extracted solutions were separated by the column chromatography.

1 g of work clothes fragments was placed in a 500 ml eggplant-shaped flask with 100 ml acetone and heated at 150°C on a sand bath for 30 min. After filtering with a glass filter (3G160), the solution was extracted again with 100 ml methanol for 30 min. We concentrated the extract solution to 10 ml by rotary evaporator (2).

Identification of the components in the work clothes

We analyzed the extract solution by using column chromatography. We identified the separated chemicals using Fourier infrared absorption spectrophotometry (FT-IR) (3, 4) and the gas chromatography/mass spectrometry (GC/MS) (4, 5).

Fourier infrared absorption spectrophotometry (FT-IR). The separated solutions were each put in

an agate mortar separately and dried at 60°C. A pellet (3 mm id) for FT-IR was made from the dried material mixed with potassium bromide (KBr). The infrared absorption spectrum was measured using a Fourier-transform infrared spectrophotometer (60SXR).

Gas chromatography/Mass spectrometry (GC/MS). 1 ml of each separated solution was injected. The conditions were as follows: apparatus: MAT 90 mass spectrometer (Finnigan, Bremen, Germany); column: 5% phenylmethyl silicon (0.25 μ m thickness), DB-5MS (J&W), 0.25 mm id $\times$ 30 m length; carrier gas: helium 1.5 ml/min; column temperature: 50°C (3 min), rising by 10°C/min to 320°C (5 min), then cooling; injection mode: 1 μ l; injection temperature: 280°C; ionization mode: electron ionization (EI) 70eV.

Prick and scratch testing. We performed prick/scratch testing with extracts, reading at 15 and 30 min. We used histamine hydrochloride 1% aq. as a positive control. We tested distilled water and white petrolatum as negative controls. Water-soluble materials were examined by prick testing. Materials dispersed in petrolatum were examined by scratch testing. Readings were graded according to Lahti and Turjanmaa (6), as follows: no reaction; 2+ 1/2 size of histamine reaction; 3+ size of histamine reaction; 4+ larger than histamine reaction.

Table 1. Chemicals detected in each solution

No.	Elution	Chemicals detected
0	acetone and methanol	DOP, DBP and fatty acid ester
1	hexane	paraffin
2	hexane: chloroform	silicon
3	chloroform	DOP, DBP
4	chloroform: methanol	DBP

Results

Analyzed chemicals (Fig. 1, Tables 1, 2)

Summer work clothes. We detected the following chemicals in the extract and separated solutions:

di(2-ethylhexyl) phthalate (DOP), di(2-n-butyl) phthalate (DBP) and fatty acid ester in the extract, paraffin in the hexane elution, silicon in the hexane: chloroform elution, DOP, DBP and polyester oligomer in the chloroform elution, DBP in the chloroform: methanol elution.

Winter work clothes. We detected the following chemicals in the extract and separated solutions: di(2-ethylhexyl) phthalate (DOP), di(2-n-butyl) phthalate (DBP) and fatty acid ester in the extract, paraffin in the hexane elution, silicon in the hexane: chloroform elution, DOP, DBP and fatty acid ester in the chloroform elution, DBP in the chloroform: methanol elution.

Prick and scratch testing (Fig. 2)

The results of the prick and scratch testing are shown in Table 2. We confirmed the positive reactions to the separated solutions of no. 0 (the whole extract), nos. 3 and 4 for summer work clothes, no. 0 (the whole extract, Fig. 2), nos. 3 and 4 for winter work clothes. DOP, a component of summer and winter work clothes, also showed positive reactions. DBP, with a similar chemical structure to DOP, also reacted positively.

Discussion

We experienced a case of contact urticaria due to work clothes. When we carried out prick/scratch testing, we confirmed positive results with the extract solution of work clothes. We also confirmed positive reactions for the separated solutions nos.

Table 2. Results of prick/scratch testing

Materials	Conc./ vehicle	15-min reading	30-min reading
no. 0 (S, W)	5% pet.	4+	4+
no. 1 (S)	5% pet.	—	—
no. 2 (S, W)	5% pet.	—	—
no. 3 (W, W)	5% pet.	4+	4+
no. 4 (W)	5% pet.	4+	4+
DOP	2% pet.	4+	4+
DBP	2% pet.	4+	4+
extraction residue	as is	—	—
ethanol	as is	—	—
stearyl alcohol	2% eth.	—	—
histamine hydrochloride	1% aq.	wheal and flare	wheal and flare
white petrolatum	as is	—	—
distilled water	as is	—	—

S: summer clothes. W: winter clothes.

0, 3 and 4 of the summer work clothes, and nos. 0, 3 and 4 of the winter work clothes, and both DOP and DBP at the 15-min reading. In nos. 0 and 3 of the summer work clothes and nos. 0 and 3 of the winter work clothes, DOP was detected. We observed a positive reaction to DBP at both 15-min and 30-min readings. In nos. 0, 3 and 4 of the summer work clothes and nos. 0, 3 and 4 of the winter work clothes, DBP was detected. Because part of the chemical structure of DBP is very similar to part of the chemical structure of DOP (Fig. 3), we considered that the positive reaction to DBP at the 15-min and the 30-min readings were a cross-reactions to DOP. Petrolatum, ethanol and distilled water were negative.

DOP is a plasticizer used in making PVC prod-



Fig. 2. Positive skin reactions (left side: summer clothes; right side: winter clothes).

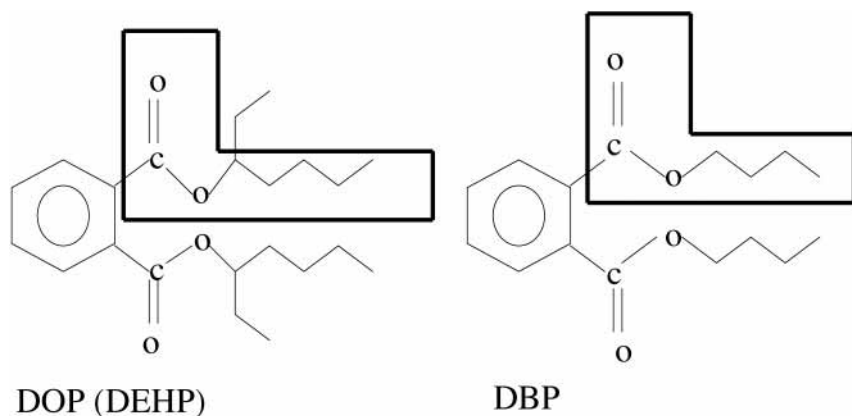


Fig. 3. Chemical structures of DOP and DBP.

ucts. Many plasticizers are used for making many kinds of PVC products. There are vast amounts of PVC products in the world. It is a very difficult and a constant problem for this patient to avoid PVC products in his daily life and working environment. He had thus been suffering from stage 3 CUS (7). The symptoms continue to be a serious problem in his daily life and he is always anxious. Whenever he handles things in daily life, he always puts on cotton gloves. There are many medical instruments and articles made of PVC, such as stethoscopes, oxygen masks, tubes, needles for drip infusions, medical gloves, some medical wear, and so on. With stage 3 or 4 (anaphylactoid) CUS due to DOP, prevention is very difficult and the patient may experience feelings of helplessness.

There have been previous reports of allergic reactions to PVC: contact dermatitis (8–11); contact urticaria (12); and asthma (13). Health hazards of PVC have recently been reviewed (14). In the future, our expectation is that the number of cases of PVC allergy like these will increase. We strongly advise the use not only of latex-free but also of PVC (DOP)-free medical instruments.

References

1. Sugiura K, Sugiura M, Hayakawa R, Sasaki K. Di(2-ethylhexyl) phthalate (DOP) in the dotted (Polyvinyl chloride) PVC grip of cotton gloves as a cause of contact urticaria syndrome. *Contact Dermatitis* 2000; 43: 237–238.
2. Hayakawa R, Matsunaga K, Kojima S, Kaniwa M, Nakamura A. Naphthol AS as a cause of pigmented contact dermatitis. *Contact Dermatitis* 1985; 13: 20–25.
3. Japanese Standard Association. *General rules for molecular absorptiometric analysis*. JIS handbook. 1st edition. Tokyo: Heibunsha, 1993: 235–244.
4. Geroge Schwedt. *Taschenatlas der Analytik*, 1st edition. New York: George Thieme Verlag, 1992.
5. Japanese Standard Association. *General rules for analytical methods in gas chromatography mass spectrometry*. JIS Handbook. Tokyo: Heibunsha, 1993: 296–301.
6. Lahti A, Turjanmaa K. Prick and use tests with 6 glove brands in patients with immediate allergy to rubber proteins. *Contact Dermatitis* 1992; 26: 259–262.
7. Amin S, Maibach H I. Introduction. In: Amin S, Lahti A, Maibach H I (eds): *Contact urticaria syndrome*. Boca Raton, New York: CRC Press, 1997: 1–4.
8. Kanerva L, Jolanki R, Estlander T. Organic pigment as a cause of plastic glove dermatitis. *Contact Dermatitis* 1985; 13: 41–43.
9. Koch P, Nickolaus G. Allergic contact dermatitis and mercury exanthem due to mercury chloride in plastic boots. *Contact Dermatitis* 1996; 34: 405–409.
10. Estlander T, Jolanki R, Kanerva L. Dermatitis and urticaria from rubber and plastic gloves. *Contact Dermatitis* 1986; 14: 20–25.
11. Monma S, Tsunoda T. Two cases of contact dermatitis due to polyvinyl chloride gloves. *Environ Dermatol* 1999; 6 (suppl 1): 84.
12. Mitchell J C. Contact urticaria from plastic shower curtains. *Contact Dermatitis* 1983; 9: 329.
13. Lee H S, Yap I, Wang Y T, Lee C S, Tan K T, Poh S C. Occupational asthma due to unheated polyvinylchloride resin dust. *Br J Indust Medicine* 1989; 46: 820–822.
14. Hayakawa R, Sugiura K, Sugiura M. Health Hazards due to polyvinyl-chloride (PVC). *Environ Dermatol* 2000; 7: 48–51.

Address:

Sugiura Keiji
Department of Environmental Dermatology
Nagoya University School of Medicine
65 Tsurumai-cho
Showa-ku, Nagoya, 466-8550
Japan