

Contact allergy to 2,5-dimercapto-1,3,4-thiadiazole and phenyl- α -naphthylamine, allergens in industrial greases and lubricant oils – contact allergy to water-insoluble greases is uncommon but needs to be considered in some workers

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Background: Industrial lubricants are usually made of petroleum and contain no water. Industrial greases and neat oils (insoluble metalworking oils) cause contact allergy relatively seldom, and reported allergies to the components of engine oils, such as hydraulic oils, are extremely scarce.

Objective: The aim was to describe patients with contact allergy to the components of industrial lubricants.

Results: We describe 2 patients with allergic reactions to 2,5-dimercapto-1,3,4-thiadiazole. Their allergies derived from guide-way oil and grease. Guide-way oils are lubricants for metalworking machines. Machinists may have continuous skin contact to these oils, as the oils are leaked to the circulating metalworking fluid system and form the so-called 'tramp oil'. We also report a new case with allergy to phenyl- α -naphthylamine in grease.

Conclusion: 2,5-dimercapto-1,3,4-thiadiazole is an aromatic compound used in oils and greases. It has previously caused contact allergy to workers who have handled the pure chemical, but to our knowledge, there are no previous reports of contact allergy from products containing the chemical in a relatively low concentration. 1 of our 2 cases had been sensitized from grease and the other from a guide-way oil. The latter case shows that machinists may become sensitized to lubricants that leak to the metalworking fluid system.

Key words: assembler; CAS 1072-71-5; CAS 72676-55-2; guide-way oil; machinist; metalworking fluid; occupational; phenyl- α -naphthylamine; tramp oil. © Blackwell Munksgaard, 2007.

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Industrial lubricants, such as greases, various engine oils, and neat oils (insoluble metalworking oils), cause allergic contact dermatitis relatively seldom (1, 2). The most commonly reported allergen in *greases* is **phenyl- α -naphthylamine (PAN;** CAS 90-30-2) (2–7) used as an antioxidant. A single case of allergic contact dermatitis caused by another antioxidant, **diphenylamine** (CAS 122-39-4), has also been reported (8). Regarding allergens in *neat oils*, there are 2 previous reports with a total of 5 patients allergic to an extreme pressure additive, **zinc,bis [(O,O'-di-2-ethylhexyl)dithio-**

phosphate] (2-ethylhexyl zinc dithiophosphate; **EHZDTP**, CAS 4259-15-8) (9, 10). Another extreme pressure additive, **dipentene** (CAS 138-86-3), in honing oil caused 3 independent cases of contact allergy in the UK (11). **Epoxide 7** (CAS 55838-67-0) in grinding oil caused allergic contact dermatitis in 3 patients (12). Stabilized chlorinated paraffin fraction in neat oil (possibly an **epoxy stabilizer** within it) caused an outbreak of contact dermatitis in 12 factory workers in the UK (13). 2 cases of contact allergy to another stabilizer, a **cycloaliphatic epoxy resin**

[**1,2-cyclohexanedicarbocyclic acid, bis(oxiranylmethyl)ester**, CAS 5493-45-8], in neat oil have also been reported from Denmark (14). In machinists, there are 2 reports of contact allergy to **tertiary-butylhydroquinone** (CAS 1948-33-0), an antioxidant, which was used in a vegetable oil based metalworking fluid and in a *hydraulic oil* (15, 16). There is also a case of allergic contact dermatitis from **coconut diethanolamide** (cocamide DEA; CAS 68603-42-9) in a hydraulic mining oil (17).

At the Finnish Institute of Occupational Health (FIOH), we have had only a few cases of contact allergy to industrial lubricants in this decade, 2 from greases and 1 from guide-way oil. In this article, we describe the patients in detail. The allergens in the greases were PAN and 2,5-dimercapto-1,3,4-thiadiazole, and the allergen in the guide-way oil was also 2,5-dimercapto-1,3,4-thiadiazole.

Materials and Methods

Patch tests

We reviewed the test files at FIOH from January 2000 to March 2007 for allergic reactions (+/++/+++) to the following allergens in greases and lubricants: 2,5-dimercapto-1,3,4-thiadiazole (2% in petrolatum, in-house preparation made from Oloa 4452X, a chemical delivered by the French manufacturer (Chevron Oronite, France) of the guide-way oil of patient 1, see below), PAN [1% in pet., in-house preparation (5)], tertiary butyl hydroquinone (1% pet., Chemotechnique, Vellinge, Sweden), EHSDTP [in-house preparation of 1% Additin 3180 in pet.; Additin 3180 contains 78% EHSDTP and 22% mineral oil (9)], Coconut diethanolamide (0.5% in pet., Chemotechnique), and Dipentene (1% in pet., Chemotechnique). The patch tests were performed using the Finn Chambers on Scanpore tape (Epitest, Tuusula, Finland).

We have not tested diphenylamine at all. Cycloaliphatic epoxy resins have not been included in the oil series, so they have not been tested in patients exposed to oils and lubricants.

Results

During the study period **2,5-dimercapto-1,3,4-thiadiazole** was tested in 112 patients, and 2 of them an allergic reaction (Cases 1 and 2 below). **PAN** was tested in 148 patients, and there were 2 allergic reactions: 1 of them is described below (Case 3), and the other patient's allergic reaction probably represented cross-allergy to black rubber chemicals and textile dyes, because his greases were negative on patch testing and according to the information of the manufacturer did not contain naphthylamines. **Tertiary butyl hydroquinone**

was tested in 289 patients, but there were no clearly allergic reactions, only 2 doubtful reactions and 3 irritant reactions. **EHSDTP** was tested in 249 patients, but there were no allergic or irritant reactions. **Coconut diethanolamide** was tested in 1224 patients, and there were 13 allergic reactions. None of the reactions could be connected to lubricants, most of them derived from liquid soaps. **Dipentene** was tested in 294 patients, but there were no allergic reactions to it.

Case reports

Patient 1 was a 50-year-old male computer numerical control machinist who had previously had occasional skin symptoms on various parts of his body, including foot dermatitis while using protection shoes. In 1999 he developed hand dermatitis for the first time, and it healed during sick leaves. In 2001, in patch testing (the standard, epoxy, ethanolamine, plastics, and glues, oils and cooling fluids series, concentration titration series of formaldehyde and patient's own products) he reacted to neomycin sulfate (+++), bacitracine (+++), terpene phenol resin 5% (+), fragrance mix (?+), metalworking fluid at 5% (?+), and 3.2% (+?), and to guide-way oil at 20% (+?). 8 months later 5 components of the metalworking fluid and 3 components of the guide-way oil were tested, and the patient had an allergic reaction to 1 component of the guide-way oil, dimercaptothiadiazole (DMTD; trade name Oloa 4452X): 20% +, 10%?+, 3.2%?+, 1%?+. 4 months later 2,5-Dimercapto-1,3,4-thiadiazole was tested for the second time: 2% +, 1% -, 0.32%, and 0.1% mild follicular reaction (?+). 18 control patients were negative to 2% 2,5-dimercapto-1,3,4-thiadiazole. The allergy to terpene phenol resin probably derived from his protection shoes.

Patient 2 was a 52-year-old male lorry assembler who developed work-related eczema on his eyelids and around his eyes in 2003. In 2005 on patch testing at FIOH (standard, antimicrobials, oils, and metalworking fluids, epoxy, plastics and glues, isocyanates, coco fatty acid derivatives, and own products) he reacted to his centre lubrication grease (as such; ++) and 2,5-dimercapto-1,3,4-thiadiazole (1%, ++). 6 months later, after many inquiries, the manufacturer of the centre grease informed us that it contained 0.25% 2,5-dimercapto-1,3,4-thiadiazole (CAS 1072-71-5) derivative and 0.25% 5,5-dithiobis(1,3,4-thiadiazole-2(3H)-thione (CAS 72676-55-2; 2,5-dimercapto-1,3,4-thiadiazole dimer). In the meanwhile, we had tested the patient for the second time with the dilution series of the centre grease: 100–3.2% concentrations gave ++ reactions, and 1% gave a + reaction. 5

control patients were negative to 100% and 10% centre grease. On the 3rd patch test session he had strong allergic reactions (++) to the 2,5-dimercapto-1,3,4-thiadiazole derivative 2–0.06%, and to 2,5-dimercapto-1,3,4-thiadiazole dimer 2–0.06% (lower concentrations were not tested).

Patient 3 was a 50-year-old male hydraulic assembler in a plant producing explosives. He had had atopic dermatitis since childhood and hand dermatitis since the 1980s. His hand dermatitis exacerbated in 1998. In 2001, on FIOH patch tests (standard, epoxy, plastics and glues, oils, and metalworking fluids, coco fatty acid derivatives, methacrylates, formaldehyde resins, and own products) the patient reacted to cocamide diethanolamide (cocamide DEA; ++), PAN (+++), and from the workplace materials to gunpowder containing ethylene glycol dinitrate (10%; ++), and a grease (?+). The grease was analysed by gas chromatography and found to contain a very small amount (<0.01%) of pure PAN. The oxidized products of PAN could not be analysed because of lack of reference preparation. The source of cocamide DEA allergy remained unknown.

Discussion

Greases, lubricant engine oils, and neat oils are all insoluble to water. They are most often produced from petroleum, but synthetic hydrocarbons are used for demanding conditions. Because these lubricants contain no water, biocides are not routinely required. However, various chemicals may be added to modify the properties of the products, such as oxidation inhibitors, extreme-pressure additives (especially in neat oils), and corrosion inhibitors. Many of these additives are potential skin sensitizers, but in the literature, there are only a few reports of contact allergy to these products, and at our institute only isolated cases have appeared every now and then.

Lubricating oils contain long paraffinic hydrocarbons (alkanes) and **greases** are oils to which thickening agents, most often fatty acid soaps, have been added. Most lubricating oils and greases contain oxidation inhibitors (antioxidants or metal deactivators). Diphenylamine and PAN are among the commonly used oxidation inhibitors in greases and they can be used also in neat oils (18). 2-mercaptobenzothiazole (MBT) can be used in greases as a copper deactivator. We have not found any cases of MBT allergy in the literature in connection with the use of greases or other lubricants. **Neat oils** are used as metalworking fluids when lubrication of a machining process is

more important than cooling it, as in fine grinding and honing. They contain naphthenic or paraffinic oils and other chemicals such as extreme pressure additives, scavengers (e.g. epoxides), and diluents. Besides MBT, epoxy compounds are other contact allergens that might have relevance to the use of lubricants, as epoxy compounds may be used to stabilize chlorinated paraffins, especially in neat oils.

Patient 1 was allergic to the guide-way oil used in the machine, and more specifically to 1 of its components, 2,5-dimercapto-1,3,4-thiadiazole. Guide-way oils are used to lubricate the metalworking machine itself, and they leak to the circulating metalworking fluid forming what is referred to as 'tramp oil'. Machinists may have continuous skin contact to the guide-way oil and other machine oils because of the leakage. Because 2,5-dimercapto-1,3,4-thiadiazole is a rare contact allergen, and it was found to be a component of the guide-way oil used in the metalworking machine, this case shows that the leakage of the engine oils to the metalworking fluid may cause sensitization. At FIOH, we have previously investigated a machinist whose formaldehyde allergy probably derived from formaldehyde in his guide-way oil, liquid soap, and metalworking fluid (19).

2,5-Dimercapto-1,3,4-thiadiazole is a heterocyclic compound that is used for instance in the production of copper corrosion inhibitors for engine oils, flame retardants, and photographic development chemicals. 7 cases of allergic contact dermatitis from the pure chemical have been reported in a manufacturing plant (20). It is also a possible component of metalworking fluids (18). To our knowledge, there are no previous reports of contact allergy caused by 2,5-dimercapto-1,3,4-thiadiazole in industrial greases, metalworking fluids or other products which contain the chemical in a low concentration.

We have had both PAN and 2,5-dimercapto-1,3,4-thiadiazole in our patch test series of oils and metalworking fluids, but there are no commercial test preparations of these allergens. In lack of in-house test substances, contact allergy to these compounds can be diagnosed only by testing patients' own products. Industrial greases and neat oils can usually be tested as is, but a short dilution series of, for instance 100%, 32%, and 10% in pet. makes it easier to differentiate between irritant and allergic reactions (21). For the patch testing of guide-way oils and other lubricant oils, we have used a single concentration of 20% in pet.. If a product gives seemingly allergic reactions and few control patients are negative, we try to get the ingredients from the manufacturer for patch testing. As Case 2 showed, it is sometimes hard to

get information on the composition of a product. Regarding PAN, the patient may react only to an oxidation product of the chemical (produced in the grease and patch test preparation during storage/use) and remain negative to freshly made PAN test preparation (4). If needed, the oxidation of a fresh sample of PAN may be enhanced by addition of, for instance hydrogen peroxide.

In conclusion, contact allergy to water-insoluble lubricants is rare. The petroleum-based hydrocarbons do not sensitize, but the various additives may cause contact allergy. We describe a new allergen in lubricants, 2,5-dimercapto-1,3,4-thiadiazole, which caused allergic contact dermatitis in 2 patients, a machinist and an assembler, the first of whom was sensitized from a guide-way oil of a metalworking machine and the other from a lubricant grease. In addition, 1 of our patients was sensitized to PAN, the most common allergen in lubricants.

References

- Geier J, Uter W, Lessmann H, Frosch P J. Patch testing with metalworking fluids from the patient's workplace. *Contact Dermatitis* 2004; 51: 172–179.
- Svedman C, Isaksson M, Zimerson E, Bruze M. Occupational contact dermatitis from a grease. *Dermatitis* 2004; 15: 41–44.
- Boman A, Hagelthorn G, Jeansson I, Karlberg A T, Rystedt I, Wahlberg J E. Phenyl-alpha-naphthylamine – case report and guinea pig studies. *Contact Dermatitis* 1980; 6: 299–300.
- Jolanki R, Alanko K, Vainiotalo S, Estlander T, Kanerva L. Occupational compound allergy to an industrial grease caused by an oxidation product of phenyl-alpha-naphthylamine. *Contact Dermatitis* 2000; 43: 122–123.
- Kalimo K, Jolanki R, Estlander T, Kanerva L. Contact allergy to antioxidants in industrial greases. *Contact Dermatitis* 1989; 20: 151–152.
- Carmichael A J, Foulds I S. Isolated naphthylamine allergy to phenyl-alpha-naphthylamine. *Contact Dermatitis* 1990; 22: 298–299.
- Freeman S. Allergic contact dermatitis due to an industrial grease caused by the antioxidant phenyl-alpha-naphthylamine. *Am J Contact Dermat* 1991; 2: 117–118.
- Herve Bazin B, Fousseureau J, Cavelier C. Allergy to diphenylamine from an industrial grease. *Contact Dermatitis* 1986; 14: 116.
- Kanerva L, Tupasela O, Jolanki R. Occupational allergic contact dermatitis from ethylhexylzinc dithiophosphate and fatty acid polydiethanolamide in cutting fluids. *Contact Dermatitis* 2001; 44: 193–194.
- Isaksson M, Frick M, Gruvberger B, Ponten A, Bruze M. Occupational allergic contact dermatitis from the extreme pressure (EP) additive zinc, bis ((O, O'-di-2-ethylhexyl) dithiophosphate) in neat oils. *Contact Dermatitis* 2002; 46: 248–249.
- Rycroft R J. Allergic contact dermatitis from dipentene in honing oil. *Contact Dermatitis* 1980; 6: 325–329.
- Rycroft R J. Allergic contact sensitization to Epoxide 7 in grinding oil. *Contact Dermatitis* 1980; 6: 316–320.
- Scerri L, Dalziel K L. Occupational contact sensitization to the stabilized chlorinated paraffin fraction in neat cutting oil. *Am J Contact Dermat* 1996; 7: 35–37.
- Jensen C D, Andersen K E. Two cases of occupational allergic contact dermatitis from a cycloaliphatic epoxy resin in a neat oil: case report. *Environ Health* 2003; 2: 3.
- Meding B. Occupational contact dermatitis from tertiary-butylhydroquinone (TBHQ) in a cutting fluid. *Contact Dermatitis* 1996; 34: 224.
- Aalto-Korte K. Allergic contact dermatitis from tertiary-butylhydroquinone (TBHQ) in a vegetable hydraulic oil. *Contact Dermatitis* 2000; 43: 303.
- Hindson C, Lawlor F. Coconut diethanolamide in a hydraulic mining oil. *Contact Dermatitis* 1983; 9: 168.
- Forschungsgemeinschaft D. Metal working fluids. In: *Occupational Toxicants Critical data Evaluation for MAK Values and Classification of Carcinogens*, Vol. 20, Greim H (ed.): Weinheim, Wiley-VCH, 2003: 197–215.
- Suuronen K, Aalto-Korte K, Piipari R, Tuomi T, Jolanki R. Occupational dermatitis and allergic respiratory diseases in Finnish metalworking machinists. *Occupational Medicine* 2007; 57: 277–283.
- O'Driscoll J, Beck M, Taylor S. Occupational contact allergy to 2,5-dimercapto-1,3,4-thiadiazole. *Contact Dermatitis* 1990; 23: 268–269.
- Jolanki R, Estlander T, Alanko K, Kanerva L. Patch testing with a patient's own materials handled at work. In: *Handbook of Occupational Dermatology*, Kanerva L, Elsner P, Wahlberg J E, Maibach H I (eds): Berlin, Springer, 2000: 375–384.

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