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CONTACT DERMATITIS

Airborne irritant contact dermatitis and conjunctivitis after occupational exposure to chlorothalonil in textiles

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Chlorothalonil (tetrachloro-1,3-benzenedicarbonitrile, CAS 1897-45-6) is a pesticide that has been on the market for many years. It is used as a fungicide in agriculture, horticulture, and floriculture; as a wood preservative; and in paint. We report an epidemic of airborne irritant contact dermatitis, conjunctivitis, and upper airway complaints among seamstresses in a Portuguese trailer tent factory, which we attribute to chlorothalonil. All exposed workers had work-related skin symptoms. After patch testing, we showed that none of these were of allergic origin. Instead of allergic reactions, we noticed a delayed type of irritation after 72 hr to chlorothalonil and to the textile extracts containing high concentrations of chlorothalonil. Although allergic and irritant contact dermatitis from chlorothalonil has been described before, this is, as far as we know, the first time that a delayed type of dermatitis, conjunctivitis, and upper airway irritation after exposure to chlorothalonil in tent-cloth is described.

Key words: airborne irritant contact dermatitis; chlorothalonil; occupational exposure; fungicides; pesticides; tent; textile. © Blackwell Munksgaard, 2007.

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The purpose of our study was to detect the aetiology of work-related health complaints among workers in a textile factory. A European textile market leader in manufacturing high-quality tent cloth for family and trailer tents was confronted with skin and mucosal complaints among workers from several workshops throughout Europe, which used their fabrics. These health problems were most prominent in their Portuguese plant and had led to some commotion among the workers.

In this plant, the problem occurred in a workshop where the tent cloth was cut and sewn. From the original 11 workers, 3 had already resigned because of the health complaints. The workers reported erythema; itch and scaling on eyelids, face, and arms; conjunctivitis; and a sore throat. The symptoms appeared after a few hours of exposure to specific batches of the tent cloth and disappeared during weekends and vacations. There were no symptoms when they worked with other batches.

Materials and Methods

Subjects

All 11 workers who had been exposed to the fabrics, all of whom had reported skin and airway complaints, were examined: 8 still worked for the company and 3 had resigned because of their health problems. 5 workers without exposure to the fabrics served as control group: they did not have the reported health complaints. Cases and controls were all women, 22–47 years old. The duration of employment varied from 7 months to 15 years.

Questionnaire and medical history

To survey the dermatological complaints and exposures to environmental factors, the Nordic Occupational Skin Questionnaire 2002 (1) was used. The work-related mucosal health complaints were investigated with a questionnaire that was previously developed by our own expert

centre. Both questionnaires were translated in Portuguese by a certified translator. The completed questionnaires were translated into Dutch by the same translator. With the help of the translator, a medical history was taken by an occupational physician trained in occupational dermatology.

Patch testing

Patch testing was performed with TRUE test and van der Bend square chambers on Medipore tape. We patch tested with European standard series, extended with 12 additional substances used in our clinic, a textile series (see Table 1), and a dilution series from tent cloth extracts and solutions of all materials the seamstresses were exposed to. Tent cloths and solutions were supplied by the manufacturer of the tent cloth. Freeze-dried extracts in water, alcohol, and acetone were made from 3 different coloured cotton tent cloths (blue-green, grey, and dark blue), and tested in a dilution of 10%, 1%, and 0.1% in petrolatum (pet.). 6 solutions were tested: 3 textile finishes (I, II, and II) and 3 dyes. The finishes and dyes were tested pure and in a dilution of 10%, 1%, and 0.1% in pet.

Table 1. Textile series

Concentration	Allergen
4.5% aq.	Dimethyloldihydroxyethylene urea (Fp CPN)
5% aq.	Dimethyloldihydroxyethylene urea modified (Fix ECO)
5% pet.	Ethylene urea melamineform mix (Fp AC)
4.5% aq.	DMDHI (Fix NF)
10% pet.	Urea formaldehyde
7% pet.	Melamine formaldehyde
1% pet.	Disperse blue 3
1% pet.	Disperse blue 35
1% pet.	Disperse blue 85
1% pet.	Disperse blue 106
1% pet.	Disperse blue 124
1% pet.	Disperse blue 153
1% pet.	Disperse yellow 3
1% pet.	Disperse yellow 9
1% pet.	Disperse orange 1
1% pet.	Disperse orange 3
1% pet.	Disperse brown 1
1% pet.	Disperse red 1
1% pet.	Disperse red 17
5% pet.	Direct orange 34
5% pet.	Acid yellow 61
1% pet.	Reactive violet 5
1% pet.	Basic red 46
1% pet.	Reactive black 5
1% pet.	Reactive blue 21
1% pet.	Reactive blue 238
1% pet.	Reactive orange 107
1% pet.	Reactive red 123
5% pet.	Acid red 118
5% pet.	Acid red 359
1% pet.	Acid yellow 36
0.1% pet.	Isophoronediamine

DMDHI, 1,3-Dimethyl-4,5-dihydroxyimidazolidinon-z.

The patches were removed after 48 hr. Readings were carried out after 48 and 72 hr by 3 different persons: a dermatologist, an occupational physician, and a nurse practitioner, all experienced in patch testing and reading.

Prick testing

To evaluate the atopic diathesis of the employees, prick testing was performed with 19 inhalation allergens: tree, grass, and weed pollen; animals' and birds' allergens; house dust mites; and moulds.

Workplace survey

A workplace survey was performed by a registered occupational health nurse to identify tasks and possible exposure to allergens or irritants. 6 of the 8 workers with skin, eye, and upper airway complaints worked as seamstress. From the other 2, 1 inspected and folded the complete tents and the other had to cut all the tent cloth. All 8 employees worked in the same unit. The unit had no industrial vacuum cleaning system to remove the textile dust at the source and was ventilated by opening the windows. As personal protection device, all workers wore aprons and sleeves over their own clothes. Some workers started to wear dust masks when the health complaints occurred. Gloves were not used.

The tent cloth was delivered in 100-m rolls, packed in plastic. Other materials worked with were polyvinyl chloride, curtain fabrics, zippers, and sewing thread. The rolls were opened by the cutter (this worker had the most complaints). During this procedure, dust was released into the work environment. After cutting the cloth, the cutter distributed the cloths among the seamstresses. All seamstresses had their own sewing machine. Sewing the different pieces of tent cloth together produced a small amount of dust. The workplace was swept daily and the working area was completely cleaned once a week. The daily and the weekly cleaning activities were done by the workers themselves.

Results

Questionnaire and medical history

In spring 2003, the first workers had developed health complaints: swollen red eyelids, conjunctivitis, and a sore throat. After the summer holidays, the number of workers with these health complaints increased. The workers noted a difference between several batches: some batches gave more health complaints than others, although

these batches showed no difference in colour or material. In spring 2004, the health complaints increased until the summer holidays. During and after the summer holidays, none of the workers had health complaints until the beginning of autumn. During the health survey (October 2004), none of the workers had dermatological or pulmonary complaints

Patch testing

The results of patch testing are shown in Table 2 (only the positive and irritant reactions are shown). The positive reactions to nickel sulfate and thiomersal were judged as not relevant for the complaints. The tent cloth extracts, finish, and dye series showed only irritant reactions: they were concentration dependent, test chamber shaped, sharply demarcated erythematous without other skin changes, and without pruritus. Most reactions occurred at 72 hr to the alcohol and acetone extract of the blue-green and grey, both 10% in pet. and to 1 of the finishes (II) tested pure and 10% in pet.

Striking findings were that 7 of the 8 still exposed workers showed no reaction after 48 hr. After 72 hr, 5–6 of these 8 workers showed a reaction to the alcohol and/or acetone tent cloth extracts and to finish II. The worker with an irritation reaction at 48 as well as 72 hr had been absent from work for 8 weeks preceding patch testing because of other health problems. In the control group, 3 of 5 nonexposed workers showed irritation reactions to the tent cloth extracts and finish II after 48 hr. The 3 formerly exposed workers, who had resigned, reacted all after 48 hr to the alcohol extracts from the tent cloth. After 72 hr, all exposed workers and 4 of 5 controls showed irritant reactions to the alcohol and acetone extract and to finish II. None of the 16 tested persons reacted on the 1% and 0.1% dilutions of the extracts, dye, or finish.

Prick testing

3 of the 8 exposed employees had a positive prick test to 1 or more of the inhalation allergens. 2 of these 3 also had a positive medical history for atopy.

Follow-up

In May 2005, the local dermatologist documented a new outbreak of dermatitis at the plant. Because the tent cloth supplier was out of stock of cloth treated with finish I and III, the factory was supplied with cloth treated with finish II. Batches treated with finish I and III did not seem to cause any health problems. Study of the Medical Safety Data Sheets (MSDS) of all 3 finishes resulted in the conclusion that the main difference between these finishes was the composition with regard to fungicides: finish II contained chlorothalonil, while the other 2 contained tebuconazol.

Again the workers showed a typical pattern of eyelid dermatitis and conjunctivitis, and they complained of sore throat and oral secretions with blood or tasting like blood. Although again the working area had fairly good ventilation, the atmosphere felt uncomfortable. The visiting

Table 2. Patch test results in 11 workers with skin/mucosal symptoms and 5 controls

	BG al 10%		BG ac 10%		G al 10%		G ac 10%		Finish II pure		Finish II 10% pet.		BG as is		B as is		G as is	
Worker	D2	D3	D2	D3	D2	D3	D2	D3	D2	D3	D2	D3	D2	D3	D2	D3	D2	D3
E 1		Irr						Irr		Irr		Irr						
E 2																		
E 3		Irr		Irr		Irr		Irr		Irr		Irr		Irr		Irr		
E4		Irr		Irr		Irr		Irr		Irr		Irr		Irr				
E 5																		
E 6		Irr		Irr		Irr		Irr										
E 7		Irr		Irr		Irr		Irr				Irr						
E 8	Irr	Irr		Irr	Irr	Irr	Irr	Irr		Irr				Irr		Irr		Irr
E 9	Irr	Irr		Irr	Irr	Irr		Irr		Irr								
E 10	Irr	Irr		Irr	Irr	Irr		Irr		Irr		Irr						
E 11	Irr	Irr	Irr	Irr	Irr	Irr	Irr	Irr	Irr	Irr		Irr						
C 1		Irr		Irr		Irr		Irr		Irr								
C 2	Irr	Irr		Irr	Irr	Irr	Irr	Irr	Irr	Irr		Irr				Irr		
C 3	Irr	Irr	Irr	Irr	Irr	Irr	Irr	Irr		Irr				Irr		Irr		Irr
C 4			Irr		Irr		Irr	Irr	Irr	Irr		Irr						
C 5	Irr	Irr	Irr	Irr	Irr		Irr	Irr	Irr	Irr		Irr		Irr		Irr		Irr

E 1, exposed worker 1; C 1, control person 1; BG al 10%, blue-green tent cloth, extracted in alcohol, diluted in 10% pet.; B as is, blue tent cloth patch tested as is; BG ac 10%, blue-green tent cloth, extracted in acetone, diluted in 10% pet.; G as is, grey tent cloth patch tested as is; G al 10%, grey tent cloth, extracted in alcohol, diluted in 10% pet.; G ac 10%, grey tent cloth, extracted in acetone, diluted in 10% pet.; BG as is, blue-green tent cloth patch tested as is; Irr, irritant reaction.

dermatologist also noticed some trouble with eyelid pruritus on the second day in the factory.

The workers were patch tested again with the Portuguese standard series, pesticide series, plastic and glues series, tebuconazol 1 and 5% pet., econazol 1% alc (Chemotechnique, Vellinge, Sweden), miconazol 1% alc (Chemotechnique), and clotrimazol 5% pet. (Oftalder, Linda a Velha, Portugal). Tests were applied on Finn Chambers® on Scanpor tape.

Chlorothalonil powder (supplied by the manufacturer of the tent cloth) was dissolved at 0.01% in pet., 0.01% and 1% in acetone, and 0.01% in distilled water. Liquids were immediately placed in large Leukotests tapes (with the cotton portion in the middle) and taped on the workers' backs within less than 20 min. Pet. was tested in Finn Chambers®. After 48 hr (D2), all tests were removed at the factory and readings performed within 30 min. Second readings were performed at 72 hr (D3) at the factory. The results of the readings are presented in Table 3. Tebuconazol tested 1 and 5% pet. in Finn Chambers® was negative in all subjects. Chlorothalonil 0.01% acetone and 0.01% pet. tested in 7 controls were all negative.

Discussion

We report an epidemic of work-related health complaints (see Table 4), among seamstresses in a Portuguese tent factory, where all 11 exposed workers were affected. We concluded that the workers suffered from occupational contact dermatitis and conjunctivitis caused by an airborne exposure factor. Airborne contact dermatitis can have an allergic and irritant origin (2–4) and can be accompanied by conjunctivitis (2).

After patch testing with the European/Portuguese standard series, textile series, and dilution series from tent cloth extracts and solutions of all exposed materials, we concluded that the airborne contact dermatitis had an irritant origin. This conclusion was based on the following:

(1) the distribution of complaints among the exposed and nonexposed workers: the more these workers were exposed, the more complaints were reported. Workers without exposure had no complaints;
(2) the patch test reactions to all exposed materials and ingredients.

Table 3. Patch test results with chlorothalonil in 4 affected workers during the second outbreak of the dermatitis

	0.01% pet.		1% acetone		0.01% acetone		0.01% water	
Worker	D2	D3	D2	D3	D2	D3	D2	D3
E 1	Irr	—	—	—	—	—	Irr	Irr
E 3	Irr	Irr	—	Irr	—	—	Irr	Irr
E 4	—	Irr	—	Irr	—	—	—	Irr
E 5	—	—	NT	NT	—	—	—	—

E 1, exposed worker 1; Irr, irritant reaction; NT, not tested.

Table 4. Reported health complaints

Worker	Eye lid	Dermatitis elsewhere	Conjunctivitis	Sore throat
E 1	Pruritus, erythema, scaling	Arms	No	Yes
E 2	Pruritus, erythema, scaling, swelling	No	Yes	Yes
E 3	Pruritus, erythema, scaling	Arms	Yes	No
E 4	Erythema, burning sensation	Hands	Yes	Yes
E 5	Pruritus, erythema, scaling, swelling	No	Yes	No
E 6	Pruritus, scaling, swelling	No	Yes	Yes
E 7	Pruritus, scaling	No	Yes	No
E 8	Erythema, burning sensation	Cheeks	Yes	No
E 9	Pruritus, erythema, scaling	No	No	No
E 10	Erythema, burning sensation	Cheeks	Yes	Yes
E 11	Pruritus, erythema, scaling	Arms	No	No

E 1, exposed worker 1.

We could exclude an allergic origin of the complaints. Instead, we noticed delayed-type irritant reactions after 72 hr. We observed this irritant reaction to the alcohol and acetone extracts and to finish II in all exposed workers. Moreover, the most important argument for an irritant reaction is that we also observed this reaction in 4 of 5 controls. None of the 16 tested persons reacted on the 1% and 0.1% dilutions of the extracts, dye, or finish. This delayed-type reaction was confirmed by patch testing with chlorothalonil 0.01% in pet., acetone, and water. Although uncommon, delayed and crescendo irritant reactions have been described before, while a possible explanation is lacking (5–7). Our observation of a delayed-type irritant reaction did not match the appearance of symptoms within a few hours of exposure, as reported by the exposed workers. In our opinion, this is an apparent discrepancy that can be explained by the fact that the patch test was performed on not previously exposed, and therefore not already irritated, skin.

Based on the results of the patch testing in combination with the findings after the new outbreak, we concluded that the most likely source of the irritant exposure was finish II, containing chlorothalonil. Chlorothalonil (tetrachloro-1,3-benzenedicarbonitrile, CAS 1897-45-6) is a widely used

fungicide in agriculture, horticulture, and floriculture; as a wood preservative; and in paint. Allergic contact dermatitis because of contact with chlorothalonil has been described in woodworkers (8–10), fruit and vegetable growers (11–13), floriculturists (14), and after working with paint (15, 16). Other reported skin complaints are contact urticaria and erythema dyschromicum perstans (17, 18). Although less frequently described, contact with chlorothalonil can also have an effect on the bronchopulmonary system. Clinical signs can vary from occupational asthma to irritation of eye, nose, and throat (19–21). Although most publications report allergic contact dermatitis (8–16, 19), several authors mention the irritant properties of chlorothalonil (10, 22, 23, 24). Bruynzeel and van Ketel (14) even described a delayed crescendo irritant reaction to chlorothalonil 1% pet. in their control group. We first suspected the irritant reactions in our subjects to have been caused by a high concentration of chlorothalonil, thereby hiding a true allergic response in the exposed group. Study of the MSDS of finish II showed a concentration of 3% chlorothalonil. Converted to the test concentrations we used, this means that we had tested the chlorothalonil in a concentration of 3%, 0.3%, 0.03%, and 0.003% in pet. With this in mind, the irritant reactions to the pure finish (3% chlorothalonil) and the 10% dilution (0.3% chlorothalonil) are understandable because these concentrations are higher than the 0.01% concentration, which had no irritant reaction in control persons (8, 9).The second test series after the new outbreak was done with chlorothalonil 0.01% pet., acetone, and water. Flannigan et al. (24) reported a mild irritation below the threshold for clinical problems after exposure to 0.01% chlorothalonil in acetone. The negative reactions of the workers after testing with chlorothalonil 0.01% in pet., acetone, and water could exclude sensitization to chlorothalonil. Moreover with a sensitization, the workers would have reacted to the 1% and 0.1% dilution (0.03% and 0.003% chlorothalonil). Boman et al. (22) showed positive allergic reactions in animal tests with these low–patch test concentrations in sensitized animals and Lidén (16) recognized a positive allergic reaction on a patch test concentration as low as 0.0001% aq. None of our tested workers showed a reaction on the low concentrations of the dilution series.

The high concentration of chlorothalonil in the finish and the long periods of storage of the tent cloth in a plastic wrap suggest a high air concentration of chlorothalonil-contaminated tent cloth dust in some areas of the working space. Unfortunately, we were not able to measure the concentration of chlorothalonil in the ambient air.

Based on our finding that an airborne exposure with low concentrations of chlorothalonil can cause skin and airway irritant reactions, we advise to use chlorothalonil-treated fabrics only in open spaces or with sufficient ventilation and industrial vacuum cleaning at the source of the exposure. Chlorothalonil-treated fabrics should have warnings on its packing, especially when the packing is airtight.

References

1. Susitaival P, Flyvholm M A, Meding B, Kanerva L, Lindberg M, Svensson A, Olafsson J H. Nordic Occupational Skin Questionnaire (NOSQ-2002): a new tool for surveying occupational skin diseases and exposure. *Contact Dermatitis* 2003: 49: 70–76.
2. Angelini G, Vena G A. Airborne contact dermatitis. *Clin Dermatol* 1992: 10: 123–131.
3. Lachapelle J M. Industrial airborne irritant or allergic contact dermatitis. *Contact Dermatitis* 1986: 14: 137–145.
4. Huygens S, Goossens A. An update on airborne contact dermatitis. *Contact Dermatitis* 2001: 44: 1–6.
5. Malten K E, der Arend J A, Wiggers R E. Delayed irritation: hexanediol diacrylate and butanediol diacrylate. *Contact Dermatitis* 1979: 5: 178–184.
6. Bruynzeel D P, van Ketel W G, Scheper R J, von Blomberg-van der Flier B M E. Delayed time course of irritation by sodium lauryl sulfate: observations on threshold reactions. *Contact Dermatitis* 1982: 8: 236–239.
7. Löffler H, Effendy I. Crescendo reactions to sodium lauryl sulfate and retinoic acid in irritant patch tests. *Contact Dermatitis* 1997: 37: 47–48.
8. Bach B, Pedersen N B. Contact dermatitis from a wood preservative containing tetrachloroisophthalonitrile. *Contact Dermatitis* 1980: 6: 142.
9. Spindeldreier A, Deichmann B. Kontaktdermatitis auf ein Holzschutzmittel mit neuer fungizider Wirksubstanz. *Dermatosen in Beruf und Umwelt* 1980: 28: 88–90.
10. Johnsson M, Buhagen M, Leira H L, Solvang S. Fungicide-induced contact dermatitis. *Contact Dermatitis* 1983: 9: 285–288.
11. Penagos H. Contact dermatitis causes by pesticides among banana plantation workers in Panama. *Int J Occup Environ Health* 2002: 8: 14–18.
12. Penagos H, Ruepert C, Partanen T, Wesseling C. Pesticide patch test series for the assesment of allergic contact dermatitis among banana plantation workers in Panama. *Dermatitis* 2004: 15: 137–145.
13. Horiuchi Y, Ando K. Contact dermatitis due to pesticides for agricultural use. *Jap J Dermatol* 1980: 90: 289.
14. Bruynzeel D P, Ketel van W G. Contact dermatitis due to chlorothalonil in floriculture. *Contact Dermatitis* 1986: 14: 67–68.
15. Meding B. Contact dermatitis from tetrachloroisophthalonitrile. *Contact Dermatitis* 1986: 15: 187.
16. Lidén C. Facial dermatitis caused by chlorothalonil in a paint. *Contact Dermatitis* 1990: 22: 206–211.
17. Penagos H, Jimenez V, Fallas V, O'Malley M, Maibach H I. Chlorothalonil, a possible cause of erythema dyschromicum perstans (ashy dermatitis). *Contact Dermatitis* 1996: 35: 214–218.
18. Dannaker C J, Maibach H I, O'Malley M. Contact urticaria and anaphylaxis to the fungicide chlorothalonil. *Cutis* 1993: 52: 312–315.

19. Huang J, Aoyama K, Ueda T, Matsushita T. Respiratory effects on skin allergy in workers exposed to tetrachloroisophthalonitrile. *Bull Environ Contam Toxicol* 1995: 55: 320–324.
20. Honda I, Kohrogi H, Ando M, Araki S, Ueno T, Futatsuka M, Ueda A. Occupational asthma induced by the fungicide tetrachloroisophthalonitrile. *Thorax* 1992: 47: 760–761.
21. Draper A, Cullinan P, Campbell C, Jones M, Newman Taylor A. Occupational asthma from fungicide fluazinam and chlorothalonil. *Occup Environ Med* 2003: 60: 76–77.
22. Boman A, Montelius J, Rissanen R L, Lidén C. Sensitizing potential of chlorothalonil in the guinea pig and the mouse. *Contact Dermatitis* 2000: 43: 273–279.
23. Flannigan S A, Tucker S B. Influence of the vehicle on irritant contact dermatitis. *Contact Dermatitis* 1985: 12: 177–178.
24. Flannigan S A, Tucker S B, Calderon V Jr. Irritant dermatitis form tetrachloroisophthalonitrile. *Contact Dermatitis* 1986: 14: 258–259.

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