

ORIGINAL ARTICLE

Tertiary prevention of occupational skin diseases: Prevalence of allergic contact dermatitis and pattern of patch test results

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Background: Allergic contact dermatitis (ACD) is one of the most common occupational skin diseases (OSDs). Its prevalence and the causative allergens differ between occupations.**Objectives:** To evaluate the prevalence of ACD and the pattern of patch test results of patients taking part in a tertiary individual prevention programme (TIP) for OSD in Germany.**Patients and Methods:** In a retrospective cohort study, the data of 3411 TIP patients patch tested between 2007 and 2016 were analysed.**Results:** In 2687 (78.8%) patients, work-related skin disease was diagnosed, mostly hand dermatitis. The highest proportion of face dermatitis was seen in painters (8.1%). ACD was most common in painters (56.8%), hairdressers (45.8%), construction workers (31.5%), gardeners/florists (26.7%), and metalworkers (26.5%). On average, hairdressers had the youngest age (31.4 ± 12.6 years, $P < 0.0001$) and the shortest time in the profession prior to the TIP (mean 13.7 years). The pattern of patch test reactivity showed occupation-specific differences related to work exposures.**Conclusions:** Identification of occupational groups at risk for ACD and relevant allergens may help in the development and implementation of targeted prevention strategies. Our data suggest that there should be a particular focus on hairdressers and painters.

KEYWORDS

contact allergy, contact dermatitis, hand eczema, occupational skin diseases, patch test, work-related

1 | INTRODUCTION

Occupational skin diseases (OSDs) are among the most common occupational diseases in industrial countries.^{1,2} They are associated with a poor prognosis and constitute a considerable socio-economic burden.^{3–5} The majority of OSDs consist of contact dermatitis of the hands resulting from wet work and exposure to skin irritants and/or contact allergens.² In general, work-related irritant contact dermatitis (ICD) is more frequent than allergic contact dermatitis (ACD).⁶ However, ACD is considered to confer a higher severity and worse prognosis of occupational hand dermatitis, resulting more often in change of profession or not remaining in the workforce.^{3,7}

In Germany, patients with severe skin diseases suspected to be of occupational origin are offered to take part in an inpatient/outpatient

tertiary individual prevention programme (TIP) funded by the statutory accident insurances. It has been shown that the TIP is associated with significant improvements in severity of OSD, quality of life, ability to return to work, and ability to remain in the workforce.^{6,8,9} As part of the diagnostic work-up during the TIP, patch tests are regularly performed. When a relevant contact allergy is detected, targeted preventive measures are elaborated to enable the best possible avoidance of allergen exposure both at the workplace and in leisure time. This includes suggestions for replacement of allergen-containing products and selection of adequate protective gloves.

Previous studies have shown that the prevalence of work-related ACD and the spectrum of causative contact allergens differ substantially between occupations.^{10,11} This is mainly attributable to different allergen exposures in the respective professions. Also, the extent of

exposure varies according to the work tasks and the possibilities of applying protective measures, such as protective gloves. The identification of occupational groups at risk for ACD and relevant allergens will help in the development and implementation of targeted prevention strategies for the respective sectors and agents. Hence, we analysed the occupation-specific prevalence of ACD and the pattern of patch test reactivity of patients with OSD taking part in the TIP.

2 | PATIENTS AND METHODS

2.1 | Study population and study design

This retrospective study was based on pseudonymized medical histories, clinical data and patch test results that were routinely submitted to the Information Network of Departments of Dermatology (IVDK) central office at the University of Göttingen. The structure and routine operating procedure of the IVDK have been described elsewhere in detail.¹² Data are subject to standardized quality control and are analysed according to international standards.^{13,14} For this analysis, we selected the submitted data of all patients patch tested during the TIP in the 2 dermatological centres of the Institute for Interdisciplinary Dermatological Prevention and Rehabilitation (iDerm) at the University of Osnabrück and at the BG Hospital Hamburg, Germany, between January 2007 and December 2016. Participants in the TIP are largely representative of the population of patients in Germany with severe skin disease suspected to be of occupational origin who did not respond sufficiently to secondary outpatient prevention measures.^{6,8,9} During the 3-week inpatient phase of the TIP, the patients were seen by trained dermatologists, who took a detailed history and thoroughly assessed the aetiology of the presented skin diseases. The diagnosis and location of the skin lesions, and demographic information including age, sex, and current profession, were recorded. The relationship between occupational exposures and skin disease was documented as “yes”, “no”, or “unclear”. For the present analysis, only patients with skin diseases finally considered to be of occupational aetiology after thorough diagnostic work-up during the TIP were further investigated. The majority of patients had been patch tested with the German baseline series of contact allergens and, when required, with additional substances/test series. In only a few cases was no patch test performed. The main reasons were that the observed skin disease was unlikely to be caused by contact allergy or that sufficient patch testing had been performed prior to the TIP. ACD was diagnosed in patients with a positive patch test reaction to at least 1 allergen, with exposure ascertained by patient history, documented workplace visits, and inspection of product labels or safety data sheets, which was considered to be relevant for the current eczema.

Patch tests were performed and read according to international guidelines, refined by the German Contact Dermatitis Research Group (DKG).¹⁵ Patch test reactions documented on day (D) 3 were included in the evaluation. In only a few exceptional cases, when a reading was performed on D4 instead, was this reaction selected. Patch test reactions were considered to be positive if they were characterized by erythema plus infiltration, papules, and/or vesicles (+, ++, or +++).

Because of changes in the test recommendations of the DKG over time, some allergens that used to be in special test series had been moved to the baseline series or vice versa. Therefore, patch test results for these allergens are presented in context with the baseline series and also with additional special series.

2.2 | Data analysis

Data analysis was performed in the IVDK central office at the University of Göttingen with the sas 9.4 program package (SAS Institute, Cary, North Carolina). Concerning the proportions of positive test reactions and items of population characteristics, statistically significant differences at a 5% level were concluded from non-overlapping 95% confidence intervals (CIs) when separate subgroups were compared. Differences in the distribution of age and years in profession until the TIP among the different occupational groups were analysed with the Kruskal-Wallis test, and considered to be significant at $P < 0.05$.

3 | RESULTS

3.1 | Study population

Data of 3411 TIP patients patch tested in the two centres in Osnabrück and Hamburg between January 2007 and December 2016 had been routinely sent to the IVDK central office. Only those who were finally diagnosed with a work-related skin disease ($n = 2687$, 78.8%) were further investigated in this analysis (Table 1). Of these, 1582 patients (58.9%) were women. The average age was 43.3 years (standard deviation, ± 12.6 years). The 10 most frequent occupational groups and their specific characteristics are shown in Table 1. The highest numbers of patients worked as hospital nurses ($n = 443$, 16.5%), elderly care nurses ($n = 329$, 12.2%), mechanics ($n = 264$, 9.8%), and hairdressers ($n = 262$, 9.8%). Female patients were more common among hospital nurses, elderly care nurses, hairdressers, cleaning personnel, gardeners/florists, and food handlers, whereas a substantially higher number of male patients worked as mechanics, metalworkers, construction workers, and painters. The age distribution differed significantly between the occupational groups (Kruskal-Wallis test; $P < 0.0001$). A closer analysis showed that hairdressers were significantly younger (average age of 31.4 ± 12.6 years) and cleaning personnel were significantly older (average age of 50.5 ± 8.1 years) than patients in the other occupational groups, among which the age distribution did not differ significantly. In all groups, mainly the hands were affected. Only rarely were facial skin lesions observed. The highest proportion was seen in painters (8.1%). More than half of the patients ($n = 1510$, 56.2%) were diagnosed with past or present atopic dermatitis. This diagnosis was more common in female-dominated occupational groups. In most patients, an overlap of combined aetiologies was documented. In general, ICD was more common than ACD (44.0% vs 22.3%), with the exception of painters: 32.4% with ICD vs 56.8% with ACD. Other occupational groups with a high prevalence of ACD were hairdressers (45.8%), construction workers (31.5%), gardeners/florists (26.7%), and metalworkers (26.5%). The

TABLE 1 Demographic data of the 10 most frequent occupational groups among TIP patients with work-related skin diseases

	All patients N = 2687	Hospital nurses N = 443	Elderly care nurses N = 329	Mechanics N = 264	Hairdressers N = 262	Food handlers ^a N = 121
Mean age ± SD (years)	43.3 ± 12.6	45.3 ± 11.8	44.2 ± 11.9	44.9 ± 11.9	31.4 ± 12.6 ^b	41.6 ± 12.0
Females, n (%; 95%CI)	1582 (58.9; 57.0-60.7)	393 (88.7; 85.4-91.5)	305 (92.7; 89.3-95.3)	13 (4.9; 2.6-8.3)	241 (92.0; 88.0-95.0)	68 (56.2; 46.9-65.2)
Hand dermatitis, n (%; 95%CI)	2567 (95.5; 94.7-96.3)	430 (97.1; 95.0-98.4)	322 (97.9; 95.7-99.1)	245 (92.8; 89.0-95.6)	255 (97.3; 94.6-98.9)	118 (97.5; 92.9-99.5)
Face dermatitis, n (%; 95%CI)	33 (1.2; 0.8-1.7)	5 (1.1; 0.4-2.6)	3 (0.9; 0.2-2.6)	7 (2.7; 1.1-5.4)	1 (0.4; 0.0-2.1)	0 (0.0; 0.0-2.4)
Past or present AD, n (%; 95%CI)	1510 (56.2; 54.3-58.1)	272 (61.4; 56.7-66.0)	226 (68.7; 63.4-73.7)	120 (45.5; 39.3-51.7)	153 (58.4; 52.2-64.4)	80 (66.1; 57.0-74.5)
Current diagnosis ^c , n (%; 95%CI)						
ICD	1183 (44.0; 42.1-45.9)	219 (49.4; 44.7-54.2)	165 (50.2; 44.6-55.7)	102 (38.6; 32.7-44.8)	123 (46.9; 40.8-53.2)	48 (39.7; 30.9-49.0)
ACD	599 (22.3; 20.7-23.9)	61 (13.8; 10.7-17.3)	41 (12.5; 9.1-16.5)	61 (23.1; 18.2-28.7)	120 (45.8; 39.7-52.0)	17 (14.0; 8.4-21.5)
AD	1181 (44.0; 42.1-45.9)	216 (48.8; 44.0-53.5)	173 (52.6; 47.0-58.1)	99 (37.5; 31.6-43.6)	100 (38.2; 32.3-44.3)	64 (52.9; 43.6-62.0)
Years in profession prior to the TIP (mean ± SD)	18.1 ± 12.1	22.2 ± 12.2	14.8 ± 9.2	21.1 ± 12.6	13.7 ± 12.5	16.6 ± 11.2
	Cleaning personnel N = 102	Metalworkers ^d N = 83	Construction workers N = 73	Gardeners/florists N = 45	Painters N = 37	
Mean age ± SD (years)	50.5 ± 8.1	46.2 ± 10.6	45.6 ± 10.7	44.0 ± 11.0	47.2 ± 11.8 ^b	
Females, n (%; 95%CI)	97 (95.1; 88.9-98.4)	3 (3.6; 0.8-10.2)	0 (0.0; 0.0-4.0)	30 (66.7; 51.1-80.0)	1 (2.7; 0.1-14.2)	
Hand dermatitis, n (%; 95%CI)	102 (100.0; 97.1-100.0)	82 (98.8; 93.5-100.0)	65 (89.0; 79.5-95.1)	42 (93.3; 81.7-98.6)	32 (86.5; 71.2-95.5)	
Face dermatitis, n (%; 95%CI)	0 (0.0; 0.0-2.9)	0 (0.0; 0.0-3.5)	2 (2.7; 0.3-9.5)	0 (0.0; 0.0-6.4)	3 (8.1; 1.7-21.9)	
Past or present AD, n (%; 95%CI)	55 (53.9; 43.8-63.8)	27 (32.5; 22.6-43.7)	29 (39.7; 28.5-51.9)	27 (60.0; 44.3-74.3)	17 (45.9; 29.5-63.1)	
Current diagnosis, n (%; 95%CI)						
ICD	51 (50.0; 39.9-60.1)	37 (44.6; 33.7-55.9)	34 (46.6; 34.8-58.6)	19 (42.2; 27.2-57.9)	12 (32.4; 18.0-49.8)	
ACD	24 (23.5; 15.7-33.0)	22 (26.5; 17.4-37.3)	23 (31.5; 21.2-43.4)	12 (26.7; 14.6-41.9)	21 (56.8; 39.5-72.9)	
AD	43 (42.2; 32.4-52.3)	22 (26.5; 17.4-37.3)	25 (34.2; 23.5-46.3)	22 (48.9; 33.7-64.2)	10 (27.0; 13.8-44.1)	
Years in profession prior to the TIP (mean ± SD)	14.8 ± 9.5	18.8 ± 13.0	20.3 ± 12.6	20.7 ± 10.8	27.7 ± 12.7	

Abbreviations: ACD, allergic contact dermatitis; AD, atopic contact dermatitis; CI, confidence interval; ICD, irritant contact dermatitis; SD, standard deviation; TIP, tertiary individual prevention programme.

^a Chefs, kitchen helpers, butchers, and bakers^b $P < 0.0001$ (Kruskal-Wallis test).^c ≥ 1 possible.^d Lathe operators, milling cutters, and grinding machine operators exposed to metalworking fluids.

TABLE 2 Allergens of the baseline, preservatives and rubber series with positive patch test reactions in ≥5% of patients of at least 1 occupational group. All allergens in petrolatum, except where indicated otherwise

	Hospital nurses N = 443				Elderly care nurses N = 329				Mechanics N = 264				Hairdressers N = 262				Food handlers N = 121						
	Concentration (%)	Tested (n)	Positive (n)	% (95%CI)	Tested (n)	Positive (n)	% (95%CI)	Tested (n)	Positive (n)	% (95%CI)	Tested (n)	Positive (n)	% (95%CI)	Tested (n)	Positive (n)	% (95%CI)							
Baseline series																							
Nickel sulfate	5	328	46	14.0 (10.5-18.3)	236	32	13.6 (9.5-18.6)	212	12	5.7 (3.0-9.7)	185	29	15.7 (10.8-21.7)	85	14	16.5 (9.3-26.1)							
Cobalt chloride	1	375	21	5.6 (3.5-8.4)	271	21	7.7 (4.9-11.6)	218	11	5.0 (2.5-8.8)	209	15	7.2 (4.1-11.6)	97	6	6.2 (2.3-13.0)							
Potassium dichromate	0.5	391	26	6.6 (4.4-9.6)	286	17	5.9 (3.5-9.3)	218	10	4.6 (2.2-8.3)	215	5	2.3 (0.8-5.3)	99	6	6.1 (2.3-12.7)							
MCI/MI	0.01 aq.	397	29	7.3 (4.9-10.3)	288	20	6.9 (4.3-10.5)	219	22	10.0 (6.4-14.8)	216	28	13.0 (8.8-18.2)	97	7	7.2 (3.0-14.3)							
MI	0.05 aq.	383	20	5.2 (3.2-7.9)	288	22	7.6 (4.8-11.3)	200	15	7.5 (4.3-12.1)	195	22	11.3 (7.2-16.6)	93	7	7.5 (3.1-14.9)							
MDBGN	0.2	339	21	6.2 (3.9-9.3)	248	15	6.0 (3.4-9.8)	185	13	7.0 (3.8-11.7)	176	8	4.5 (2.0-8.8)	85	4	4.7 (1.3-11.6)							
IPBC	0.2	404	14	3.5 (1.9-7.1)	303	11	3.6 (1.8-6.4)	227	4	1.8 (0.5-4.5)	222	7	3.2 (1.3-6.4)	100	3	3.0 (0.6-8.5)							
Formaldehyde	1 aq.	397	10	2.5 (1.2-4.6)	287	8	2.8 (1.2-5.4)	222	6	2.7 (1.0-5.8)	215	5	2.3 (0.8-5.3)	99	2	2.0 (0.2-7.1)							
Fragrance mix I	8	367	46	12.5 (9.3-16.4)	274	47	17.2 (12.9-22.1)	202	14	6.9 (3.8-11.4)	210	23	11.0 (7.1-16.0)	95	8	8.4 (3.7-15.9)							
Fragrance mix II	14	373	35	9.4 (6.6-12.8)	277	19	6.9 (4.2-10.5)	211	9	4.3 (2.0-7.9)	211	11	5.2 (2.6-9.1)	97	3	3.1 (0.6-8.8)							
Myroxylon pereirae	25	394	32	8.1 (5.6-11.3)	286	28	9.8 (6.6-13.8)	219	19	8.7 (5.3-13.2)	212	7	3.3 (1.3-6.7)	100	7	7.0 (2.9-13.9)							
Cananga odorata (Ylang ylang [I + II] oil)	10	366	7	1.9 (0.8-3.9)	279	10	3.6 (1.7-6.5)	181	6	3.3 (1.2-7.1)	175	3	1.7 (0.4-4.9)	80	2	2.5 (0.3-8.7)							
Preservatives series																							
Compositae mix ^a	5	171	4	2.3 (0.6-5.9)	138	8	5.8 (2.5-11.1)	93	3	3.2 (0.7-9.1)	133	1	0.8 (0.0-4.1)	50	4	8.0 (2.2-19.2)							
Compositae mix II ^b	5	248	4	1.6 (0.4-4.1)	180	2	1.1 (0.1-4.0)	144	2	1.4 (0.2-4.9)	96	0	0.0 (0.0-3.8)	54	2	3.7 (0.5-12.7)							
Colophonium	20	394	10	2.5 (1.2-4.6)	285	10	3.5 (1.7-6.4)	219	14	6.4 (3.5-10.5)	215	5	2.3 (0.8-5.3)	99	7	7.1 (2.9-14.0)							
Epoxy resin	1	266	3	1.1 (0.2-3.3)	208	0	0.0 (0.0-1.8)	200	3	1.5 (0.3-4.3)	145	1	0.7 (0.0-3.8)	63	0	0.0 (0.0-5.7)							
Thiuram mix ^c	1	381	31	8.1 (5.6-11.4)	282	18	6.4 (3.8-9.9)	211	9	4.3 (2.0-7.9)	205	10	4.9 (2.4-8.8)	96	10	10.4 (5.1-18.3)							
ZDEC	1	396	7	1.8 (0.7-3.6)	288	6	2.1 (0.8-4.5)	218	2	0.9 (0.1-3.3)	216	2	0.9 (0.1-3.3)	99	5	5.1 (1.7-11.4)							
Mercapto mix ^d	1	395	2	0.5 (0.1-1.8)	290	1	0.3 (0.0-1.9)	220	2	0.9 (0.1-3.2)	216	1	0.5 (0.0-2.6)	99	1	1.0 (0.0-5.5)							
Preservatives series																							
MI	0.05 aq.	385	20	5.2 (3.2-7.9)	289	22	7.6 (4.8-11.3)	209	15	7.2 (4.1-11.6)	203	22	10.8 (6.9-15.9)	94	7	7.4 (3.0-14.7)							
IPBC	0.2	409	14	3.4 (1.9-5.7)	308	11	3.6 (1.8-6.3)	236	5	2.1 (0.7-4.9)	233	8	3.4 (1.5-6.7)	105	3	2.9 (0.6-8.1)							
Rubber series																							
TMTD	0.25	396	13	3.3 (1.8-5.5)	302	4	1.3 (0.4-3.4)	228	5	2.2 (0.7-5.0)	234	3	1.3 (0.3-3.7)	104	3	2.9 (0.6-8.2)							
TMTM	0.25	397	22	5.5 (3.5-8.3)	302	9	3.0 (1.4-5.6)	228	7	3.1 (1.2-6.2)	234	7	3.0 (1.2-6.1)	103	5	4.9 (1.6-11.0)							
TETD	0.25	395	25	6.3 (4.1-9.2)	302	18	6.0 (3.6-9.3)	228	2	0.9 (0.1-3.1)	235	11	4.7 (2.4-8.2)	104	8	7.7 (3.4-14.6)							
ZDEC	1	376	7	1.9 (0.8-3.8)	281	6	2.1 (0.8-4.6)	208	1	0.5 (0.0-2.6)	205	1	0.5 (0.0-2.7)	92	5	5.4 (1.8-12.2)							
Cleaning personnel N = 102																							
Concentration (%)				Posn	Tested (n)	Positive (n)	Rate, % (95%CI)	Metalworkers N = 83				Construction workers N = 73				Gardeners N = 45				Painters N = 37			
Baseline series																							
Nickel sulfate	5	73	10	13.7 (6.8-23.8)	71	4	5.6 (1.6-13.8)	55	3	5.5 (1.1-15.1)	39	2	5.1 (0.6-17.3)	29	0	0.0 (0.0-11.9)							
Cobalt chloride	1	85	5	5.9 (1.9-13.2)	73	1	1.4 (0.0-7.4)	56	4	7.1 (2.0-17.3)	42	4	9.5 (2.7-22.6)	31	2	6.5 (0.8-21.4)							
Potassium dichromate	0.5	91	7	7.7 (3.1-15.2)	73	1	1.4 (0.0-7.4)	54	9	16.7 (7.9-29.3)	42	3	7.1 (1.5-19.5)	31	0	0.0 (0.0-11.2)							
MCI/MI	0.01 aq.	92	6	6.5 (2.4-13.7)	74	3	4.1 (0.8-11.4)	55	2	3.6 (0.4-12.5)	42	2	4.8 (0.6-16.2)	33	6	18.2 (7.0-35.5)							

MI	0.05 aq.	88	7	8.0 (3.3-15.7)	71	5	7.0 (2.3-15.7)	56	2	3.6 (0.4-12.3)	37	3	8.1 (1.7-21.9)	32	8	25.0 (11.5-43.4)
MDBGN	0.2	72	6	8.3 (3.1-17.3)	65	3	4.6 (1.0-12.9)	43	3	7.0 (1.5-19.1)	35	1	2.9 (0.1-14.9)	28	2	7.1 (0.9-23.5)
IPBC	0.2	90	5	5.6 (1.8-12.5)	77	3	3.9 (0.8-11.0)	62	1	1.6 (0.0-8.7)	39	0	0.0 (0.0-9.0)	34	2	5.9 (0.7-19.7)
Formaldehyde	1 aq.	92	5	5.4 (1.8-12.2)	76	6	7.9 (3.0-16.4)	55	0	0.0 (0.0-6.5)	42	1	2.4 (0.1-12.6)	31	0	0.0 (0.0-11.2)
Fragrance mix I	8	86	8	9.3 (4.1-17.5)	73	9	12.3 (5.8-22.1)	51	0	0.0 (0.0-7.0)	38	1	2.6 (0.1-13.8)	30	2	6.7 (0.8-22.1)
Fragrance mix II	14	86	7	8.1 (3.3-16.1)	72	2	2.8 (0.3-9.7)	52	3	5.8 (1.2-15.9)	41	2	4.9 (0.6-16.5)	31	0	0.0 (0.0-11.2)
Myroxylon pereirae	25	91	5	5.5 (1.8-12.4)	74	2	2.7 (0.3-9.4)	54	4	7.4 (2.1-17.9)	42	0	0.0 (0.0-8.4)	31	3	9.7 (2.0-25.8)
Cananga odorata (Ylang ylang [I + II] oil)	10	83	5	6.0 (2.0-13.5)	58	1	1.7 (0.0-9.2)	50	0	0.0 (0.0-7.1)	36	1	2.8 (0.1-14.5)	28	0	0.0 (0.0-12.3)
Compositae mix ^a	5	41	2	4.9 (0.6-16.5)	35	0	0.0 (0.0-10.0)	28	1	3.6 (0.1-18.3)	19	5	26.3 (9.1-51.2)	11	0	0.0 (0.0-28.5)
Compositae mix II ^b	5	53	3	5.7 (1.2-15.7)	44	0	0.0 (0.0-8.0)	32	0	0.0 (0.0-10.9)	23	3	13.0 (2.8-33.6)	23	1	4.3 (0.1-21.9)
Colophonium	20	91	2	2.2 (0.3-7.7)	74	9	12.2 (5.7-21.8)	55	0	0.0 (0.0-6.5)	41	6	14.6 (5.6-29.2)	30	2	6.7 (0.8-22.1)
Epoxy resin	1	58	1	1.7 (0.0-9.2)	66	0	0.0 (0.0-5.4)	56	6	10.7 (4.0-21.9)	38	0	0.0 (0.0-9.3)	31	7	22.6 (9.6-41.1)
Thiuram mix ^c	1	85	12	14.1 (7.5-23.4)	74	1	1.4 (0.0-7.3)	55	10	18.2 (9.1-30.9)	40	2	5.0 (0.6-16.9)	29	2	6.9 (0.8-22.8)
ZDCE	1	90	3	3.3 (0.7-9.4)	73	0	0.0 (0.0-4.9)	56	0	0.0 (0.0-6.4)	42	1	2.4 (0.1-12.6)	31	0	0.0 (0.0-11.2)
Mercapto mix ^d	1	91	3	3.3 (0.7-9.3)	74	0	0.0 (0.0-4.9)	55	2	3.6 (0.4-12.5)	42	0	0.0 (0.0-8.4)	31	2	6.5 (0.8-21.4)
Preservatives series																
MI	0.05	90	8	8.9 (3.9-16.8)	71	5	7.0 (2.3-15.7)	57	3	5.3 (1.1-14.6)	37	3	8.1 (1.7-21.9)	31	8	25.8 (11.9-44.6)
IPBC	0.2	91	5	5.5 (1.8-12.4)	78	3	3.8 (0.8-10.8)	64	1	1.6 (0.0-8.4)	40	0	0.0 (0.0-8.8)	32	2	6.3 (0.8-20.8)
Rubber series																
TMTD	0.25	92	2	2.2 (0.3-7.6)	76	0	0.0 (0.0-4.7)	61	6	9.8 (3.7-20.2)	40	1	2.5 (0.1-13.2)	30	1	3.3 (0.1-17.2)
TMTM	0.25	92	1	1.1 (0.0-5.9)	76	1	1.3 (0.0-7.1)	61	9	14.8 (7.0-26.2)	40	3	7.5 (1.6-20.4)	30	2	6.7 (0.8-22.1)
TETD	0.25	93	8	8.6 (3.8-16.2)	76	1	1.3 (0.0-7.1)	61	7	11.5 (4.7-22.2)	40	2	5.0 (0.6-16.9)	30	1	3.3 (0.1-17.2)
ZDEC	1	86	2	2.3 (0.3-8.1)	69	0	0.0 (0.0-5.2)	55	0	0.0 (0.0-6.5)	39	1	2.6 (0.1-13.5)	28	0	0.0 (0.0-12.3)

Abbreviations: Cl, confidence interval; IPBC, iodopropenyl butylcarbamate; MCI, methylchloroisothiazolinone; MDBGN, methylthiuram disulfide; TETD, tetraethylthiuram disulfide; disulfide; TMTD, tetramethylthiuram disulfide; TMTM, tetramethylthiuram monosulfide; ZDEC, zinc diethyldithiocarbamate.

^a Contains *Tanacetum vulgare*, *Arnica montana*, parthenolide, *Camomilla romana*, and *Achillea millefolium*.

^b Contains *Tanacetum vulgare*, *Arnica montana*, parthenolide, *Camomilla recutita*, *Anthemis nobilis*, and *Achillea millefolium*.

^c Contains dipentamethylenethiuram disulfide (DPTD), TETD, TMTD, and TMTM.

^d Contains N-cyclohexyl-2-benzothiazole sulfonamide, dibenzothiazyl disulfide, and morpholinylmercaptobenzothiazole.

percentages of the diagnoses ACD and ICD do not add up to 100%, because, in some patients, other skin conditions, such as atopic dermatitis or psoriasis aggravated by occupational factors, were considered to be work-related. The distribution of years in profession prior to the TIP was heterogeneous, and differed significantly among the occupational groups (Kuskal-Wallis test; $P < 0.0001$). The shortest durations were seen in hairdressers (13.7 years), elderly care nurses (14.8 years), and cleaning personnel (14.8 years), and the longest in painters (27.7 years).

3.2 | Patch test results

Tables 2 and S1a-f show the frequency of reactions to allergens eliciting positive patch reactions in $\geq 5\%$ of patch tested patients in at least one occupational group.

Contact allergy to nickel was more common in female-dominated occupational groups (5.1%-16.5%) than in male-dominated occupational groups (0%-5.7%). The prevalence of contact allergy to cobalt was fairly similar in all occupational groups (5.0%-9.5%), apart from metalworkers, in which the prevalence was very low (1.4%, 95%CI: 0%-7.4%).

Hospital nurses ($n = 443$) were commonly sensitized to the preservatives methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI), MI, methyldibromo glutaronitrile (MDBGN), as well as to thiuram mix and its components tetramethylthiuram monosulfide and tetraethylthiuram disulfide. In addition, contact allergies to fragrances were frequent in hospital nurses, as indicated by positive patch test reactions to fragrance mix I (12.5%, 95%CI: 9.3%-16.4%), fragrance mix II (9.4%, 95%CI: 6.6%-12.8%), and *Myroxylon pereirae* (balsam of Peru; 8.1%, 95%CI: 5.6%-11.3%). High prevalences of contact allergies to disinfectants such as glutaraldehyde and povidone iodine were also found. Elderly care nurses ($n = 329$) had a similar spectrum of common contact allergies. The prevalences of contact allergy to fragrance mix I (17.2%, 95%CI: 12.9%-22.1%) and *M. pereirae* (9.8%, 95%CI: 6.6%-13.8%) were even higher, whereas the proportion of contact allergy to fragrance mix II (6.9%, 95%CI: 4.2%-10.5%) was lower than in hospital nurses. Contact allergies to MCI/MI and MI, MDBGN and thiurams were also common in elderly care nurses, and a higher proportion of these than of hospital nurses were sensitized to Compositae mix.

Mechanics ($n = 264$) were frequently sensitized to colophonium, fragrance mix, and *M. pereirae*. Contact allergies to MCI/MI, MI and MDBGN were also common. Hairdressers ($n = 264$) were 1 of the occupational groups with the highest frequency of contact allergies to MCI/MI, namely 13.0% (95%CI: 8.8%-18.2%), and MI (in baseline series: 11.3%, 95%CI: 7.2%-16.6%). They were also frequently sensitized to fragrance mix I and II. Moreover, contact allergies to substances present in hairdressing products were commonly found, including ammonium persulfate (27.2%, 95%CI: 21.4%-33.6%), *p*-phenylenediamine (23.5%, 95%CI: 17.4%-30.6%), and toluene-2,5-diamine (25.2%, 95%CI: 19.7%-31.4%). Contact allergy to glyceryl monothioglycolate was less frequent (5.6%, 95%CI: 2.9%-9.5%).

Food handlers ($n = 121$) included chefs, kitchen helpers, butchers, and bakers. Common contact allergens in this occupational group were MCI/MI, MI, and fragrances. Food handlers had high prevalences

of contact allergies to Compositae mix and colophonium. Sensitization to thiuram mix and its components tetramethylthiuram disulfide and zinc diethylthiocarbamate was also frequent. Cleaning personnel ($n = 102$) were commonly sensitized to preservatives such as MCI/MI, MI, MDBGN, and iodopropynyl butylcarbamate, as well as to fragrances. Cleaners belonged to the occupational groups with the highest prevalence of contact allergy to thiuram mix (14.1%, 95%CI: 7.5%-23.4%) and its component tetraethylthiuram disulfide (8.6%, 95%CI: 3.8%-16.2%). In addition, contact allergies to the disinfectants/preservatives glutaraldehyde (12.4%, 95%CI: 6.3%-21.0%) formaldehyde (5.4%, 95%CI: 1.8%-12.2%) and glyoxal trimer (5.7%, 95%CI: 1.9%-12.8%) were frequent.

Metalworkers included lathe operators, milling cutters and grinding machine operators exposed to metalworking fluids. These had high prevalences of contact allergies to fragrance mix, formaldehyde and formaldehyde releasers such as benzylhemiformal, methylen-bis(methyloxazolidin), 7-ethylbicyclooxazolidine, and 4,4-dimethyloxazolidine, and to colophonium and abietic acid and other components of metalworking fluids, including iodopropynyl butylcarbamate and monoethanolamine. The prevalence of contact allergy to MI when tested in the baseline series was 7.0% (95%CI: 2.3%-15.7%). By far the highest prevalence of contact allergy to chromium was found in construction workers (16.7%, 95%CI: 7.9%-29.3%). In addition, they were frequently sensitized to epoxy resin (10.7%, 95%CI: 4.0%-21.9%) and 1,6-hexanediol diglycidyl ether (5.7%, 95%CI: 1.2%-15.7%). Common contact allergens also included thiurams, MDBGN, *M. pereirae*, and fragrance mix II.

Gardeners/florists had the highest prevalences of contact allergy to colophonium (14.6.0%, 95%CI: 5.6%-29.2%), Compositae mix (26.3%, 95%CI: 9.1%-51.2%), and Compositae mix II (13.0%, 95%CI: 2.8%-33.6%). Moreover, contact allergies to single Compositae components, thiurams and MI were very frequent. Painters had the highest prevalences of contact allergy to MCI/MI (18.2%, 95%CI: 7.0%-35.5%), MI (in baseline series: 25.0%, 95%CI: 11.5%-43.4%), octylisothiazolinone (11.5%, 95%CI: 2.4%-30.2%), and benzisothiazolinone (7.7%, 95%CI: 0.9%-25.1%). Moreover, painters were frequently sensitized to epoxy resin (22.6%, 95%CI: 9.6%-41.1%), components of epoxy resin systems, and hydroxyethylacrylate. Contact allergies to fragrance mix, *M. pereirae*, colophonium, MDBGN and iodopropynyl butylcarbamate were also frequent. Other common contact allergies were to mercapto mix and to thiuram mix and its component tetramethylthiuram monosulfide.

4 | DISCUSSION

The present results confirm that ACD is common in patients taking part in a TIP for severe OSD, notwithstanding the observation that, in most occupations, ACD is less frequent than ICD.⁶ The prevalence of ACD and the pattern of patch test reactivity showed occupation-specific differences related to the respective exposures at work. On average, 22.3% of the patients suffered from ACD. It was most common in painters (56.8%), hairdressers (45.8%), construction workers (31.5%), gardeners/florists (26.7%), and metalworkers (26.5%). It was less often diagnosed in nurses and food handlers, suggesting that, in these occupations, protective measures are better established, or

exposure to (strong) contact sensitizers is less common than irritant exposure or can be more readily prevented by protective strategies, such as wearing of gloves.

Sensitization to MCI/MI and MI was common in most occupational groups, probably because of the widespread use of MI in cosmetics and also in industrial products in the past.^{16,17} This led to an epidemic of contact sensitization to MI across Europe, also causing a high proportion of allergic reactions to MCI/MI.¹⁸ Only recently was MI banned from use in leave-on cosmetic products within the EU. However, its use in industrial products is still not restricted. In the present study, painters had the highest prevalence of contact allergy to MCI/MI and MI, and also to octylisothiazolinone and benzisothiazolinone. These preservatives are commonly found in water-based paints and varnishes,^{16,19,20} explaining the high frequency of contact allergy to isothiazolinones in painters, as already reported by others.^{10,21–23} In particular, MI has become a major problem in painters. Replacement is apparently difficult, and preventive measures are not always effective or possible, especially as airborne ACD caused by MI in paints is not uncommon,²⁴ which is underlined by the high proportion of face dermatitis among painters in our analysis. As reported by others,^{10,23,25,26} painters were, in addition, frequently sensitized to epoxy resin and epoxy resin system components, which are used in wall and floor coatings, varnishes, or glues, and may also cause airborne ACD.^{26,27} The increased prevalence of contact allergy to hydroxyethylacrylate is probably related to its occurrence in lacquers and varnishes.²⁸

Because of extensive occupational exposure to potent allergens, ACD is also a common cause of OSD in hairdressers.^{10,29} In line with other studies, the most important allergens in hairdressers were the precursors of oxidative hair dyes *p*-phenylenediamine and toluene-2,5-diamine, and the bleaching substance ammonium persulfate.^{11,30,31} Remarkably, we still found 12 hairdressers who were sensitized to glyceryl monothioglycolate, which was voluntarily withdrawn from the German market in 1995.³² Among them, 4 had started working in 2004 or later. In these, exposure from imported perm wave products must be considered. Extensive exposure to perfumed and preserved hair products may explain the high proportion of contact allergy to fragrances, MCI/MI and MI in hairdressers. In accordance with this, Uter et al reported a higher prevalence of contact allergy to MCI/MI among female hairdressers than among hairdressers' clients.³⁰ The exposure to strong sensitizers and the high amount of wet work results in an early onset of OSD in hairdressers, often already during apprenticeship.^{33,34} Accordingly, hairdressers in the present study were significantly younger when taking part in the TIP than patients from other occupational groups. In addition, the time in the profession prior to the TIP was the shortest in hairdressers. Complete avoidance of harmful exposures at work is often difficult for hairdressers, as replacement of the relevant allergens is not feasible, and the wearing of protective gloves during all work procedures (eg, hair cutting) is not yet accepted everywhere. Therefore, in particular, young hairdressers with OSD tend to leave the occupation.^{34,35} A previous study showed that hairdressers had by far the worst prognosis with regard to remaining in the original occupation after taking part in the TIP.⁹

Contact allergy to chromium (tested as hexavalent chromium) resulting from exposure to wet cement was the most frequent occupational sensitization in bricklayers and construction workers for

decades. Since 2005, a EU Directive has restricted the use of cement containing >2 ppm of water-soluble hexavalent chromium. In Europe, this has led to a decrease in the frequency of chromium allergy and dermatitis, particularly in men³⁶ and in the building trade.³⁷ However, occupational chromium allergy still occasionally occurs, for example, because of lack of work hygiene.³⁸ Accordingly, only 2 of the 9 chromium-sensitized construction workers had started working after implementation of the above-mentioned EU regulation. In line with other investigations,^{10,25,26} we found that construction workers were also frequently sensitized to epoxy resin and 1,6-hexanediol diglycidyl ether, which is related to the increasing use of epoxy resin systems in the building trade in recent years.³⁷ This is alarming, because the protective effect of protective gloves against components of epoxy resin systems is limited, and airborne ACD is common.^{26,27} Both factors worsen the prognosis for remaining in the building trade, for example, in sensitized floor-layers or tile-setters.

Contact allergy to nickel is very common in the general population,³⁹ and is mainly caused by ear piercing and the wearing of nickel-releasing costume jewellery, explaining the higher prevalence in women.^{40,41} Thus, the higher frequency of nickel allergy in female-dominated occupational groups in the present study was probably not related to increased exposure to nickel in these occupations, but rather to higher non-occupational exposure to nickel in women than in men. The prevalence of contact allergy to cobalt was fairly similar in all occupational groups, which may also point to relevant non-occupational exposures to cobalt from various consumer items.⁴² As described previously,^{43,44} metalworkers were frequently sensitized to typical components of metalworking fluids, such as formaldehyde and formaldehyde releasers, colophonium and its major allergen abietic acid, and iodopropynyl butylcarbamate and monoethanolamine.

Nurses were frequently sensitized to MCI/MI and MI, but also to fragrances. The majority of nurses are women, and thus, to a high extent, are non-occupationally exposed to fragrances and preservatives in cosmetics and household products. However, in nurses, occupational contact with scented and preserved skin care products is frequent, in particular in elderly care nurses.^{45,46} In accordance with the occupational exposure to disinfectants, hospital nurses had a high prevalence of contact allergy to glutaraldehyde and povidone iodine, even though false-positive patch test reactions to povidone iodine must be considered.⁴⁷ As described previously, sensitization to formaldehyde was less common.⁴⁵ This is probably related to the decreased use of formaldehyde and formaldehyde releasers in German healthcare institutions. However, contact allergy to formaldehyde was still frequent in cleaning personnel. The increased prevalence of contact allergy to Compositae mix in nurses caring for the elderly might be explained by exposure to plant-derived components in skin care products.⁴⁸ Contact allergies to colophonium and to Compositae and their major allergenic sesquiterpene lactone components in gardeners/florists and food handlers are, instead, related to their occupational exposure to plants containing these allergens or cross-reactivity.^{48,49}

Since use of the preservative MDBGN in cosmetic products was banned by the European Commission in 2008, the prevalence of contact allergy to MDBGN has substantially decreased, and is usually only of historical relevance.^{50,51} For many years, contact allergies to rubber

components, and in particular thiurams, have played a major role in occupational ACD.^{52,53} Even though thiurams are now often replaced by dithiocarbamates or mercaptobenzothiazole derivatives, the main exposure to thiurams at work is the wearing of water-impermeable protective gloves.^{45,54–56} Consequently, contact allergies to thiurams were common in occupations in which such gloves are frequently worn, in particular in cleaning personnel, gardeners/florists, and food handlers. This is in line with other studies.^{10,55,57,58} As reported previously,¹⁰ thiuram allergy was also common in construction workers. Notably, thiurams and dithiocarbamates constitute a redox pair, and may be transformed into each other. A possible explanation for the persistent high frequency of contact allergies to thiurams despite decreased use is that, in the patch test, thiurams might constitute a better marker of sensitization to the dithiocarbamate/thiuram redox pair than dithiocarbamates.⁵⁹

4.1 | Limitations of the study

The data presented originate from a well-documented, large set of patients with severe OSD. It is likely that the prevalence of ACD is higher in the presented cohort than in other studies on patients with OSD because ACD may have complicated the outpatient management of these patients. In particular, ACD caused by allergens that are difficult to avoid at the workplace or are responsible for airborne ACD may have led to participation in the TIP. Hence, no conclusions concerning the prevalence of ACD in patients with less severe OSD can be drawn. In the course of the 10 years covered, occupational exposure to some allergens and patch test series and recommendations have changed, which implies that not every single patient of a particular occupational group was tested with an identical set of allergens. However, as can be seen from Tables 2 and S1a–f, this is a minor problem. We only considered the patients' current occupations (which led to the TIP). Some patients may have had a different occupation with a different allergen exposure earlier. However, according to our clinical experience, there are very few such cases, and they do not significantly affect the results. No time trend analysis with regard to frequencies of specific contact allergies was possible, owing to the limited number of patients. Occupational exposure to some allergens has already been reduced in recent years by regulatory efforts. However, the results show that other allergens remain an imminent or increasing problem, and should be targeted by prevention strategies, such as raising awareness, health education, and legal regulations.

In conclusion, the results presented indicate that patients with severe OSD (mostly contact dermatitis) who are eligible for the TIP show occupation-specific patterns of patch test results. Among these patients, hairdressers and painters, in particular, suffer from ACD. Even though the TIP is a successful approach to managing patients with OSD, relevant contact allergies may worsen the prognosis and reduce the chance of remaining in the profession afterwards. The results confirm that occupational exposure to allergens must be further reduced in order to decrease the burden of OSD. The development of prevention strategies is particularly important for hairdressers and painters.

Conflict of interest

The authors declare no potential conflict of interests.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Table S1a: Allergens of the disinfectants series with positive patch test reactions in $\geq 5\%$ of patients of at least one occupational group

			Hospital nurses n=443			Elderly care nurses n=329			Food handlers n=121			Cleaning personnel n=102		
	Conc %	Veh	Test n	Pos n	Rate % [95% CI]	Test n	Pos n	Rate % [95% CI]	Test n	Pos n	Rate % [95% CI]	Test n	Pos n	Rate % [95% CI]
Glutaraldehyde	0.30	Pet	404	21	5.2 [3.2-7.8]	291	9	3.1 [1.4-5.8]	101	5	5.0 [1.6-11.2]	89	11	12.4 [6.3-21.0]
Povidon Iodine	10.00	Aqu	410	37	9.0 [6.4-12.2]	302	22	7.3 [4.6-10.8]	103	2	1.9 [0.2-6.8]	91	4	4.4 [1.2-10.9]
Glyoxal Trimer (Dihydrat)	1.00	Pet	402	10	2.5 [1.2-4.5]	291	0	0.0 [0.0-1.3]	101	0	0.0 [0.0-3.6]	88	5	5.7 [1.9-12.8]

Aqu=water, Pet=petrolatum, Conc=test concentration, Veh=vehicle

Table S1b: Allergens of the hairdressers' series with positive patch test reactions in $\geq 5\%$ of patients of at least one occupational group

			Hairdressers n=262		
	Conc %	Veh	Test n	Pos n	Rate % [95% CI]
Ammoniumpersulfate	2.50	Pet	217	59	27.2 [21.4-33.6]
Glycerylmonothioglycolate	1.00	Pet	216	12	5.6 [2.9-9.5]
p-Phenylenediamine (free base)(CI 76060)	1.00	Pet	170	40	23.5 [17.4-30.6]
Toluene 2,5-diamine (free base)	1.00	Pet	226	57	25.2 [19.7-31.4]

Pet=petrolatum, Conc=test concentration, Veh=vehicle

Table S1c: Allergens of the plants series with positive patch test reactions in $\geq 5\%$ of patients of at least one occupational group

			Gardeners n=45		
	Conc %	Veh	Test n	Pos n	Rate % [95% CI]
Sesquiterpene lactone mix	0.10	Pet	37	8	21.6 [9.8-38.2]
<i>Tanacetum vulgare</i> (tansy)	1.00	Pet	38	7	18.4 [7.7-34.3]
<i>Parthenolide</i> (feverfew)	0.10	Pet	36	9	25.0 [12.1-42.2]
<i>Chamomilla romana</i> (Roman chamomile)	1.00	Pet	18	2	11.1 [1.4-34.7]

<i>Achillea millefolium</i> (yarrow)	1.00	Pet	38	4	10.5 [2.9-24.8]
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Pet=petrolatum, Conc=test concentration, Veh=vehicle

Table S1d: Allergens of the biocides series with positive patch test reactions in $\geq 5\%$ of patients of at least one occupational group

			Mechanics n=264			Painters n=37		
	Conc %	Veh	Test n	Pos n	Rate % [95% CI]	Test n	Pos	Rate % [95% CI]
Octylisothiazolinone	0.03	Pet	143	2	1.4 [0.2-5.0]	26	3	11.5 [2.4-30.2]
1,2-Benzisothiazolin-3-one, sodium salt	0.10	Pet	141	3	2.1 [0.4-6.1]	26	2	7.7 [0.9-25.1]
Methylisothiazolinone	0.05	Aqu	140	12	8.6 [4.5-14.5]	23	8	34.8 [16.4-57.3]
Iodopropynyl butylcarbamate	0.20	Pet	142	4	2.8 [0.8-7.1]	25	2	8.0 [1.0-26.0]

Aqu=water, Pet=petrolatum, Conc=test concentration, Veh=vehicle

Table S1e: Allergens of the metal working fluids series with positive patch test reactions in $\geq 5\%$ of patients of at least one occupational group

			Metal workers n=83		
	Conc %	Veh	Test n	Pos n	Rate % [95% CI]
Abietic acid	10.00	Pet	52	8	15.4 [6.9-28.1]
Benzylhemiformal	1.00	Pet	53	4	7.5 [2.1-18.2]
Methylen-bis(methyloxazolidine)	1.00	Pet	56	5	8.9 [3.0-19.6]
7-Ethylbicyclooxazolidine (Bioban CS 1246)	1.00	Pet	54	3	5.6 [1.2 - 15.4]
4,4-Dimethyloxazolidine (Bioban CS 1135)	1.00	Pet	54	8	14.8 [6.6 - 27.1]
Monoethanolamine (MEA)	2.00	Pet	55	3	5.5 [1.1-15.1]
Methylisothiazolinone	0.05	Aqu	55	4	7.3 [2.0-17.6]
Iodopropynyl butylcarbamate	0.20	Pet	54	3	5.6 [1.2-15.4]

Aqu=water, Pet=petrolatum, Conc=test concentration, Veh=vehicle

Table S1f: Allergens of the resins and glues series with positive patch test reactions in $\geq 5\%$ of patients of at least one occupational group

			Construction workers n=73			Painters n=37		
	Conc %	Veh	Test n	Pos n	Rate % [95% CI]	Test n	Pos n	Rate % [95% CI]
Phenyl glycidyl ether	0.25	Pet	52	1	1.9 [0.0-10.3]	30	2	6.7 [0.8-22.1]
1,6-Hexanediol diglycidyl ether	0.25	Pet	53	3	5.7 [1.2-15.7]	30	5	16.7 [5.6-34.7]
1,4-Butanediol diglycidyl ether	0.25	Pet	53	1	1.9 [0.0-10.1]	30	3	10.0 [2.1-26.5]
m-Xylylenediamine	0.10	Pet	49	1	2.0 [0.1-10.9]	30	3	10.0 [2.1-26.5]
Isophorone diamine (IPD)	0.50	Pet	52	0	0.0 [0.0-6.8]	30	3	10.0 [2.1-26.5]
Trimethylhexane-1,6-diamine (isomer mix)	0.50	Pet	49	0	0.0 [0.0-7.3]	28	2	7.1 [0.9-23.5]
4,4'-Diaminodiphenylmethane	0.50	Pet	52	1	1.9 [0.0-10.3]	29	2	6.9 [0.8-22.8]
Hydroxyethyl acrylate	0.10	Pet	53	0	0.0 [0.0-6.7]	30	2	6.7 [0.8-22.1]

Pet=petrolatum, Conc=test concentration, Veh=vehicle