

Characteristics of chromium-allergic dermatitis patients prior to regulatory intervention for chromium in leather: a questionnaire study

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Summary

Background. Chromium-tanned leather articles currently constitute the most important cause of contact allergy to chromium in Denmark. A regulation on the content of hexavalent chromium in leather was adopted in November 2013 by the EU member states.

Objectives. To characterize patients with chromium allergy and their disease, to serve as a baseline for future studies on the potential effect of the new regulation on chromium in leather.

Methods. A questionnaire case-control study was performed on 155 dermatitis patients with positive patch test reactions to potassium dichromate and a matched control group of 621 dermatitis patients. Comparisons were made by use of a χ^2 -test and the Mann-Whitney *U*-test. Logistic regression analyses were used to test for associations.

Results. Sixty-six per cent of chromium-allergic patients had a positive history of contact dermatitis caused by leather exposure. They had a significantly lower quality of life ($p < 0.001$), a higher prevalence of dermatitis during the last year ($p = 0.008$), a higher use of medication during the past 12 months ($p = 0.001$) and a higher prevalence of sick leave ($p = 0.007$) than patients in the control group.

Conclusions. Chromium-allergic patients have more severe and more chronic contact dermatitis. Their primary chromium exposure comes from leather articles.

Key words: allergic chromium dermatitis; allergy; chromate; chromium; chromium allergy; dermatitis; leather; metal.

Chromium is an important allergen. Reports of severe allergic contact dermatitis caused by chromium-containing articles have been published

since the beginning of the 18th century (1). However, as chromium was an unknown allergen at the time, it could only be reported indirectly, and chromium was not mentioned as such. For example, in 1908, it was described as 'la gale du ciment' by Martial et al. (2). Importantly, the association between these clinical observations and chromium as an allergen was not established until the middle of the 20th century (3–5).

Historically, the primary cause of chromium contact allergy has been occupational exposure to cement. A reduction of the chromium content in cement to 2 ppm in Europe was an effective intervention that reduced the prevalence of chromium allergy among construction workers in Denmark (6) and other EU member states

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(7–9). Surprisingly, since the early 1990s, an increase in allergic chromium dermatitis, presumably caused by skin contact with leather products, has been observed in Denmark (10). Leather articles are currently considered to constitute the most important cause of contact allergy to chromium in consumers (11–13). A regulation on the content of hexavalent chromium in leather was recently approved by EU member states (14). It was adopted by consensus in November 2013, with a 12-month period before entry into force, and is expected to limit the leather chromium allergy problem.

Contact dermatitis in chromium-allergic patients is often chronic and resistant to therapy, despite patients' efforts to avoid allergen contact (15–18). This study aimed to characterize patients with positive patch test reactions to chromium (referred to as chromium-allergic patients) from a tertiary clinic in Denmark. We performed a questionnaire study to determine both previous and present allergen exposures, and to evaluate the impact of chromium allergy on disease severity and quality of life. This study serves as a baseline for future studies on the potential effects of the new regulation on chromium in leather.

Materials and Methods

Study population

In the period 1 January 2003 to 31 December 2012, a total of 8064 patients with dermatitis were patch tested at the department of Dermato-Allergology, Gentofte Hospital, Denmark. We included all patients ($n = 196$) who had at least one positive patch test reaction to potassium dichromate (0.5% in petrolatum). For each case, we found 4 controls ($n = 784$) who had dermatitis but negative patch test results with potassium dichromate (0.5% pet.) and cobalt chloride (1% pet.); patients with a positive patch test reaction to cobalt chloride form part of another study in preparation. Patients were matched for age, sex, year of patch testing, and occupation. Their home addresses were obtained from the Danish central personal register (19), which is a unique register of social information and health services. Patients were excluded if they did not wish to be contacted for research purposes, had unknown addresses, or were no longer alive. The two groups finally consisted of 155 cases and 621 controls. Hence, a total of 776 patients with no significant differences in the matched variables were eligible for the study.

Patch testing

Patch testing was performed with the European baseline series [Trolab allergens (Hermal, Reinbek, Germany)]

with Finn Chambers® (8 mm; Epitest Ltd, Oy, Finland) on Scanpor® tape (Norgesplaster A/S, Alpharma, Venesla, Norway). Dosing of the chamber was performed with 20 mg of the test preparation. Potassium dichromate (0.5% pet.) was used for testing. Patch test readings were performed according to the recommendations of the ICDRG (20), with an exposure time of 48 hr and readings being performed on D2, D3 or D4, and D7. Patch test reactions designated as 1+, 2+ or 3+ were interpreted as positive reactions. An irritant responses and doubtful (+?) or negative readings were interpreted as negative responses.

Questionnaire

We developed a questionnaire to identify possible differences between the two study groups. The questions were in Danish, and are shown in Table 1, translated into English.

To evaluate disease severity, our questions aimed to determine the impact on occupational performance (e.g. loss of job, change of job because of dermatitis, sick leave, and effect of dermatitis on work), medical needs over the past 12 months (e.g. use of healthcare system and medication), personal perception of disease severity on a visual analogue scale (VAS) (e.g. worst-case and current dermatitis, and effect of dermatitis on leisure time), number of anatomical regions affected by dermatitis, and an estimate of their quality of life [Dermatology Life Quality Index (DLQI) (21)]. The DLQI is a validated 10-question questionnaire assessing the impact of the skin disease on the patient's life during the last week. The validated official Danish-language version was used (22), and formal permission for use was given by the authors.

We sent out the questionnaire in January 2014; 4 weeks later, non-respondents received a reminder, and the study was closed for data entry after another 4 weeks.

Statistical analysis

Comparisons were made by use of the χ^2 -test. A logistic regression analysis was performed with 'chromium allergy' as the dependent variable, and 'atopic dermatitis', 'hand dermatitis' and 'foot dermatitis' as the independent variables. Testing of data for normality was performed with the Shapiro–Wilk test. VAS score data and the DLQI score had a non-parametric distribution, and were analysed with the Mann–Whitney *U*-test to determine whether there was a statistically significant difference between the medians.

The DLQI score was calculated according to published instructions (23), which result in a score between 0 and 30, with a high score indicating a lower quality of life.

Table 1. Questions included in the questionnaire sent to the cohort

Where on your body did you have rash/eczema when your skin condition started? (Please tick more than one box if appropriate)

Scalp; Face; Neck; Upper arms; Lower arms; Hands; Chest/stomach; Legs; Feet; other part of body, where?

Have you had rash/eczema during the last 12 months?

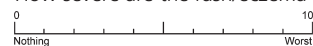
No; Yes, all the time; Yes, more than half the time; Yes, about half the time; Yes, less than half the time

Where was the rash/eczema last time? (Please tick more than one box if appropriate)

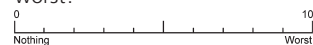
Scalp; Face; Neck; Upper arms; Lower arms; Hands; Chest/stomach; Legs; Feet; other part of body, where?

How would you assess the severity of the rash/eczema using a scale of 0 to 10, where 0 corresponds to no rash/eczema and 10 correspond to the worst imaginable rash/eczema? Mark on the line.

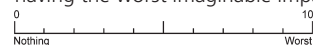
How severe are the rash/eczema today?



How severe were the rash/eczema when they were at their worst?



In your working life, how severely do you think rash/eczema affected you, on a scale of 0 to 10, where 0 corresponds to having no impact and 10 corresponds to having the worst imaginable impact? Mark on the line.



In your current job, do you have contact with things that cause you rash/eczema?

No; No, unemployed/retired; Don't know; Yes

If yes, are they any of the following products? (Please tick more than one box if appropriate)

Leather shoes; Leather gloves; Tools; Screws; Metalwork; Cement; Wood protection; Other.

Have you been in contact with products that caused you rash/eczema in previous jobs?

No; Don't know; Yes

If yes, were they any of the following products? (Please tick more than one box if appropriate)

Leather shoes; Leather gloves; Tools; Screws; Metalwork; Cement; Wood protection; Other.

Does the rash/eczema improve when you are away from your normal work, e.g. at weekends or when you are on holiday?

No; Yes, sometimes; Yes, usually; Yes, always; Don't know/no longer have eczema.

When you have had rash/eczema, how has it affected your daily life? Please tick ☐ whether you agree/disagree with the following statements.

I must often take special precautions:

Agree; Disagree

I am frequently bothered by eczema and itching:

Agree; Disagree

I have been on sick leave from my job:

Agree; Disagree

I have had to change occupation:

Agree; Disagree

I have become unemployed:

Agree; Disagree

I have retired: **Agree; Disagree**

It has not particularly affected my daily life:

Agree; Disagree

Other, please write:

Has a doctor ever told you that you have asthma?

No; Yes; Don't know

Have you ever had itchy skin, which you have scratched and rubbed a lot?

No; Yes

Have you had itchy skin, which you have scratched and rubbed a lot in the last 12 months?

No; Yes

A diagnosis of atopic dermatitis was defined according to the UK diagnostic criteria (24), without the possibility of objectifying visual flexural dermatitis. The patient must have had an itchy skin condition during the past 12 months plus three or more of the following: (i) onset before the age of 2 years, (ii) a history

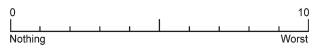
of flexural involvement, (iii) a history of a generally dry skin, and (iv) a personal history of other atopic diseases.

All results were expressed as odds ratios (ORs) with 95% confidence intervals, and the threshold for statistical significance was predefined as a *p*-value of < 0.05.

Table 1. Continued

How long had you been employed in this job when you first had a patch test? (e.g. 2 years and 3 months)

In your leisure time, how would you assess how severely the rash/eczema have affected you, using a scale of 0 to 10, where 0 corresponds to having no impact and 10 corresponds to having the worst imaginable impact? Mark on the line.



During your leisure time, have you ever been in contact with products that caused you rash/eczema?

No; Yes

If yes, were they any of the following products? (Please tick more than one box if appropriate)

Leather shoes; Leather gloves; Tools; Screws; Metalwork; Watch straps; Cement; Wood protection; Other.

How has your rash/eczema been treated in the last 12 months? (Please tick more than one box if appropriate)

No treatment; Moisturiser cream; Hormone cream / ointment (also called steroid cream);

Protopic or Elidel; Penicillin or other types of antibiotics; Corticosteroid tablets; Hay fever-/anti-itch tablets; Herbal medicine;

Immunosuppressant tablets (e.g. methotrexate (MTX), azathioprine (Imurel) etc.); Light treatment; Other, please write:

Have you visited a general practitioner in the last year because of your rash/eczema?

Yes, once; Yes, 2-5 times; Yes, more than 5 times; No

Have you visited a dermatologist in the last year because of your rash/eczema?

No; Yes, once; Yes, 2-5 times; Yes, more than 5 times

Has a doctor ever told you that you have hay fever?

No; Yes; Don't know

How old were you when your skin condition started?

Less than 2 years old; Between 2 and 5 years old; Between 6 and 10 years old; More than 10 years old

Has your skin condition ever been present on your insides of elbows, back of the knees, ankles, neck or around the eyes?

No; Yes

If yes, has the skin condition been present on your insides of elbows, back of the knees, insteps, neck or around the eyes in the last 12 months?

No; Yes

Have you ever suffered from dry skin all over your body?

No; Yes

If yes, have you suffered from dry skin all over your body in the last 12 months?

No; Yes

Data were analysed with IBMTM SPSSTM Statistics (SPSS Inc., Chicago, IL, USA) for WindowsTM (release 19.0).

Results

The overall response rate was 73% (564/776); 78.1% (n = 121) in the chromium-allergic group, and 71.3% (n = 443) in the control group ($p = 0.196$).

Patient characteristics

Patient characteristics are summarized in Table 2. Women were the dominant sex, with 71.1% (n = 86) in the chromium-allergic group; the mean age was 58.47 years (standard deviation 13.9), and more than half of chromium-allergic patients were between 50 and 70 years of age. The prevalence of atopic dermatitis did

Table 2. Characteristics

	Chromium-allergic patients (n = 121), % (n)	Control patients without chromium allergy (n = 443), % (n)	Odds ratio (95% confidence interval)	p-value*
Sex				
Female	71.1 (86)	71.8 (318)	0.97 (0.62–1.51)	0.878 [†]
Age group (years)				0.979 [†]
20–49	24.0 (29)	24.4 (108)	0.98 (0.61–1.56)	
50–59	28.1 (34)	28.9 (128)	0.96 (0.61–1.50)	
60–69	27.3 (33)	26.6 (118)	1.03 (0.66–1.62)	
69–79	14.0 (17)	14.9 (66)	0.93 (0.52–1.66)	
> 80	6.6 (8)	5.2 (23)	1.29 (0.56–2.97)	
Atopic dermatitis	24.0 (29)	17.4 (77)	1.50 (0.92–2.43)	0.100
Occupational causation	23.1 (28)	19.9 (88)	1.21 (0.75–1.97)	0.429 [‡]
Initial location of dermatitis				
Scalp	14.0 (17)	18.1 (80)	0.74 (0.42–1.31)	0.300
Face	14.0 (17)	32.7 (145)	0.34 (0.19–0.58)	< 0.001
Neck	13.2 (16)	15.6 (69)	0.83 (0.46–1.48)	0.521
Upper arm	13.2 (16)	11.1 (49)	1.22 (0.67–2.24)	0.509
Forearm	24.0 (29)	19.6 (87)	1.29 (0.80–2.08)	0.297
Hand	74.4 (90)	49.4 (219)	2.97 (1.90–4.65)	< 0.001
Back	16.5 (20)	12.4 (55)	1.40 (0.80–2.44)	0.238
Chest/abdomen	16.5 (20)	17.4 (77)	0.94 (0.55–1.61)	0.826
Leg	28.1 (34)	19.6 (87)	1.60 (1.01–2.53)	0.045
Foot	48.8 (59)	14.4 (64)	5.63 (3.61–8.79)	< 0.001
Other location	4.1 (5)	5.4 (24)	0.75 (0.28–2.02)	0.816
Present location of dermatitis				
Scalp	11.6 (14)	13.3 (59)	0.85 (0.46–1.58)	0.612
Face	21.5 (26)	29.3 (130)	0.66 (0.41–1.06)	0.087
Neck	17.4 (21)	12.4 (55)	1.48 (0.86–2.56)	0.158
Upper arm	7.4 (9)	6.5 (29)	1.15 (0.53–2.49)	0.729
Forearm	22.3 (27)	13.5 (60)	1.83 (1.10–3.04)	0.018
Hand	67.8 (82)	44.0 (195)	2.67 (1.75–4.09)	< 0.001
Back	13.2 (16)	10.6 (47)	1.28 (0.70–2.36)	0.419
Chest/abdomen	8.3 (10)	12.2 (54)	0.65 (0.32–1.32)	0.228
Leg	29.8 (36)	16.9 (75)	2.08 (1.31–3.30)	0.002
Foot	48.8 (59)	12.2 (54)	6.86 (4.34–10.82)	< 0.001
Other location	5.0 (6)	3.6 (16)	1.39 (0.53–3.64)	0.498
Initial no. of locations with dermatitis				
0	5.0 (6)	12.0 (53)	0.38 (0.16–0.92)	< 0.001[‡]
1	32.2 (39)	44.9 (199)	0.58 (0.38–0.89)	
2–4	35.5 (43)	31.8 (141)	1.18 (0.77–1.80)	
5–8	25.6 (31)	10.2 (45)	3.05 (1.83–5.08)	
> 8	1.7 (2)	1.1 (5)	1.47 (0.28–7.68)	
Total no. (median)	2	1		
Present no. of locations with dermatitis				
0	3.3 (4)	6.3 (28)	0.51 (0.17–1.47)	0.002[‡]
1	29.8 (36)	43.6 (193)	0.55 (0.36–0.85)	
2–4	42.1 (51)	33.6 (149)	1.44 (0.95–2.17)	
5–8	21.5 (26)	14.2 (63)	1.65 (0.99–2.75)	
> 8	3.3 (4)	2.3 (10)	1.48 (0.46–4.81)	
Total no. (median)	2	2		

*Chi-square or Fisher's exact test (if n ≤ 5 or less).

[†]Control group matched on variable.[‡]Mann–Whitney test.Significant results ($p < 0.05$) are shown in bold.

not differ significantly between the case and control groups (24.0% versus 17.4%, OR 1.5, $p = 0.100$).

The initial location of dermatitis was significantly more often on the hands (74.4% versus 49.4%, OR 2.97, $p < 0.001$) and on the feet (48.8% versus 14.4%, OR 5.63, $p < 0.001$) among chromium-allergic patients. The location of current dermatitis showed a similar pattern, with significantly higher prevalence rates of hand dermatitis (67.8% versus 44.0%, OR 2.67, $p < 0.001$) and foot dermatitis (48.8% versus 12.2%, OR 6.86, $p < 0.001$). A logistic regression analysis was performed with 'chromium allergy' as the dependent variable, and with 'atopic dermatitis', 'hand dermatitis' and 'foot dermatitis' as the independent variables. No associations between atopic dermatitis and chromium allergy were found ($p > 0.05$).

Exposures to chromium

Exposures causing dermatitis are summarized in Table 3. For simplicity, these exposures were divided into three separate categories: (i) leather articles, (ii) tools, and (iii) cement. Each of these contained four subdivisions: (i) present workplace exposures, (ii) former workplace exposures, (iii) spare-time exposures and (iv) any kind of exposure.

Regarding a positive history of leather exposure, a significant difference was observed between chromium-allergic patients and controls (66.1% versus 12.6%, OR 13.48, $p < 0.001$). The highest prevalence of leather exposure resulting in dermatitis derived from leisure-time activities (61.2% versus 12.0%, OR 11.59, $p < 0.001$). For comparison, the prevalence rates of leather exposure at the present workplace and former workplace were, respectively, 11.6% versus 1.1% (OR 11.46, $p < 0.001$) and 15.7% versus 1.4% (OR 13.57, $p < 0.001$) in the two groups.

Regarding dermatitis caused by exposure to work tools, an overall significant difference between the two groups was observed (19.8% versus 5.4%, OR 4.32, $p < 0.001$). Moreover, differences were observed for spare-time exposure (11.6% versus 3.2%, OR 4.00, $p < 0.001$), exposure at the present workplace (5.8% versus 1.6%, OR 3.83, $p = 0.016$), and exposure at the former workplace (5.8% versus 2.3%, OR 2.66, $p = 0.044$).

There was a significant difference between the groups with regard to cement exposure (9.9% versus 3.6%, OR 2.94, $p = 0.005$). Spare-time exposure to cement causing dermatitis was significant (7.4% versus 3.2%, OR 2.46, $p = 0.035$). However, present workplace exposure showed significant differences (4.1% versus 0.7%, OR 6.32, $p = 0.014$), whereas no difference was observed

for former workplaces (1.7% versus 0.9%, OR 1.84, $p = 0.614$).

Disease severity

The occupational consequences of having contact dermatitis are summarized in Table 4. Chromium-allergic patients changed their jobs (16.5% versus 8.1%, OR 2.24, $p = 0.006$) and took sick leave (28.1% versus 17.2%, OR 1.89, $p = 0.007$) significantly more often than controls. Loss of job because of dermatitis also occurred markedly more often among chromium-allergic patients (10.7% versus 5.9%, OR 1.93, $p = 0.061$).

The medical status of patients is summarized in Table 4. The 1-year prevalence of having dermatitis was significantly higher in chromium-allergic patients than in controls (76.9% versus 64.1%, OR 1.86, $p = 0.008$). However, chromium-allergic patients did not visit their general practitioner (36.4% versus 31.2%, $p = 0.270$) or a dermatologist (33.9% versus 26.2%, $p = 0.094$) more often than the controls. Regarding the total use of medication in the groups, the control group had a significantly higher proportion of patients without a need for any medication during the last 12 months (12.4% versus 26.2%, OR 0.34, $p = 0.001$). However, chromium-allergic patients had a higher use of topical corticosteroids (66.9% versus 38.8%, OR 3.19, $p < 0.001$) and antibiotics (14% versus 5.2%, OR 2.96, $p = 0.001$) than controls. Chromium-allergic patients also had more frequent use of emollients (61.2% versus 43.3%, OR 2.06, $p = 0.001$).

The patients' perception of their own disease severity evaluated on a VAS is summarized in Table 5. Chromium-allergic patients had a significantly higher score than controls ($p = 0.011$). Chromium-allergic patients also had a significantly higher score for worst-case dermatitis ($p < 0.001$). For the question on the effect of the disease on work duties and spare time, a significantly higher score was observed in chromium-allergic patients.

The number of anatomical regions with dermatitis at present, and at the time of disease onset, is summarized in Table 2. There were significantly more regions with dermatitis in chromium-allergic patients than in controls, both for the initial situation ($p > 0.001$) and for present-day status ($p < 0.021$).

Table 5 summarizes the analysed total DLQI score. The complete DLQI score was significantly higher among chromium-allergic patients ($p < 0.001$). Chromium-allergic patients had a significantly affected quality of life in three of the six categories. Among these, the 'symptoms and feelings' category was significantly

Table 3. Exposure causing dermatitis

	Chromium-allergic patients (n = 121), % (n)	Controls (n = 443), % (n)	Odds ratio (95% confidence interval)	p-value*
Leather				
At present workplace	15.7 (19)	1.4 (6)	13.57 (5.28–34.83)	< 0.001
At earlier workplace	11.6 (14)	1.1 (5)	11.46 (4.04–32.52)	< 0.001
In spare time	61.2 (74)	12.0 (53)	11.59 (7.28–18.44)	< 0.001
Any leather exposure	66.1 (80)	12.6 (56)	13.48 (8.43–21.56)	< 0.001
Work tools				
At present workplace	5.8 (7)	1.6 (7)	3.82 (1.31–11.12)	0.008
At earlier workplace	5.8 (7)	2.3 (10)	2.66 (0.99–7.14)	0.044
In spare time	11.6 (14)	3.2 (14)	4.01 (1.85–8.66)	< 0.001
Any tool exposure	19.8 (24)	5.4 (24)	4.32 (2.35–7.93)	< 0.001
Cement				
At present workplace	4.1 (5)	0.7 (3)	6.32 (1.49–26.84)	0.014
At earlier workplace	1.7 (2)	0.9 (4)	1.84 (0.33–10.19)	0.614
In spare time	7.4 (9)	3.2 (14)	2.46 (1.04–5.83)	0.035
Any cement exposure	9.9 (12)	3.6 (16)	2.94 (1.35–6.39)	0.005

*Chi-square or Fisher's exact test (if $n \leq 5$).Significant results ($p < 0.05$) are shown in bold.**Table 4.** Occupational and medical status

	Chromium-allergic patients (n = 121), % (n)	Controls (n = 443), % (n)	Odds ratio (95% confidence interval)	p-value*
Occupational status				
Loss of job	10.7 (13)	5.9 (26)	1.93 (0.96–3.88)	0.061
Change of job	16.5 (20)	8.1 (36)	2.24 (1.24–4.03)	0.006
Sick leave from job	28.1 (34)	17.2 (76)	1.89 (1.18–3.01)	0.007
Medical status during past 12 months				
Dermatitis	76.9 (93)	64.1 (284)	1.86 (1.17–2.96)	0.008
General practitioner consultation	36.4 (44)	31.2 (138)	1.26 (0.83–1.92)	0.270
Dermatologist consultation	33.9 (41)	26.2 (116)	1.44 (0.94–2.22)	0.094
No topical/systemic medicine	12.4 (15)	26.2 (116)	0.40 (0.22–0.71)	0.001
Emollient	61.2 (74)	43.3 (192)	2.06 (1.36–3.10)	0.001
Topical corticosteroid	66.9 (81)	38.8 (172)	3.19 (2.09–4.88)	< 0.001
Topical/systemic antibiotics	14.0 (17)	5.2 (23)	2.98 (1.54–5.79)	0.001

*Chi-square or Fisher's exact test (if $n \leq 5$).Significant results ($p < 0.05$) are shown in bold.

increased ($p = 0.002$), along with the 'daily activities' category ($p < 0.001$) and the leisure category ($p = 0.039$). No significant differences were found among the 'work and school' ($p = 0.072$) category, the personal relationships category ($p = 0.114$), and the treatment category ($p = 0.119$).

Discussion

The patient population in this study is selective, as it was collected at a tertiary contact dermatitis clinic. A predominance of women (71.1%) with a

non-occupational primary cause (77.9%) was found among chromium-allergic patients. In the period from 1989 to 1994, Zachariae et al. (25) found that 61% of their chromium-allergic patients were women, and concluded that occupational cement contact had become a less important cause of chromium dermatitis, as a direct result of the cement regulation from 1983. The characteristics found in other studies (10, 25), with similar demographic populations, are similar to ours, and support the idea that a change in the epidemiology of chromium dermatitis has occurred, with a shift from mainly cement exposure in men to leather exposure in women.

Table 5. Dermatology Life Quality Index (DLQI) and severity

	Chromium-allergic patients (n = 112)	Controls (n = 410)	p-value*
DLQI score			
Median (IQR)	3 (1–7)	1 (0–4)	> 0.001
Range	0–26	0–23	–
Dermatitis today (VAS)			
Median (IQR)	2 (1–5)	1.5 (0.5–4)	0.011
Range	0–10	0–10	–
Dermatitis worst case (VAS)			
Median (IQR)	9 (8–10)	8 (7–9)	< 0.001
Range	0.5–10	0–10	–
Effect on work (VAS)			
Median (IQR)	5 (1.5–8)	4 (1–7)	0.018
Range	0–10	0–10	–
Effect on spare time (VAS)			
Median (IQR)	5 (2–7)	3.5 (1–6.5)	0.001
Range	0–10	0–10	–

IQR, interquartile range; VAS, visual analogue scale.

*Non-parametric data distribution: Mann–Whitney U-test.

Significant results ($p < 0.05$) are shown in bold.

Regarding the distribution of dermatitis in chromium-allergic patients, hand and foot dermatitis was very frequent. A potential confounder could be atopic dermatitis, which is known to be associated with hand dermatitis (26, 27). However, a logistic regression analysis rejected this.

Regarding current exposures, in Europe at least, leather seems to be the most important cause of chromium allergic contact dermatitis. Other potential sources of chromium exposure include cosmetics, mobile phones, tattoo ink, paint, detergents, and bleaches, and metal alloys used in various consumer products and medical implants (28). A recent Danish study from our clinic (10) showed that 55% of chromium-allergic patients had clinically relevant leather exposure. Notably, an increase from 1% to 3.3% in the overall prevalence of chromium allergy was observed when data from 1995 to 2007 were compared, and this increase was mainly attributable to leather. Our present study showed, in a similar way and mainly based on the same patient information, that ~66% of chromium-allergic patients had clinically relevant leather exposure. This might be explained by an increase use of leather articles over time, or might just be a result of an increased awareness about leather articles as a source of chromium.

Work tools represented a non-negligible source for eliciting allergic contact dermatitis among chromium-allergic patients, with almost 20% reporting a history of dermatitis caused by tools. This finding is consistent with a previous study showing that 75% of examined metal discs released chromium in amounts

above the chemical reporting limit (29). A recent study from January 2014 (30) analysed dental work tools, and chromium release was found from all of the examined tools in small but non-negligible amounts ($n = 21$).

Cement exposure causing dermatitis cannot be ignored as a possible relevant factor when relevant exposure is evaluated, as our results showed a significant difference from the control group. The number of cases with a positive history of cement dermatitis remained below 10% in chromium-allergic patients. Cement has a shelf-life of 2 months when opened and 10 months when it is sealed; the risk of cement suddenly releasing chromium in higher amounts than expected as a result of the shelf-life could be a reason for cement remaining a problem. Our findings showed that cement exposure primarily resulted from leisure-time activity. A recent Danish analysis showed that chromium contact dermatitis is still occupationally associated with tile setters (31). Cements for both private and occupational use are produced and legislated by the same procedures, and cases of occupational exposure still exist, owing to inadequate use of protective equipment and work safety in concrete work (32). Therefore, cement remains a relevant subject when chromium allergy is discussed, and, as well as considering protective equipment when handling cement, the shelf-life of cement could be an important factor. The measured disease severity is similar to the findings of other studies (16–18, 33).

This study confirms that chromium allergy is associated with severe hand and foot dermatitis and a poor prognosis. As a result of the changing epidemiology of chromium allergy, older studies focused mainly on occupational dermatitis when looking at the prognosis. Fregert (33) showed, in 1975, that chromium allergy had a poor prognosis, with a tendency to chronicity, and that men were more badly affected, as a result of their occupation. Similar conclusions were drawn on occupational chromium dermatitis in 1992 by Halbert et al. (17), who showed that more than half of the patients continued to have symptoms even though they changed their occupation, and rigorously attempted to avoid chromium. This study's results also showed chromium dermatitis to be responsible for sick leave, loss of work skills, and financial loss. In a more recent study from 2009, Hald et al. (16) identified allergens associated with the greatest initial severity of clinical symptoms and the worst prognosis; they concluded that chromium contact allergy showed the worst prognosis.

Our study shows the same trends as observed above. Chromium-allergic patients had a more severe and chronic course, according to the variables of their medical status, during the past 12 months. No trend was observed in the number of patients visiting their general

practitioner or dermatologist, but they reported more frequent dermatitis, more use of emollients, and more use of medicine. A higher use of topical medicaments containing corticosteroids was observed – this is interpreted as a direct indication of activity of their skin disease. The higher frequency of topical antibiotic use could be an indicator of superinfections among patients with chromium allergy. Our study also showed a trend of chromium allergy to be responsible for more loss of time from work according to sick leave, and loss of work skills according to change of job. These quantitative results are supported by chromium-allergic patients' own perception of disease severity, and the DLQI score showing a negative effect on quality of life regarding leisure time, daily activities and symptoms and feelings among chromium-allergic patients. Other studies (34, 35) focusing on quality of life, and primarily hand dermatitis, had a higher DLQI score in their patient cohorts; these studies differed regarding factors such as age, sex, test year, duration, and atopic dermatitis. Our study population was selected after treatment, and we had a retrospective study period of 10 years, which could be an explanation for the relatively low DLQI score, as a result of both recall bias, adaptation of disease, and correct treatment of the proper diagnosis. Overall, our study shows that chromium-positive patients have a significantly negatively affected quality of life as compared with a matched dermatitis control group.

Regarding the clinical healing of dermatitis among chromium-allergic patients, there was a small improvement in the prevalence of hand dermatitis, although no improvement was observed for foot dermatitis. This lack of clinical improvement confirms the hypothesis of the chronic nature of chromium allergy. Even though the epidemiology of the disease has changed, the difficulty in

avoiding the allergen remains an obstacle; Fregert (33) came to the same conclusion in 1975, in a study showing that chromium allergy also resulted in a poorer prognosis than other allergens that can more easily be avoided.

This study has shown an increase in the disease burden of the group of patients with chromium allergy as compared with the control group, which, as could be expected, affects the chromium-allergic patient's own perception of the disease severity, and has a direct impact on their quality of life.

Conclusion

In this study, we characterized the demographics of today's chromium-allergic patients, the disease severity, and the most common traits of allergy caused by chromium. Our results agree with the observation that chromium allergy causes more severe and chronic contact dermatitis than other contact allergies. In this study, we also found leather articles to be of great importance, which shows the importance of leather regulation in the EU.

This work is important in view of current regulations; follow-up studies, ideally after 5 and 10 years, will be required to measure the impact of the newly introduced leather regulation, and to monitor incident cases of chromium allergy and their causative exposures.

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