

Contact sensitization to modern dressings: a multicentre study on 354 patients with chronic leg ulcers

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Summary

Background. Modern dressings (MDs) may have a low sensitization rate, but there is a lack of prospective studies in patients with chronic leg ulcers (CLUs) to evaluate this.

Objectives. To determine the rate of sensitization (contact allergy) to MDs and substances present in dressings.

Patients and methods. A prospective multicentre study was carried out in patients with CLUs at five French dermatology departments; patch tests were performed with the European baseline series and with an additional 27 individual allergens and 10 MDs.

Results. Among 354 patients (226 women and 128 men) with CLUs, 59.6% had at least one positive patch test reaction to an MD and 19% had at least one sensitization to an MD. The number of positive test reactions per patient was correlated with the duration of ulcerative disease, but not with ulcer duration, the cause of the ulcer, or the presence of surrounding eczematous lesions. For 11 of 45 patients sensitized to Ialuset cream[®], more detailed information could be obtained with sensitization to sodium dehydroacetate (5 cases) or Lanette SX[®] (3 cases).

Conclusions. Sensitization to MDs is not rare. It is absolutely necessary to label all components of MDs on their packaging and to avoid some sensitizing molecules, such as colophonium derivatives or any strong sensitizers.

Key words: chronic leg ulcer; contact allergy; medical devices; modern dressings; patch tests.

Chronic leg ulcers (CLUs) are common, affecting 1–7% of the population aged > 65 years (1) and 0.12–1.1% of the population worldwide (2). Long duration of illness, a local inflammatory milieu, damage to the skin barrier, and the use of many topical medicaments and molecules that are strong sensitizers, together with occlusive bandages promoting skin penetration by allergens, frequently lead

to contact sensitization (contact allergy), and consequently to allergic contact dermatitis (1, 3–11). Previous studies have shown high frequencies of contact allergies to topical drugs and ointments. Barbaud et al. (5) showed that 73% of 423 patients had at least one positive patch test reaction, and that most of these patients had polysensitization. Machet et al. (1) found that 72% of 1185 cases published from 1991 to 2003 had a positive patch test reaction. The introduction of modern dressings (MDs) for wounds provides several advantages for leg ulcer patients, such as improved healing, less pain, fewer wound infections, and improved quality of life. They may have a lower risk of inducing cutaneous sensitization. However, this

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is currently unknown. The main objective of this study was to determine the rate of sensitization to MDs and to components of dressings or topical drugs that are frequently used for patients suffering from CLUs. We also investigated the potential relationships between the number of positive reactions and ulcer duration, ulcerative disease duration, the type of CLU, and the existence of leg eczema. We also evaluated the relevance of patch tests for testing CLU.

Patients and Methods

Over a period of 42 months, a prospective multicentre study was conducted, including 354 consecutive patients in five participating dermatology centres. All patients could be patch tested and had a known cause of CLU. The ulcer must have been present for > 1 month. Patients must not have taken immunosuppressive drugs in the month before being enrolled or applied topical corticosteroids to patch test sites in the week before. For each patient, the following information was collected: age, sex, duration of the current ulcer and the ulcerative disease, cause of the ulcer, medical history (psoriasis, atopic dermatitis, stasis dermatitis, rosacea, and contact dermatitis), and the presence of eczematous lesions surrounding the ulcer or at other sites. All patients were patch tested with the European baseline series updated in 2008, involving 27 allergens and a series designed for patients with CLUs (Table 1). On the basis of a previously published study (5), all substances giving > 1.5% positive patch test reactions were included in this specific series. Moreover, some other molecules frequently used in MDs were added, after being diluted following de Groot's guidelines (12). In addition, when possible, all products used by patients were tested (antiseptics, topical corticosteroids, dressings, and ointments). The special series for CLUs contained 27 commercially available allergens (Chemotechnique Diagnostics, Vellinge, Sweden, or Hermal Trolab, Reinbeck, Germany). All patients were also tested with 10 MDs 'as is' for each class of MD: charcoal dressings [Carbonet® (Smith & Nephew Laboratory, Le Mans, France)]; alginate dressings [Algosteril® (Brothier Laboratory, Nanterre, France)]; hydrocellular dressings and dressings with ibuprofen [Biatain® adhesive part and non-adhesive part, and Biatain Ibu® (Coloplast Laboratory, Rosny-sous-Bois, France) and Mepilex® (Mölnlycke Health Care Laboratory, Wasquehal, France)]; hydrogel dressings [Hydroclean gel® (Hartmann Laboratory, Selest, France)]; hydrofibre dressings [Aquacel® (ConvaTec Laboratory, Garenne-Colombes, France)]; hydrocolloid dressings [Duoderm E® (ConvaTec Laboratory)]; Ialuset cream® (Genevrier Laboratory, Antibes, France); and

Table 1. Special series on chronic leg ulcers (allergens, concentrations, vehicles, and results)

Allergens	Concentrations and vehicles	No. sensitized (%) [without the 45 patients sensitized to Ialuset cream®]
Triethanolamine	2.5% pet.	1 (0.3) [0% of 309 patients]
Propylene glycol	5% pet.	5 (1.4) [1.6]
Sorbitan sesquioleate	20% pet.	7 (2) [1.6]
Cetearyl (cetostearyl) alcohol	20% pet.	16 (4.5) [2.9]
Amerchol® L101	50% pet.	19 (5.4) [5.5]
Polyethylene glycol	'as is' (100%)	2 (0.6) [0]
Chlorocresol	1% pet.	5 (1.4) [1.6]
Chlorhexidine digluconate	0.5% aqua	3 (0.8) [0.9]
Benzalkonium chloride	0.1% pet.	25 (7) [6.1]
Phenoxyethanol	1% pet.	1 (0.3) [0.3]
Sodium metabisulfite	1% pet.	17 (4.8) [4.8]
Dodecyl gallate	0.5% pet.	2 (0.6) [0.3]
Octyl gallate	0.3% pet.	2 (0.6) [0.3]
Lidocaine hydrochloride	5% pet.	2 (0.6) [0.6]
Prilocaine hydrochloride	5% pet.	1 (0.3) [0.3]
Silver nitrate	2% aqua	0 [0]
Urgotul SAG®	As is	4 (1.1) [1]
Bacitracin	5% pet.	3 (0.8) [0.6]
Povidone-iodine	2% aqua	14 (4) [2.9]
Cetrimide	0.1% aqua	7 (2) [2.3]
Eosin	50% pet.	5 (1.4) [1.3]
Carboxymethylcellulose	2% pet.	3 (0.8) [0.6]
Aclometasone-17,21-dipropionate	1% pet.	2 (0.6) [0.6]
Hydrocortisone-17-butyrate	0.1% pet.	4 (1.1) [1.3]
Methylethacrylate	2% pet.	0 [0]
Ethyleneglycol dimethacrylate	2% pet.	2 (0.6) [0.6]
Ibuprofen	10% pet.	1 (0.3) [0.3]
Carbonet®	As is	1 (0.3) [0]
Algosteril®	Humidified	6 (1.7) [1.6]
Biatain standard® adhesive part	As is	14 (4) [4.2]
Biatain standard® non-adhesive part	As is	5 (1.4) [1.6]
Mepilex®	As is	5 (1.4) [1.3]
Hydroclean gel®	As is	3 (0.8) [1]
Ialuset cream®	As is	45 (12.7) [0]
Biatain Ibu®	As is	2 (0.6) [0.6]
Aquacel®	Humidified	5 (1.4) [1.6]
Duoderm E®	As is	18 (5.1) [5.2]

interface dressings to test silver sulfadiazine, which could not be obtained in a pure form to be tested [Urgotul SAG® (Urgo Laboratory, Chenove, France)]. Dressings used by patients were also tested as is [Versiva® (ConvaTec Laboratory), Allevyn heel® (Smith & Nephew Laboratory), and Intrasis gel® (Smith & Nephew Laboratory)].

Patch tests were performed on the upper back under IQ Chambers® (Chemotechnique Diagnostics, Vellinge, Sweden); reactions were read at D2 and D4 or D5, and recorded according to ICDRG recommendations. Doubtful erythematous reactions without infiltration were considered to be negative.

Data were processed with SAS 9.3 (SAS Institute Inc., Cary NC, USA). Categorical variables were compared among the groups of patients by use of a chi-squared analysis. When this could not be used for quantitative variables, a Fisher test was used. To compare quantitative and qualitative variables, the analysis was conducted with Student's test. Results for continuous variables are expressed as mean and standard deviation (SD), and comparisons to investigate the relationships among continuous variables and groups were analysed by one-way ANOVA and the Bartlett test. Significance was set at the $p < 0.05$ level for all comparisons. This study was approved by the president of the local institutional ethic committee of University Hospital of Nancy.

Results

In the five centres, 354 patients (226 women and 128 men, without a statistically significantly different sex ratio from one centre to another) were included (242 patients from Nancy, 38 from Thionville, 32 from Angers, 31 from Dijon, and 11 from Montpellier). The mean age was 75.3 years, without statistically significant differences among centres, based on Fisher's test (74.9 for Nancy, 77.3 for Thionville, 76.5 for Angers, 76.6 for Dijon, and 71.4 for Montpellier). There were no statistically significant differences in ulcer duration ($p = 0.1435$) or ulcerative disease duration ($p = 0.7536$) from one centre to another (27.3 and 60.7 months for Nancy, 13.18 and 83.61 months for Thionville, 8.89 and 51.21 months for Angers, 27 and 47.7 months for Dijon, and 12 and 113.8 months for Montpellier). The causes were venous insufficiency in 191 cases, mixed arterial and venous causes in 72 cases, atherosclerosis in 21 cases, hypertensive leg ulcer in 14 cases, and other causes in 56 cases. There was no difference in the main causes of CLU among centres. Surrounding eczematous lesions were observed in 112 of 354 (32%) cases, and surrounding erythema was observed in 215 of 354 (61%) of cases. However, there was a statistically significant difference between the frequency of these lesions among centres, as surrounding eczematous lesions were described in 84% of cases in Dijon and in only 13% in Nancy, whereas surrounding erythema was found in 3.2% of cases in Dijon but in 72% in Nancy.

Among all patients, 60% (211/354) had at least one positive patch test reaction (61.2% in Nancy, 63.2% in

Thionville, 46.8% in Angers, 58% in Dijon, and 54.5% in Montpellier) and 25.4% (90/354) had more than two positive patch test reactions. The mean number of positive patch test reactions per person among the 211 sensitized patients was 2.30 (1–9) per patient. None of these patients had an angry back.

Table 2 summarizes the results for the European baseline series. Sixty-eight patients (19.2%) were sensitized by MDs: 45 (12.7%) by Ialuset cream®, 28 (7.9%) by hydrocellular products (1 Versiva®, 1 Allevyn heel®, 5 Mepilex®, 14 Biatain® adhesive part, 5 Biatain® non-adhesive part, and 2 Biatain Ibu®), 18 (5.1%) by a hydrocolloid (Duoderm E®), 7 (2%) by hydrogels (3 Hydroclean gel®, 3 Intracel gel®, and 1 Urgo hydrogel®), 6 (1.7%) by alginates (Algosteril®), 5 (1.4%) by hydrofibres (Aquacel®), and 8 (2.3%) by an interface dressing (4 Urgotul SAG® and 4 Urgotul®). Regarding new components of MDs, 3 (0.8%) patients were sensitized by carboxymethylcellulose (CMC) and 4 (1.1%) were sensitized by Urgotul SAG® containing silver sulfadiazine. Among the 3 patients sensitized to CMC, all were also sensitized to hydrocellulars and 1 was sensitized to hydrocolloids. Among preservatives and antioxidants, the most frequent sensitizations were observed with benzalkonium chloride (7.1% of cases), sodium metabisulfite (4.8%), methylidibromo glutaronitrile and phenoxyethanol (1.7%), paraben mix (1.4%), and methylchloroisothiazolinone/methylisothiazolinone (1.4%). Excipients and emulsifiers led to positive results with Amerchol L101® (5.4%), cetearyl alcohol (cetostearyl alcohol) (4.5%), sorbitan sesquileate (2%), propylene glycol (1.4%), polyethylene glycol (0.6%), and triethanolamine (0.3%). Among 45 patients sensitized to Ialuset cream®, 11 had more detailed information (this was the only laboratory that provided us with the components). In the majority of cases, Ialuset cream® sensitization was attributable to sodium dehydroacetate (5 cases) and to cetearyl alcohol (3 cases), which was a component of Lanette SX® (cetostearyl alcohol, sodium lauryl sulfate and sodium cetearyl sulfate). Nine patients were sensitized only to Ialuset cream® and 40% were also sensitized to *Myroxylon pereirae*. Because of the large number of patients sensitized to Ialuset® cream, a subgroup analysis excluding these 45 patients was carried out. The results are summarized in Tables 1 and 2.

In Fisher tests, there were associations between positive patch test reaction to lauryl (dodecyl) gallate and octyl gallate ($p = 0.0034$), fragrance mix and *M. pereirae* ($p < 0.0001$), lanolin resin and Amerchol L101® ($p = 2.96$), colophonium and *M. pereirae* ($p < 0.0001$), Biatain® and CMC ($p = 0.0171$), and lanolin alcohol and *M. pereirae* ($p = 0.0059$). No association

Table 2. European baseline series results

Allergens	Concentrations and vehicles	No. sensitized (%) [without the 45 patients sensitized to Ialuset cream®]
Potassium dichromate	0.5% pet.	12/354 (3.4) [2.9% of 309 patients]
Neomycin sulfate	20% pet.	13 (3.7) [3.6]
Thiuram mix	1% pet.	8 (2.3) [1.9]
<i>p</i> -Phenylenediamine base	1% pet.	5 (1.4) [1.3]
Cobalt chloride	1% pet.	4 (1.1) [1.2]
Benzocaine	5% pet.	0 [0]
Formaldehyde	1% aqua	4 (1.1) [1.2]
Colophonium	20% pet.	14 (4) [3.6]
Clioquinol	5% pet.	0 [0]
<i>Myroxylon pereirae</i>	25% pet.	84 (23.7) [22.7]
<i>N</i> -Isopropyl- <i>N</i> -phenyl- <i>p</i> -phenylenediamine	0.1% pet.	1 (0.3) [0]
Lanolin alcohol	30% pet.	15 (4.2) [4.5]
Mercapto mix	2% pet.	1 (0.3) [0.3]
Epoxy resin	1% pet.	2 (0.6) [0.3]
Paraben mix	16% pet.	5 (1.4) [1.3]
4-tert-Butylphenol formaldehyde resin	1% pet.	3 (0.8) [0.9]
Fragrance mix I	8% pet.	47 (13.3) [12.9]
Sesquiterpene lactone mix (alantolactone, dehydrocostus lactone, and costunolide)	0.1% pet.	6 (1.7) [1.6]
Quaternium-15	1% pet.	1 (0.3) [0.3]
Nickel sulfate	5% pet.	23 (6.5) [6.1]
Methylchloroisothiazolinone/methylisothiazolinone (3:1)	0.01% aqua	5 (1.4) [1.3]
Mercaptobenzothiazole	2% pet.	2 (0.6) [0.6]
Primin	0.01% pet.	2 (0.6) [0]
Budesonide	0.01% pet.	10 (2.8) [2.9]
Tixocortol pivalate	0.1% pet.	1 (0.3) [0.3]
Methyldibromoglutaronitrile	0.5% pet.	6 (1.7) [1.3]
Fragrance mix II	14% pet.	22 (6.2) [6.1]

was found between lanolin alcohol and cetostearyl alcohol ($p=0.2178$), Ialuset cream® and fragrance mix ($p=0.5158$) or cetostearyl alcohol ($p=0.0595$), sesquiterpene lactone mix and budesonide or hydrocortisone ($p=1$), propylene glycol and Hydroclean gel® ($p=1$), or colophonium and Duoderm E® ($p=1$). A statistically significant association ($p=0.0171$) was observed between CMC and Biatain®, but not between colophonium and Biatain® ($p=1$).

The mean duration of the current ulcer was 3.6 months in patients without any sensitization versus 4.2 months in patients who had at least one positive patch test reaction. The mean duration of ulcerative disease was 7.44 versus 14.66 years, respectively. The relationship between the duration of the current

ulcer and the rate of sensitization was not statistically significant (chi-square, $SD=8$, $p=0.0688$). However, the longer the duration of ulcerative disease, the higher the rate of sensitization ($SD=10$, $p=0.0257$). Even if the disease lasted for <1 year, 58% (105/180) of patients had at least one positive patch test reaction.

The rate of sensitization was not correlated with the cause of ulcer [8/21 (38%) patients with arterial CLUs, 45/71 (63%) with mixed arterial and venous CLUs, 113/189 (59.8%) with venous CLUs and 10/14 (71%) with hypertensive leg ulcer had at least one positive patch test reaction; $p=0.26$], the presence of a surrounding eczema (the difference was not statistically significant; $p=0.23$), or a surrounding erythema (the difference was not statistically significant; $p=0.7$).

Even though it is difficult to assess in elderly patients, relevance was certain or probable in 69% of the 75 patients sensitized to MDs and for whom we had information. The relevance was <50% for Carbonet®, Hydroclean gel® (among 3 sensitized patients, relevance was found in 1 patient), and Algosteril® (3/6). A link between relevance and healing was not found ($p=0.6475$).

Discussion

MDs do not eliminate the risk of contact sensitization in patients with CLUs. This large, prospective, multicentre study confirms that contact sensitization is very frequent (59.6%) in patients suffering from CLUs, even in patients with a short duration of ulcerative disease. This rate is lower than some recently reported rates [72.5% (1) and 73% (5)]. In the literature, the percentage of sensitization varies between 46% (4) and 82.5% (11) (Table 3). This sensitization, which results from a T cell-mediated inflammatory reaction, can be explained by a local inflammatory milieu, damage to the skin barrier, and the use of many topical medicaments and dressings, together with occlusive bandages promoting skin penetration. On the other hand, it can also be explained by a 33–64% increase in the rate of contact sensitization in elderly patients (13).

In our study, 68 of 354 (19.2%) patients were sensitized to an MD, whereas Gallenkemper et al. (18) reported 4 of 36 (11%) patients who were sensitized to an MD. In the present study, the highest sensitization rate was observed with Ialuset cream® (45 cases). As recently described by Milpied et al. (22), the main sensitizers were Lanette SX® and sodium dehydroacetate. Sensitization to Lanette SX® was attributable to cetostearyl alcohol. Hydrocellular MDs (represented in our study by Biatain®) are made of polyurethane foam with or without an adhesive part. The sensitization was more frequent with the adhesive part of Biatain® (4%) than with the

Table 3. Comparison of our results with those of previously reported cases, in percentages

References (number of patients)	Our study (354) [without laluset cream®]	Beliauskienė etal. (14) (35)	Barbaud etal. (5) (423)	Smart etal. (4) (100)	Jankičević etal. (6) (55)	Veselski etal. (15) (60)	Lim etal. (8) (44)	Machet etal. (1) (1185)	Tavadia etal. (16) (200)	Renner and Wollina (17) (39)	Reichert- Pénétrot etal. (11) (359)	Le Coz et al. (7) (50)	Gallenkemper etal. (18) (36)	Cameron etal. (19) (81)	Paramsothy etal. (20) (100)	Kulozik etal. (21) (59)
Global sensitization (%) MDs	59.6 [54] 19.2	80	73	46	73.3	61.7	61.4	72.5	68	33.3	82.5	76	77.7	67	55	50.8
Carbonet®	0.3 [0]	-	-	-	-	-	9.1	-	-	33	-	-	8	-	-	-
Hydrocellular	7.9 [7.1]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hydrocolloid	5.1 [5.2]	-	-	-	-	-	2.3	-	-	5.1	-	-	0	-	-	-
Hydrofibre	1.4 [1.6]	-	4	-	-	0	4.5	-	-	7.7	0	-	0	-	-	-
Hydrogel	2 [1.6]	-	-	-	-	-	0	-	-	7.7	-	-	0	-	-	-
Alginate	1.7 [1.6]	-	-	-	-	-	2.3	-	9.5	23	-	-	8.3	-	-	-
Interface	2.3 [1]	-	-	-	2.8	1.6	-	-	-	5.1	-	-	0	-	-	-
laluset cream®	12.7 [0]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Plant resins																
<i>Myroxylon pereirae</i>	23.7 [22.7]	20	40	10	21.3	20	9.1	25.4	14.5	10.3	39.27	40	22.2	19.7	11	3.4
Colophonium	4 [3.6]	20	7.6	9	13.3	3.33	11.3	-	-	2.6	8.07	12	13.9	3.7	6	5
Fragrance mix I	13.3 [12.9]	2.9	26.5	-	-	16	4.5	18.8	23.5	5.1	25.1	28	8.3	7.4	16	11.8
Preservatives																
Benzalkonium chloride	7 [6.1]	-	10.4	8	-	-	-	-	-	-	15.32	-	2.8	-	-	-
Sodium metabisulfite	4.8 [4.8]	-	3.1	-	-	-	-	-	-	-	-	-	-	-	-	-
Methyldibromo glutaronitrile	1.7 [1.3]	-	2.6	-	-	-	-	-	-	-	-	-	0	-	-	-
Paraben mix	1.4 [1.3]	5.7	3.1	-	12	18.3	-	-	-	2.6	6.96	8	13.9	13.5	8	11.8
MCI/MI	1.4 [1.3]	2.9	0.7	-	-	-	2.3	-	-	-	-	-	2.8	-	-	-
Excipients																
Lanolin (wool alcohol)	4.2 [4.5]	17.1	17.7	11	8	6.66	6.8	17.5	16.5	10.3	19.5	14	33.3	23	26	18.6
Amerchol LT01®	5.4 [5.5]	-	19.6	7	-	-	-	-	-	12.8	-	18	19.4	14.8	-	-
Cetostearyl (cetearyl) alcohol	4.5 [2.9]	-	5.7	6	4	-	2.3	-	3	5.1	-	-	13.9	16	-	-
Sorbitan sesquioleate	2 [1.6]	-	4	-	-	-	-	-	-	-	-	-	-	-	-	-
Propylene glycol	1.4 [1.6]	-	3.5	-	-	-	-	-	2	7.7	2.5	-	8.3	-	-	-
Triethanolamine	0.3 [0]	-	1.7	-	-	-	-	-	-	-	2.5	-	-	-	-	-
Others																
Carboxymethylcellulose	0.8 [0.6]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Silver sulfadiazine	1.1 [1]	-	-	-	-	-	-	-	4.5	-	-	-	-	-	-	-
Rubber components																
N-Isopropyl-N-phenyl- <i>p</i> -phenylenediamine	1.4 [1.3]	20	2.4	8	4	3	9.1	-	-	-	3.89	-	5.6	-	-	-
Thiuram mix	2.3 [1.9]	0	4.25	-	-	-	-	5.5	12	5.1	2.5	-	2.8	-	-	-
Mercapto mix	0.3 [0.3]	0	1.4	-	-	-	-	-	2.5	2.6	1.11	-	5.6	-	-	-
Mercapto benzothiazole	0.6 [0.6]	0	0.7	-	-	-	-	-	-	2.6	-	-	-	-	-	-

MCI/MI, methylchloroisothiazolinone/methylisothiazolinone.

non-adhesive part (1.4%). Regarding hydrocellular MDs, some cases of sensitization have been reported, with 3 cases being related to Allevyn heel® (5) and 1 case being related to Contreet® (10). In our study, there was a link between sensitization to CMC and sensitization to Biatain® ($p = 0.0171$).

Sensitization to hydrocolloid MDs has been reported in 35 previous cases (5, 10, 23–28). Even though CMC has been reported to be a sensitizer in hydrocolloids, only 1 case had cosensitization to CMC and a hydrocolloid. Rare cases of allergic contact dermatitis caused by CMC in a hydrocolloid dressing have been described (25, 27). Colophonium derivatives used in hydrocolloid dressings as tackifying agents could explain sensitization to Duoderm E® (5), but we did not find this link. Pereira et al. (24) showed that colophonium derivatives do not cross-react in all cases. Some patients have positive patch test reactions to pentaerythritol ester of hydrogenated colophonium, but do not react to colophonium or other derivatives (24). Pentaerythritol ester of hydrogenated colophonium is the main sensitizer in tackifiers. Unfortunately, patients sensitized to pentaerythritol ester of hydrogenated colophonium can have negative results when tested with colophonium, and pentaerythritol ester of hydrogenated colophonium is not commercially available for patch tests. This could explain why we did not find any association between sensitization to colophonium and sensitization hydrocolloids ($p = 1$). It seems absolutely necessary to obtain clear and complete labelling of all colophonium derivatives in all medically used products, including informative terms such as colophonium and rosin, and to obtain and test the involved colophonium derivative.

Hydrogel dressings consist of hydrophilic polymers, composed of CMC, water, and an emulsifying agent (propylene glycol). More than 40 cases of sensitization to hydrogel dressings have been reported (10, 18, 29, 16). In Gallenkemper et al. (18), all cases of sensitization to hydrogel dressings (4/36) were related to propylene glycol. In Tavadia et al. (16), only 3 of 29 patients showed cosensitization between hydrogel and propylene glycol. We did not find this link between hydrogels and propylene glycol ($p = 1$). Sensitization to propylene glycol in patients with CLUs could be explained by the fact that it has been found in MDs, corticosteroids, cosmetics, and other topical drugs.

Alginates contain calcium alginates and sometimes CMC. There is only 1 previously reported case of sensitization to alginates (15), and we report 6 new cases not related to CMC sensitization.

Hydrofibre dressings are composed of CMC. Renner and Wollina (17) reported 1 case with a positive patch

test reaction to Aquacel Ag® resulting from silver sensitization, and we had 5 cases of sensitization with Aquacel®.

Regarding interface dressings, there have been 7 reported cases of sensitization to Adaptic® (10, 30). There may be a correlation between sensitization to Adaptic® and sensitization to sorbitan sesquileate (30, 31). In the present study, 8 cases had sensitization to interface dressings, whereas only 4 cases reacted to Urgotul SAG®, which was patch tested to study silver sulfadiazine, a topical sulfonamide associated with silver.

Some studies (5, 11) have reported a link between the duration of CLU and the rate of sensitization, whereas others have not (6, 32). We did not find any such link. However, for the first time, we differentiated between the duration of the current CLU and the duration of ulcerative disease, and found an association between ulcerative disease duration and sensitization rate. Moreover, among 105 patients with an ulcerative disease duration of < 1 year, 58% were sensitized even when it was assumed that these patients had only been treated with an MD. In one of the participating centres, the rate of sensitization to the European standard series was 43% (33). In contrast to another previous study (5), there was not a statistically significant correlation between the existence of eczematous lesions or erythema surrounding the ulcer and the contact allergy. We confirm that the risk of sensitization is not correlated with the cause of the CLU.

The relevance of patch tests for patients suffering from CLUs is difficult to assess in elderly patients, because of their age and frequent modifications of their dressings and topical treatments by doctors or nurses. Despite this difficulty, we determined that patch test reactions to MDs had a current or a previous probable or certain relevance in 69% of cases. The relevance was lower (33%) in the 3 patients sensitized to Hydroclean gel® and in 50% of the 6 patients with positive patch test reactions to Algosteril®. These dressings seem to be irritants, especially Hydroclean gel®, which must be changed every day. Thus, it seems to be relevant to patch test MDs in patients with CLUs. However in many cases, we had a positive patch test reaction to an MD but, unfortunately, without any explanation regarding the responsible allergen.

In conclusion, contact allergies can occur in patients with CLUs, even if new MDs are used, and in patients with a short duration of ulcerative disease. The rate of sensitization increases with the duration of ulcerative disease, but not with the duration of the current CLU. The rate of sensitization in patients with CLUs may have diminished, but it remains high. The use of MDs does not reduce the risk of sensitization, as we report for the first time that 19% of patients with CLUs were sensitized to these products. Patch test reactions to MDs are relevant in the majority of

cases, but unfortunately, owing to the absence of labelling and cooperation among manufacturers, it is impossible in most cases to determine which allergen is responsible for sensitization to an MD. It is absolutely necessary to

label all of the components of MDs on their packaging and to avoid certain sensitizing molecules in these products, such as colophonium derivatives and any other strong sensitizer.

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