Contact allergy to lanolin: temporal changes in prevalence and association with atopic dermatitis

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doi:10.1111/cod.12872

Summary

Background. Lanolin has been tested as lanolin alcohols (30% pet.) in baseline patch test series since 1969, and this has shown clinically relevant allergic contact dermatitis cases.

Objectives. To investigate the temporal development of lanolin allergy (i.e. positive reaction to lanolin alcohols and/or Amerchol™ L-101), and the association between contact allergy to lanolin and patient characteristics from the MOAHFA index.

Methods. A retrospective observational study of consecutively patch tested dermatitis patients (n = 9577) between 1 January 2004 and 31 December 2015 with lanolin alcohols 30% pet. and Amerchol™ L-101 50% pet. was performed.

Results. The prevalence of lanolin allergy increased from 0.45% in 2004 to 1.81% in 2015. In age-adjusted and sex-adjusted analyses, weak, significant associations were found between atopic dermatitis and lanolin and lanolin alcohols allergy, respectively, but no association with Amerchol™ L-101 allergy was found. Among 9286 dermatitis patients who were tested with both allergens, 108 had a positive test reaction to either lanolin alcohols or Amerchol™ L-101, whereas only 29 patients had positive test reactions to both markers.

Conclusions. The prevalence of lanolin contact allergy has increased over a 12-year period, and inclusion of Amerchol™ L-101 will increase the chance of detecting lanolin contact allergy. Patch testing with lanolin is helpful in atopics with dermatitis and suspected cosmetic allergy.

Key words: Amerchol™ L-101; atopic dermatitis; contact allergy; face dermatitis; lanolin; lanolin alcohols.
L-101 (50% pet. and 100%) exist. It has therefore become clear that lanolin alcohols alone in the baseline series might be insufficient to detect lanolin allergy (1).

The prevalence of contact allergy to lanolin alcohols varies from 0.6% to 5.7% between various countries, with the lowest estimates in Odense, Denmark, and the highest estimates in Dortmund, Germany (6). The prevalence of lanolin allergy was relatively stable between 1969 and 1996–2000 across European patch test centres (6). Interestingly, a positive association has been observed between atopic dermatitis (AD) and lanolin contact allergy (7), possibly because of the combination of frequent exposure to lanolin in topical products and increased skin absorption in atopic skin (8, 9). However, other studies have failed to show a higher prevalence of lanolin allergy in patients with AD (10, 11), and the exact relationship therefore remains unclear.

We conducted a retrospective patient-based register study to examine the relationship between contact allergy to lanolin alcohols and Amerchol™ L-101 (a commercial product obtained from hydrolysis of wool fat, containing 10% wool wax alcohols in mineral oil), respectively, and patient characteristics from the MOAHLFA index (male sex, occupational dermatitis, a history of atopic dermatitis, the presence of leg dermatitis, the presence of hand dermatitis, the presence of face dermatitis and age > 40 years), as well as the temporal development of contact allergy to lanolin.

Methods
Consecutively patch tested dermatitis patients treated at a university hospital in Copenhagen, Denmark between 1 January 2004 and 31 December 2015 were included. All patients (n = 9577) underwent routine patch testing with the baseline series containing lanolin alcohols 30% pet. and an additional series containing Amerchol™ L-101 50% pet.

Patient data were collected from the clinical database of contact allergy hosted in the department. Information available from the database included age, MOAHLFA index, and patch test results. The definition of AD was based on the clinical impression of the treating physician.

Patch testing was performed with Finn Chambers® (8 mm; Smartpractice, Phoenix, AZ, USA) on Scanpor® tape (Norgesplaster, Alpharma, Vennesla, Norway), and allergens from Allergeaze® (SmartPractice®, Phoenix, AZ, USA) and Chemotechnique Diagnostics (Vellinge, Sweden) were used. The patch tests were applied to the upper back and occluded for 48 h. Readings were performed on day (D) 2, D3 and D5/7 according to ESCD recommendations (12). A +, ++ or +++ reaction was considered to be positive. Contact allergy was defined as at least one positive reaction at any of the three readings. Irritant, doubtful and negative test reactions were interpreted as negative.

The prevalences of the maximum reaction at different readings were calculated, and the prevalence of lanolin contact allergy was calculated on the basis of at least one positive test reaction to one of the two markers: lanolin alcohols and Amerchol™ L-101. The chi²-test was used to detect possible significant differences in lanolin allergy frequency between subgroups defined according to the MOAHLFA index, and, when required, Fisher’s exact test was used. The threshold for statistical significance was defined as a p-value of < 0.05. Two logistic regression analyses were conducted. The first had AD as the dependent variable, and age and sex as the independent variables. The second had face dermatitis as the dependent variable, and AD as the independent variable. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

All data were processed with SPSS (SPSS™ Statistics, Chicago, IL, USA; IBM PASW Statistics) for Windows™, edition 22.

Results
Table 1 shows the reactions on D2, D3 and D5/7 with positive, irritant and doubtful reactions for lanolin alcohols and Amerchol™ L-101. More doubtful than irritant test reactions were observed, and no extreme positive test reactions (+++) were noted.

Lanolin alcohols versus Amerchol™ L-101
Between 2004 and 2015, 937 dermatitis patients were patch tested with lanolin alcohols, and 9316 patients were patch tested with Amerchol™ L-101. More doubtful than irritant test reactions were observed, and no extreme positive test reactions (+++) were noted.

Temporal change in prevalence
For lanolin alcohols, an increasing prevalence of contact allergy was observed, from 0.15% in 2004 to 0.90% in 2015, and, similarly, for Amerchol™ L-101 an increasing
Table 1. Reactions by day of reading

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Day of reading</th>
<th>Lanolin alcohols 30% pet.</th>
<th>Amerchol™ L-101 50% pet.</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>D2</td>
<td>1.23 (117/9537)</td>
<td>1.79 (167/9316)</td>
</tr>
<tr>
<td></td>
<td>D3</td>
<td>2.45 (234/9537)</td>
<td>2.75 (256/9316)</td>
</tr>
<tr>
<td></td>
<td>D5/7</td>
<td>0.91 (87/9537)</td>
<td>0.87 (81/9316)</td>
</tr>
<tr>
<td>++</td>
<td>D2</td>
<td>0.07 (7/9537)</td>
<td>0.12 (11/9316)</td>
</tr>
<tr>
<td></td>
<td>D3</td>
<td>0.37 (35/9537)</td>
<td>0.43 (40/9316)</td>
</tr>
<tr>
<td></td>
<td>D5/7</td>
<td>0.13 (12/9537)</td>
<td>0.23 (21/9316)</td>
</tr>
<tr>
<td>+++</td>
<td>D2</td>
<td>0.02 (2/9537)</td>
<td>0.12 (11/9316)</td>
</tr>
<tr>
<td></td>
<td>D3</td>
<td>0.13 (12/9537)</td>
<td>0.21 (20/9316)</td>
</tr>
<tr>
<td></td>
<td>D5/7</td>
<td>0.04 (4/9537)</td>
<td>0.04 (4/9316)</td>
</tr>
<tr>
<td>IR</td>
<td>D2</td>
<td>0 (0/9537)</td>
<td>0 (0/9316)</td>
</tr>
<tr>
<td></td>
<td>D3</td>
<td>0 (0/9537)</td>
<td>0 (0/9316)</td>
</tr>
<tr>
<td></td>
<td>D5/7</td>
<td>0 (0/9537)</td>
<td>0 (0/9316)</td>
</tr>
</tbody>
</table>

IR, irritant reaction.

Readings were performed on D2, D3 and D5/7 according to ESCD recommendations. +, ++ or +++ reaction was considered to be positive, and IRs, doubtful reactions (+?) and negative test reactions were considered to be negative.

Fig. 1. Positive reactions to lanolin markers: Venn diagram of positive reactions to lanolin markers. Contact allergy was defined as at least one positive reaction at any of the three readings.

prevalence was observed, from 0.46% in 2004 to 1.52% in 2015 (Fig. 2). The overall prevalence of contact allergy to lanolin increased from 0.45% in 2004 to 1.81% in 2015.

MOAHFA

Table 2 shows the MOAHFA index for dermatitis patients patch tested between 2004 and 2015 stratified by contact allergy to lanolin alcohols and Amerchol™ L-101. Face dermatitis was significantly associated with contact allergy to lanolin alcohols, Amerchol™ L-101, and lanolin. Significant associations were found for Amerchol™ L-101 (adjusted OR 1.92; 95%CI: 1.21–3.04) and lanolin (adjusted OR 1.73; 95%CI: 1.16–2.58), but no significant association was found for lanolin alcohols (adjusted OR 1.64; 95%CI: 0.95–2.83), after adjustment for AD. Moreover, age > 40 years was also significantly associated with contact allergy to lanolin alcohols, but not with contact allergy to Amerchol™ L-101. No association was found between AD and contact allergy to lanolin alcohols, Amerchol™ L-101 or lanolin in crude data analyses, but, following adjustment for age and sex, significant associations were found for lanolin alcohols (adjusted OR 2.12; 95%CI: 1.15–3.92) and lanolin (adjusted OR 1.72; 95%CI: 1.08–2.74), and a non-significant association was found for Amerchol™ L-101 (adjusted OR 1.58; 95%CI: 0.91–2.75) (Fig. 3).

Discussion

This study showed an overall increasing prevalence of contact allergy to lanolin, from 0.45% in 2004 to 1.81% in 2015. Moreover, a weak positive association between lanolin allergy and face dermatitis and between lanolin allergy and AD were observed in the adjusted analysis. Our data emphasize the benefit of testing with two lanolin markers to detect lanolin contact allergy.

The annual proportion of positive patch test reactions to lanolin has varied in studies from different countries (5–7, 10, 11, 13–17). For example, in North America, the prevalence of patch test reactivity to lanolin alcohol 30% pet. significantly decreased from 3.7% in 1994–1996 to 1.8% in 2005–2006 (7). The overall prevalence of contact allergy to lanolin alcohols in a large study from a centre in the United Kingdom was 1.7%, and appeared to be constant during 1982–1996 (13). Notably, the prevalence of positive reactions to lanolin increased from 1.05% (only lanolin alcohols 30% in pet. was tested) to 6.29% when multiple lanolin derivatives (12 in total) were tested in the Mayo clinic, emphasizing the putative benefit of comprehensive testing (5). This shows the difficulties in detecting lanolin contact allergy with only one marker in the baseline series (18). We have no explanation for the slight increase in lanolin allergy, but there is an increase of 10% of patients with AD in our database, and the possible increased use of cosmetics could have resulted in the overall increase.

Face dermatitis was significantly associated with contact allergy to lanolin alcohols, Amerchol™ L-101 and lanolin in this study. This could be explained by the use of cosmetics on the face, because cosmetics constitute one of the most common allergen sources for lanolin (7, 19). Notably, previous studies have shown a positive association between lanolin allergy and leg dermatitis (20, 21), but more recent reports have indicated a decline in the number of reactions. For example, almost 20% of chronic leg ulcer patients had a positive reaction to
Fig. 2. Annual prevalence of contact allergy to lanolin alcohols, Amerchol™ L-101, and lanolin. The prevalence of lanolin contact allergy was calculated by one positive reaction for at least one of the two markers, namely, lanolin alcohols and Amerchol™ L-101.

Table 2. MOAHLFA index

<table>
<thead>
<tr>
<th>MOAHLFA index</th>
<th>Lanolin alcohols 30% pet.</th>
<th>Amerchol™ L-101 50% pet.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 9537</td>
<td>n = 9316</td>
</tr>
<tr>
<td>Positive reactions, % (n/n_total)</td>
<td>Negative reactions, % (n/n_total)</td>
<td>Positive reactions, % (n/n_total)</td>
</tr>
<tr>
<td>Male</td>
<td>36.2 (21/58)</td>
<td>32.6 (3088/9479)</td>
</tr>
<tr>
<td>Occupational</td>
<td>19.0 (11/58)</td>
<td>20.0 (1895/9479)</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>25.9 (15/58)</td>
<td>18.5 (1751/9479)</td>
</tr>
<tr>
<td>Hand dermatitis</td>
<td>39.7 (23/58)</td>
<td>38.1 (3614/9479)</td>
</tr>
<tr>
<td>Leg dermatitis</td>
<td>3.4 (2/58)</td>
<td>3.8 (360/9479)</td>
</tr>
<tr>
<td>Face dermatitis</td>
<td>36.2 (21/58)</td>
<td>24.8 (2350/9479)</td>
</tr>
<tr>
<td>Age &gt; 40 years</td>
<td>81.0 (47/58)</td>
<td>64.9 (6156/9479)</td>
</tr>
</tbody>
</table>

The chi²-test was used to detect possible significant differences of lanolin allergy frequency between subgroups defined by the MOAHLFA index and when required, Fisher’s exact test was used. Statistical significance indicated by bold type.

lanolin alcohols in 1994–2003, and 7.8% had a positive reaction to lanolin alcohols in 2003–2014 (21). This change can probably be explained by better treatment of leg ulcers and an increased use of prophylactic measures. Among > 600 lanolin-containing products in the United States, only 169 (27.3%) declared lanolin alcohols in the list of ingredients (5). Also, the majority of consumer products do not contain the lanolin derivative that is currently used in the patch test baseline series. These findings seem to support the importance of testing the patient’s personal products.

Contact allergy affects up to 20% of the general population (22), and the prevalence of contact allergy in patients with AD has been discussed over the years. Multiple factors can contribute to a higher risk of contact allergy in AD patients, namely, skin barrier abnormality, compromised antimicrobial defences, and the need for repeated or prolonged use of topical products, which may indeed contain lanolin (8). This study showed a positive association between AD and allergy to lanolin alcohols in the adjusted analysis, and this finding is in line with findings from a recent paediatric study (23). In contrast, a large retrospective study showed no difference in allergy
Fig. 3. Prevalence of positive patch test reactions to lanolin alcohols and Amerchol™ L-101 at different readings stratified by atopic dermatitis (AD).

to lanolin alcohols among patients with and without AD (13).

Sometimes it can be difficult even for experienced clinicians to distinguish between irritant and true allergic reactions. Geier et al. discussed Amerchol™ L-101 as a problematic allergen (24). In this respect, it has been proposed that concomitant patch testing with the skin irritant sodium lauryl sulfate (SLS) could provide valuable information regarding skin irritability, as the probability of an irritant reaction seems to be higher when the SLS test result is positive (25).

Our study emphasizes the benefit of testing with two markers to detect lanolin contact allergy. An older study found that 71.1% of patients who were sensitized to lanolin reacted only to Amerchol™ L-101 (50% and 100%), 2.2% reacted only to lanolin alcohols, and 26.7% reacted to both markers (1). Notably, the test results may vary within the same patient when testing is performed with lanolin alcohols 30% from different manufacturers (5). Furthermore, the reproducibility of a positive reaction to lanolin alcohols is considered to be fair (26). It remains unclear why patch testing with Amerchol™ L-101 may detect additional cases of lanolin allergy, given that it has a lower alcoholic fraction. Awareness is needed when testing is performed with Amerchol™ L-101, as it has irritant properties (27).

Acknowledgements

J. P. Thyssen is supported by an unrestricted grant from the Lundbeck Foundation.

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