Sir,

*Staphylococcus aureus* is a common pathogen that may colonize normal skin, but it is not a member of the normal skin flora (1, 2). In healthy individuals it is most commonly isolated from the nose, the groin and the perineum. Patients with atopic dermatitis (AD) are colonized with *S. aureus* both in lesional skin as well as in non-lesional skin in 70–100% of cases (2, 3). However, the density is higher in lesional skin compared with non-lesional skin (2, 3). The reason for the increased colonization is unclear. A higher pH in the skin of patients with AD may facilitate growth of *S. aureus* (4). Furthermore, it has been recently demonstrated that endogenous antimicrobial peptides are decreased in atopic skin (5). As regards to the role of *S. aureus* colonization for AD activity, specific *S. aureus* IgE antibodies have been found in several patients, but their presence does not correlate with disease severity (6). However, superantigen-producing *S. aureus* may trigger flares in AD (6).

In acute secondary bacterial infection of AD the orally active penicillase-resistant penicillins, such as flucloxacillin or dicloxacillin, are the drugs of choice (7). In patients with less severe and/or extensive signs of secondary bacterial infection, topical applied antibiotics have a documented effect (7). However, the increase in multi-resistant *S. aureus*, including resistance to methicillin (MRSA), fusidic acid and mupirocin, is an increasing problem (7–9).

Pentane-1,5-diol (C$_5$H$_{10}$O$_2$) is a diol or glycol, today used as plasticizer in cellulose products and adhesives, in dental composites and in brake fluid compositions and as a preservative for grain (10). However, pentane-1,5-diol is also an effective solvent, percutaneous absorption enhancer, water-binding substance and has significant anti-microbial properties (11). Compared with propane-1,2-diol (propylene glycol) pentane-1,5-diol has the following advantages: (i) a more efficient anti-microbial agent, (ii) increased percutaneous absorption of active pharmaceutical substances, (iii) less side-effects (e.g. skin and eye irritation), and (iv) at least the same water-binding capacity (10, 11). Recently we have shown, in *vitro*, that pentane-1,5-diol has a high bactericidal activity against both sensitive as well as multi-resistant bacteria including MRSA, fusidic acid-resistant *S. aureus* and vancomycin-resistant enterococci (9).

In previous comparative studies the addition of an antibiotic to a topical steroid was considerable more effective in the treatment of AD than the topical steroid alone (7). The aim of the present study was to compare the effect of a hydrocortisone cream with or without addition of pentane-1,5-diol in the treatment of AD. The effect of the two treatments on the number of *S. aureus* on the skin was also studied.

**MATERIALS AND METHODS**

A total of 63 patients, 44 females and 19 males (mean age 31 years), with AD were included in the study. The diagnosis of AD was according to the criteria given by the UK Working Party’s Diagnostic Criteria for AD (12). Thirty-two patients were treated with a cream containing 1% hydrocortisone and 25% pentane-1,5-diol (HP) and 31 patients were treated with 1% hydrocortisone cream (H) alone. The cream base was Essex cream (Schering Plough, New Jersey, USA).

The study was a controlled, double-blind comparative study between HP and H. Patients stopped all topical active treatment as well as oral antibiotics at least 2 weeks prior to the start of the study. Only moisturizers without any anti-microbial additives were allowed before and during the treatment. The treatment was twice daily for 6 weeks with follow-ups after 2, 4 and 6 weeks of treatment. The cream was applied on all lesional skin and Essex cream without any additives was allowed as a moisturizer on non-lesional skin.

The severity of AD was assessed using the SCORAD system (12). Patients were included if they had a SCORAD between 15 and 50. Patients were assessed as healed if they had a SCORAD of 4 or less at the end of treatment. Adverse events were recorded, at each visit, by both the investigator and patient.

Quantitative cultures for bacteria were taken using a modification of the Williamson-Kligman model for quantitative cultures of skin bacteria (13). Cultures were taken from lesional skin before start of treatment and then from the same area after 2, 4 and 6 weeks of treatment.

The Mann-Whitney test was used to test the difference between the two treatments as well as the difference between baseline and weeks 2, 4 and 6 of treatment. The difference was assessed for both the difference in SCORAD as well as the difference in number of *S. aureus*. Analysis was performed for both the intention to treat (ITT) and the per protocol (PP) populations.

**RESULTS**

Both treatments were effective: 68% were healed in the H group and 69% in the HP group (Table I). There was also a significant reduction in SCORAD from baseline to week 6 for both group (*p* < 0.0001 for both groups). Although the median value for SCORAD, at the end of treatment, was 7 in the HP group compared with 14 in the H group, there was no statistically significant difference between the groups. However, the SCORAD
Table I. Effect of treatment of atopic dermatitis with a cream containing 1% hydrocortisone and 25% pentane-1,5-diol (HP) compared with 1% hydrocortisone (H) cream alone

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Week</th>
<th>n</th>
<th>Mean ± SD</th>
<th>Median (range)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP</td>
<td>0</td>
<td>32</td>
<td>2.83 ± 2.24</td>
<td>3.14 (0–6.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>29</td>
<td>1.44 ± 1.89</td>
<td>0 (0–5.72)</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>31</td>
<td>1.73 ± 2.39</td>
<td>0 (0–8.48)</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>29</td>
<td>1.63 ± 2.15</td>
<td>0 (0–6.36)</td>
<td>0.031</td>
</tr>
<tr>
<td>H</td>
<td>0</td>
<td>31</td>
<td>2.49 ± 2.40</td>
<td>1.97 (0–7.15)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>30</td>
<td>2.58 ± 2.21</td>
<td>2.48 (0–6.04)</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>29</td>
<td>1.91 ± 2.50</td>
<td>1.48 (0–6.73)</td>
<td>0.70</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>27</td>
<td>1.65 ± 2.00</td>
<td>0 (0–5.43)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

*p-value is for the difference in numbers between baseline and weeks 2, 4 and 6 within the groups.

reduction continued between week 4 and 6 in the HP group as contrasted with the H group (see Table I). The reduction in numbers of S. aureus was statistically significant in the HP group not only between week 0 and week 6 (p = 0.003) but also between baseline and week 2 (p = 0.0003) (Table II). No statistically significant reduction was seen in the H group.

Only 4 minor adverse events were reported; 2 in the HP group and 2 in the H group. All were a slight burning sensation in the skin after application of the cream.

DISCUSSION

Although there was no difference in clinical efficacy between a hydrocortisone cream and a hydrocortisone cream with the addition of pentane-1,5-diol, the combination cream was superior in reducing the numbers of S. aureus. This is an interesting observation, not only because S. aureus plays an important role in the deterioration of AD but also for the treatment of bacterial skin infections in general.

An increasing problem in modern healthcare is the development of multi-resistant bacteria (2, 8, 9). Pentane-1,5-diol is a diol with the same activity against both sensitive and resistant aerobic bacteria (9). The risk for development of bacterial resistance against this compound is not a problem due to the mechanism of action of diols on membranes. The risk for toxicity, skin irritation and development of allergic reactions is very low with pentane-1,5-diol (10).

The reason why we were not able to find any difference in clinical efficacy between the treatment with hydrocortisone cream and a combination cream with pentane-1,5-diol may be due to the short treatment period. An interesting future study would be to treat secondary infected AD with the combination cream to try to prevent recurrence with a moisturizing cream containing pentane-1,5-diol.

REFERENCES