In that respect, it is interesting to note in the letter from Uter et al. (2001) that the percentage of colophony sensitive patients reacting to oakmoss is increasing with regard to the severity of their allergy. Thus the percentage of patients reacting to oakmoss is 14.7% in patients reacting to colophony with erythema only ("?"), 19.4% in those with a "+" reaction, 30% in those with a "++" reaction, and 53.3% in those with very strong ("+++"), reactions. This later figure is very similar to the one we observed (53%) on our selected patients.

We suggest that more care should be taken when stating that 12823 patients were patch tested between 1992 and 1999 to the same oakmoss material as the one we have been using in our study. Over a period of time patch test suppliers will use different batches of oakmoss material either from the same supplier or from different suppliers. The oak moss sample we have been using is identical to the material used by Trolab (Reinbek, Germany) from 1999 to now. Therefore a comparison of data can only be valid if conducted in the period 1999–2000.

We are of course well aware that oakmoss and treemoss are skin sensitizers, not only because of the presence of resin acids but also because of the presence of other sensitizers, some of which are known in the literature (Dahlquist et al., 1980). Among our 17 patients two reacted to the oakmoss from Chemotechnique (Malmö, Sweden), despite a low content of resin acid, which probably indicates a true co-sensitization to oakmoss and colophony.

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Staphylococcal Colonization in Atopic Dermatitis Treatment with Topical Tacrolimus (Fk506)

To the Editor:
Tacrolimus (FK506) is a potent immunosuppressive macrolide. Clinical trials have demonstrated that it is an effective treatment for atopic dermatitis (AD) in adults as well as in children (Kuzicka et al., 1997; Boguniewicz et al, 1998). Experience from these trials suggests that an ephemeral burning sensation is the most common drug-related side-effect; however, skin infections are a potential complication of local treatment with topical immunosuppressive agents, and a recent open-label multicenter study, involving 316 AD patients treated with 0.1% tacrolimus ointment for 6–12 months, observed skin infections at the application site in 19.8% of patients (Reitamo et al, 2000). Heavy skin colonization with Staphylococcus aureus is well established in patients with AD, even in the absence of clinical signs of skin infection, and also on normal skin (Hauer et al, 1985; Lever et al, 1988).

As tacrolimus has no antistaphylococcal activity in vitro (Kino et al., 1987), topical treatment with FK-506 might enhance S. aureus colonization by a local immunosuppressive mechanism. Therefore, we conducted a pilot study in order to determine the influence of treatment with 0.1% tacrolimus ointment on S. aureus colonization. Tacrolimus ointment 0.1% was formulated according to Aoyama et al (1995).

In 11 patients (mean age 23.2 [SD 13.8]) diagnosed with AD according to the criteria of Hannifin and Rajka (1980), we identified 40 lesional skin sites positive for S. aureus colonization. All patients had stopped systemic or topical antibiotic treatments at least 2 wk before onset of treatment with 0.1% tacrolimus ointment; the use of emollients was allowed throughout the study period. Staphylococcus aureus colonization density was measured as the number of agglutination-positive colony forming units (CFU per cm²) (Pastorex Staph-plus, Sanofi Pasteur, Marnes La Coquette, France), sampled with a mannitol salt agar contact plate (Ecobion, Carouge, Switzerland). Assessment of S. aureus colonization density at each site was done at baseline (day 0), and scheduled on days 3, 7, 14, and 21 after the onset of 0.1% tacrolimus ointment monotherapy. In total, 151 samples were realized, which represents 75.5% of the scheduled number (n = 200). Of these, 139 samples (92.1%) could be evaluated; 7.9% of the realized samples could not be processed because of technical problems. We also studied 11 S. aureus positive lesional skin sites in 11 patients (mean age 27.3 [SD 9.5]) that were treated with the vehicle alone. In order to correlate S. aureus colonization density at each site with parameters of treatment efficacy, we performed clinical grading based on the lesional score of the SCORAD index (Consensus report EPTFA), and assessed transepidermal water loss (TEWL), a parameter of skin barrier function (EP2 evaporimeter, ServoMed AB, Kinna, Sweden). Statistical comparison was made using the Wilcoxon signed-rank test, a nonparametric test; rank correlation analysis was made using the Spearman test.

During treatment with 0.1% tacrolimus ointment, TEWL and lesional score showed a significant decrease already after the third day of therapy (p < 0.03 and p < 0.001, respectively), whereas decrease of S. aureus colonization became significant at treatment day 7 (p < 0.003) (Fig1). Statistical analysis according to the Spearman test showed no correlation between the three parameters (score, TEWL, and S. aureus colonization) studied at days 0, 3, 7, 14, and 21. In 31 samples, significant but transient increases of S. aureus CFU counts, as compared with preceding levels at the same skin site, were observed at some point during the 21-d treatment period (p < 0.05), without simultaneous changes of the clinical score and TEWL.

Our results demonstrate that topical immunosuppressive therapy of AD with 0.1% tacrolimus ointment during 3 wk is associated with an overall decrease of S. aureus colonization on lesional skin. Similar results have been reported with local steroid monotherapy, which has also been shown to reduce S. aureus colonization on AD skin (Nilsson et al, 1992). These findings are consistent with the concept of inflammatory skin condition in AD, being itself a predisposing factor for colonization with S. aureus. This hypothesis has some limitation insofar as the day-to-day variation of S. aureus colonization in untreated skin of patients with AD is not known. As tacrolimus does not have a direct antistaphylococcal activity (Kino
et al., 1987), it is conceivable that the decrease of S. aureus colonization observed in this study is a consequence of the improvement of the skin surface due to the anti-inflammatory effect of the drug, and possibly also due to the emollient effect of the vehicle. This is supported by our observation that the onset of significance for the decrease of S. aureus colonization at treatment day 7 lagged behind the evolution of the clinical score and the skin barrier function, that had already significantly improved by day 3. Alternatively, S. aureus CFU density might be a more sensitive parameter of AD severity than the clinical score and TEWL, and thus lag behind the evolution of the latter during immunosuppressive local treatment. Our observation that a substantial number of samples showed transient increases in S. aureus colonies during continued treatment, despite a rapid decrease of baseline S. aureus counts at onset of immunosuppressive treatment, suggests however that S. aureus colonization is an independent disease parameter in AD, whose dynamics under topical immunosuppressive treatment need further study.

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![Figure 1. Evolution of clinical parameters during treatment of atopic dermatitis lesional skin sites with tacrolimus ointment. (A) Staphylococcus aureus colony forming units (CFU per cm²) count; (B) lesional SCORAD score; (C) transepidermal water loss (TEWL); *p < 0.05 (Wilcoxon signed-rank test).](image)