4th week. Due to skin irritation we decided to stop the treatment at the end of the 4th week. For further details, see our previous report (8).

FOLLOW-UP

Two weeks after withdrawal of the treatment the patient could tolerate outdoor light exposure for one hour. The rest of the summer he spent mainly indoors, allowing up to one hour in the sun daily. Only occasionally did he develop a faint erythema and itching on sun-exposed areas, proving that he was not fully cured. Therefore the topical mechlorethamine treatment was readministered in September 1980, but was withdrawn after 3 weeks of daily application due to irritation and a general rash the day after each application. No relapse has so far been noted (November 1980) even following outdoor visits. His skin is normal pale and the lichenification has subsided. No other treatment has been given. Only a slight cell infiltrate persisted in the dermis, as compared with the diagnostic histology before treatment. The cell infiltrate consisted mainly of mononuclear cells. There was no epidermal infiltration.

DISCUSSION

Treatment of patients with actinic reticuloid has been unsatisfactory. For patients with more or less normal light reactions, PUVA therapy may be helpful, but this treatment is practically impossible in more light-sensitive patients. Our patient, however, demonstrates that whole-body topical mechlorethamine applications may be the treatment of choice for actinic reticuloid. So far, only one actinic reticuloid patient has received mechlorethamine topically for 6 weeks, but that was 2–3 years before the diagnosis was confirmed, in the belief that he had mycosis fungoides (3). Individual factors may explain why that reported case did not respond to mechlorethamine topically. It is important that the skin is in a good condition before mechlorethamine topically is instituted, so that an adequate concentration can be used. The time before remission is considerably shortened by the soaking modality (8). The patient of Johnson et al. (3) might therefore have been treated insufficiently.

We have as yet no explanation for the beneficial effect of topical mechlorethamine treatment in actinic reticuloid. Both the etiology of the disease and the working mechanism of mechlorethamine topically are unknown. These observations, however, are not unexpected, since the dense superficial dermal infiltrate with cells which also extends into the overlying epidermis may mimic early mycosis fungoides.

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Inefficacy of Topical Methoxalen plus UVA for Palmoplantar Pustulosis

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Abstract. The effect of local application of 8-methoxypsoralen (8-MOP) and subsequent UVA irradiation on palmoplantar pustulosis (PPP) was studied in 10 patients. In 8 patients 8-MOP baths were used, and in 5 patients an

Table 1. *Results of treatment with topical psoralen and UVA*
B=bathing, O=ointment

Patient no.	Sex	Methoxalen application	Number of treatments	Total UVA dose	Maximal single dose	Therapeutic results
1	♀	B	15	8	1.2	Exacerbation
2	♀	O	34	26	1.2	None
3	♀	B	29	18	1.5	None
4	♂	B, O[a]	128	348	3.6	None
5	♀	B	35	35	4	Moderate
6	♀	B	30	40	4	Moderate
7	♂	O	65	154	4	None
8	♀	B, O[b]	17	59	7	Exacerbation
9	♀	B, O[c]	44	144	12	None
10	♀	B	40	220	12	Good

[a] Last 34 treatments, ointment.
[b] Left side, bath treatment. Right side, ointment.
[c] Last 19 treatments, ointment.

8-MOP ointment was applied, 3 patients receiving both forms of treatment. The number of treatment sessions varied from 15 to 128, with maximal UVA doses of 1.2 to 12 J/cm², and total cumulative doses of 8 to 348 J/cm². Two patients experienced a brisk phototoxic erythema and one patient developed a bullous reaction. Only 3 patients responded favourably to the treatment, 2 with moderate and 1 with good clearing of the lesions. In the remaining 7 patients either no effect (5 patients) or an exacerbation of the disease (2 patients) was seen.

Palmoplantar pustulosis (PPP) continues to pose a therapeutic problem for the practising dermatologist. The recent reports of the successful application of oral methoxalen and local UVA irradiation in the treatment of this dermatosis are, therefore, of great interest (2, 3, 4, 5). Considering the localized nature of PPP, systemic psoralen administration would seem to be unwarranted, however, as the local application of psoralen in ointments or water baths has been demonstrated to be effective in PUVA treatment, of psoriasis vulgaris for example (1, 6). Topical psoralen application eliminates both the need for protection of the eyes after irradiation, as well as the risk of systemic psoralen side effects. In this paper we report the therapeutic results of topical bath and/or ointment application of methoxypsoralen (8-MOP) and subsequent UVA irradiation in 10 patients with palmoplantar pustulosis.

MATERIAL AND METHODS

Ten patients, 9 of them women, participated in the study. The ages of the patients varied between 25 and 69 (mean 48) years. The duration of the dermatosis ranged from 9 months to 10 years (mean 3.5 years). The diagnosis was based on a typical clinical picture and the exclusion of contact sensitivity and bacterial or fungal infections.

The aqueous 8-MOP solution was prepared by adding, to 10 litres of lukewarm tap water, 6 ml of a stock solution containing 1 g/l of 8-methoxypsoralen in ethyl alcohol. The feet and hands of the patient were bathed in the 8-MOP water solution for 20 min. Thereafter, the skin was gently wiped with paper towels, and the UVA irradiation performed immediately. Alternatively, 0.1% 8-methoxalen ointment was applied for 60 min, the ointment wiped off with paper towels, and the skin area immediately subjected to UVA irradiation. The ointment base consisted of an emulsion of glycerol, polyunsaturated fatty acids and emulgators in water.

For irradiation, portable light boxes (PUVA-4, Airam Oy, Helsinki) were used, emitting in the 315–410 nm region, with maximal output at 360 nm. The output, as measured with an Airam UVM-8 radiometer ranged from 4 to 6 mW/cm² at the skin surface. As topical application of methoxalen is known to sensitize the skin much more strongly than oral medication, the starting dose of UVA irradiation was 0.1–0.2 J/cm² and increments of 0.1–0.2 J/cm² were used to reach the dose of 1 J/cm². Thereafter, dose increments of 0.3–0.5 J/cm² were applied. The maximal dose did not exceed 12 J/cm². The therapeutic result was evaluated at frequent intervals, and the final result scored as no, moderate, good, or excellent improvement. In some patients an exacerbation of the dermatosis was the outcome of the treatment.

RESULTS

The results of the treatment are set out in the Table. In 2 out of the 10 patients a moderate, and in 1 good therapeutic success was recorded, but in no patient was the response excellent, i.e. complete healing was not achieved. Of the remaining 7 patients, the clinical status remained unchanged in 5, while an

exacerbation was the outcome in 2 cases. The number of treatment sessions, the maximum individual dose, and the total UVA dose varied considerably from case to case (Table 1). Fewer than 20 treatments were accomplished in patients 1 and 8, who interrupted the treatment because of an exacerbation. Other side effects were smarting and erythema in patient 1 at a dose of 1.2 J/cm² and in patient 10 at 12 J/cm²; patient 7 experienced a severe burning with large bulla formation at 4 J/cm².

DISCUSSION

This study records poor results with topical psoralen application in the PUVA treatment of palmoplantar pustulosis, even with up to 128 treatments and total doses of up to 144–348 J/cm². These results contrast both with the favourable effect documented with topical psoralens and UVA in the treatment of psoriasis vulgaris (1, 6), and the therapeutic success reported with oral methoxalen and UVA in the treatment of PPP (2, 3, 4, 5).

In the case of 8-MOP bath application the inadequate effect might, at least partially, have resulted from a depletion of the drug from the skin during the prolonged irradiation times (up to 40 min) used in the higher UVA dosage range. After a trioxsalen bath, the photosensitivity of body skin has been shown to diminish to 50% of the starting value during the first 30 min after bathing and to 25% during the next 30 min (1). In the case of a psoralen ointment, therapeutic drug concentrations may be retained in the skin for somewhat longer periods. In one study, after removal by blotting paper of an 0.01% trioxsalen ointment, one-fourth of the photosensitivity was retained at 2 h (7). That effective sensitization of the skin was actually obtained in our study, can be inferred from the fact that 3 of the patients developed painful erythema of the treated skin areas, one developing a bullous phototoxic reaction; in only one of these patients was a favourable clinical response obtained, however.

Recently, Murray et al. reported a study in which 7 out of 15 PPP patients cleared on a treatment consisting of the application of an 0.15% 8-MOP oil emulsion and 30 irradiations with a mean clearing dose of 8 J/cm² (5). In our series 5 patients were treated with 8-MOP ointment and UVA, 4 receiving more than 30 treatments; the maximal UVA dose varied from 1.2 to 12 J/cm². None of the 5 patients showed any improvement. The discrepancy of these results and those of Murray et al. (5), could be due to chance alone, to different vehicles, different application times (60 min vs. 90 min), different UVA dosage schemes, different frequently of treatment (3 vs. 4 times a week), or any combination of these factors. Clearly, more studies are required to delineate the efficacy of topical 8-MOP and UVA treatment of palmoplantar pustulosis. In particular, systemic versus topical psoralen, psoralen solution vs. psoralen ointments, and different application and irradiation schedules should be evaluated.

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Solubility of Antimycotics: A Problem in *in vitro* Experiments

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Abstract. An investigation of how miconazole nitrate dissolved in dimethylformamide in initial concentrations of 1 000, 500, and 100 μg/ml may alter its concentration with