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TREATMENT OF PSORIASIS WITH TRIOXSALEN BATHS AND DYSPROSIUM LAMPS

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Abstract. Photochemotherapeutic treatment of psoriasis with trioxsalen baths (0.5 mg/l) for 15 minutes followed by irradiation with dysprosium lamps (Osram HQI-TS) healed or nearly healed the psoriatic lesions in 18 patients within 3–5 weeks. A control area treated with the Ingram method showed a slower healing in 9 of these patients. Methoxsalen bath was not as effective in healing at the concentration used (1 mg/l). The bath method is easy to administer and cosmetically acceptable. Sensitisation to light is maximal immediately after the bath and disappears more quickly than after painting with an alcoholic trioxsalen solution. By using baths, there is less risk of accidental burns or uneven pigmentation than with the often time-consuming local application of psoralen solutions. Toxic systemic effects, which are possible with oral treatment, are less apt to occur. The dysprosium lamps give high intensity in the UV-A region. Exposure times of 10 seconds to 8 minutes are effective in the treatment of psoriasis, where both the UV-B region itself and the UV-A in combination with trioxsalen have psoriasis-healing properties.

Key words: Photochemotherapy; Psoralens; Psoriasis; UV-light; UV-treatment

Treatment of psoriasis with light sensitisation and UV light has been common since the 1920's. Goeckermann (6) used coal tar ointments and a medium-pressure type mercury quartz lamp when he created the first effective photochemotherapeutic treatment. Ingram (8) modified the treatment to include coal tar baths, carbon arc light, and anthralin paste.

The first attempts to treat psoriasis by parenteral light sensitisation were those of Oppenheim (13), who used tryptaflavin injections plus UV-light and obtained good results in 22 of the 25 treated patients. Tulipan (21) found that peroral light sensitisation with sulfanilamid followed by UV-light treatment resulted in a healing of psoriasis. Epstein (4) later verified this finding but sulfanilamid was considered too toxic to be accepted as a treatment method.

In 1962 Allyn (1) reported healing of psoriasis after local application of psoralen plus UV-light. In 1967 Oddoze et al. (12) presented 3 patients with severe psoriasis who were healed by using peroral methoxsalen treatment and sunbathing. There have been several reports since 1972 in which the efficacy of both local and peroral psoralen plus UV-light treatment has been confirmed (10, 15, 19, 20, 23, 24, 25, 26).

MATERIALS

Chemicals

1. Trioxsalen (Triosoralen®, Paul B. Elder Co., USA) 0.05, 0.005 and 0.0005% in 70% ethanol.
2. Methoxsalen (Oxsoralen, Memphis Chemical Co., Egypt) 0.1, 0.01 and 0.001% in 70% ethanol.
3. Spiritus carbonis detergens AF 68 (a coal tar extract).
4. Anthralin, 0.1 and 0.4% paste according to Ingram (8).

Test lamps

The light-test apparatus (2) contains high pressure mercury lamps (Philips SP-500 W) and water-cooled filters that isolate the principal mercury lines, e.g. at 313 nm or 365 nm, as narrow bands of very high intensity.

Treatment lamp

A solarium was built with 8 dysprosium lamps (Osram type HQI-TS, 400 W, see Fig. 1). The dysprosium lamp is a 3×20 cm gas discharge lamp that operates at about atmospheric pressure and has a high emission of visible light. Its primary use is for illumination of large areas, e.g. sports fields. At the irradiation distance chosen for treatment (50–60 cm from the lamps), the light spreads evenly ±10% over the treatment area (0.8×2 m). During the treatment, the patient lies on a bench and is irradiated on one side at a time. The irradiance of the solarium at this distance as calculated from measurements with an EG&E type 585 spectroradiometer is as follows: UV-A, 13 mW/cm²; UV-B, 0.7 mW/cm²; UV-C, 0.17 mW/cm². Using 5 mm thich heat-resistant glass as a filter, the following values are obtained: UV-A, 9 mW/cm²; UV-B 2×10^{-3} mW/cm²; UV-C, 0.

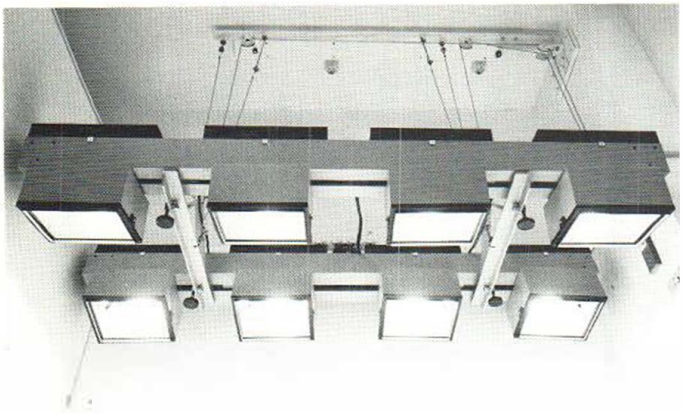

Fig. 1. The new dysprosium solarium mounted and seen looking upwards.

Comparison of trioxsalen baths with trioxsalen painting on normal skin

A comparison was made using the arms of 9 persons with normal-appearing skin. One arm was bathed for 15 min in a 10 litre bath of 37°C tap water containing 10 ml of 0.05% trioxsalen (0.5 mg/l). Test areas on this arm were irradiated immediately after the bath and again after ½ hour, 1 hour, and 24 hours with the 365 nm band of the test lamp. For each test the following doses were used: 0.3, 0.4, 0.6, 0.8, 1.0, 1.5, 2.0, 3.0, 4.0, 6.0 and sometimes 10 J/cm². Square areas were painted on the other arm with 0.05% and 0.005% trioxsalen in ethanol and irradiated 1 hour later in the same manner as the bathed arm. The erythema thresholds (MED) after 48 hours are shown in Table I and Fig. 2.

The maximum sensitisation for UV-light with trioxsalen painting occurs after 1 to 2 hours (5, 11) and then decreases slowly (Fig. 2). After bathing, the maximum sensitisation occurs immediately and is stronger than with painting. Half an hour after the bath, the sensitisation has dropped to 50% of the initial value and is equal to the maximum that can be obtained with painting and, after one hour, it has decreased to 25% of the initial value. After 24 hours, the erythema threshold is more than 10 J/cm², which corresponds to more than ½ hour of sunbathing at noon on a clear day. The erythema threshold 24 hours after trioxsalen painting is between 5 and 10 J/cm².

Comparison of dysprosium solarium and test lamps

The MED in J/cm² can be easily determined with the test lamps. It was therefore of interest to compare the irradiation times needed to produce erythema with the dysprosium solarium and with the test lamps.

Normal skin on the back was irradiated with the 313 nm band of the test lamp and the MED was determined at 24 hours. Skin painted with a trioxsalen or methoxsalen solution was irradiated 1 hour later with the 365 nm band of the test lamp and the MED was determined after 48 hours.

With the dysprosium lamps, irradiation was given with both unfiltered and glass-filtered light on 2×4 cm test

Table I. *Minimal erythema dose J/cm² read 48 hours after bathing vs. painting with trioxsalen*

Time of irradiation after treatment ...	Trioxsalen+water baths 37°C, 15 min 0.5 mg/l				Trioxsalen painting alcohol solution	
	0 min	30 min	60 min	24 h	500 mg/l 60 min	50 mg/l 60 min
Patient no.						
27	0.6	1.0	2.0	>10	1.0	3.0
28	0.3	0.6	2.0	>10	0.6	2.0
29	1.5	2.0	4.0	>10	1.0	6.0
30	0.6	1.0	3.0	>10	1.5	5.0
31	0.8	1.5	3.0	>10	2.0	4.0
32	1.5	2.0	6.0	>10	3.0	6.0
33	1.0	1.5	3.0	>10	2.0	4.0
34	2.0	4.0	>6.0	>10	2.0	>6.0
35	0.6	0.8	2.0	>10	0.8	1.0
Mean (log)	0.8	1.4	3.0	>10	1.4	3.5

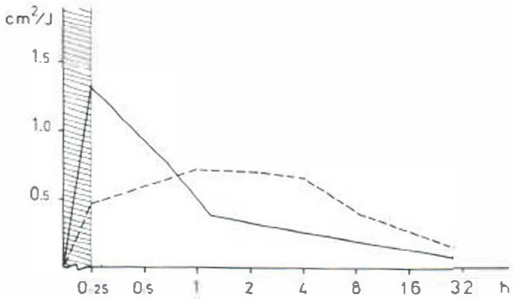

Fig. 2. Erythema sensitivity to the 365 nm band (MED) at various time intervals following: 1) Trioxsalen painting (– – –), and 2) Trioxsalen baths (—). Shadowed area= bathing time.

areas. A 1 cm² area in the middle of each test area had been painted with 0.05% trioxsalen 1 hour before irradiation. The erythema thresholds were judged after 24 hours for the non-treated skin and after 48 hours for the psoralen-treated skin. Values are given in J/cm² for the test lamps and in minutes for the dysprosium solarium. With no pretreatment of the skin, the erythema effect of 1 J/cm² with the 313 nm band of the test lamp equals 8 minutes of irradiation with unfiltered solarium light. Trioxsalen-painted skin will react with the same erythema when irradiated with 1 J/cm² of the 365 nm band or 2½ min of glass-filtered solarium light. Direct conversion to J/cm² is not possible as the spectral distributions of the light sources are different.

PSORALEN BATHING

Patients

Fourteen men and 12 women between the ages of 16 and 84 years, who had widespread psoriasis and an anamnesis of light tolerance, participated i the treatment series using trioxsalen or methoxsalen baths. All patients had a plaque type of psoriasis with the exception of one patient who had generalized pustular psoriasis. The patients visited the clinic 5 days a week for treatment in our bath- and light-treatment department. Eight of them had previously responded poorly to treatment with either coal tar or salt baths plus UV light. They had developed increased light tolerance, whereas the other 18 patients had not recently been exposed to sun or sunlamps.

Method

Psoralen baths were prepared from 0.1 litre of 0.05% trioxsalen- or 0.1% methoxsalen–alcohol solution added to 150 litres of 37°C water. The concentration of psoralen is then about 0.3 respectively 0.7 mg/l.

Eighteen patients bathed in trioxsalen and 8 in methoxsalen. The whole body, excluding the face and one arm, was immersed in the bath. The other arm was used for control treatment according to Ingram. During the bath, the arm was wrapped in a plastic bag containing 10 litres of 37°C water combined with 10 ml of the coal tar extract.

After a 15-minute bath, the patients were immediately exposed to unfiltered light from the dysprosium solarium. The average exposure times and range limits for psoralen-treated areas are listed in Table III. Usually, the light treatment was started with a 10–15 second exposure on each side for the winter-pallid, normally-pigmented skin and continued for 3–4 days. The erythema reaction that then occurred became the guide for the subsequent light doses. With only a slight irritation, the times were increased by 5–10 seconds per day. With a strong reaction the initial times were continued for another 3–4 days and, if there was then no reaction, the times were increased by 15–20 seconds per day. If the irritation was severe, the light treatment had to be carried out very carefully during the second week. Sensitive and easily irritated body areas, e.g. the face, back of the legs and, for women, the tops of the mammae, needed to be covered after half of the irradiation time. In 2 patients, a severe irritation developed with the formation of some blisters between the breasts and around the axilla. The treatment was discontinued on the affected areas for 2–3 days.

The treatment times for the second week were generally ½ to 2 minutes and, during the following weeks, the exposure times were gradually increased to 3–5 min. A copule of very light-tolerant patients had exposures up to 7 min. on each side. For the 8 patients who were light-tolerant from previous light treatment, the exposure times

Table II. *The erythema-producing dose of the test lamps (J/cm²) and the dysprosium solarium (min)*
Psoralen was painted 1 hour before irradiation and the tests read at 48 hours. Non-pretreated tests were read at 24 hours

	Light test lamp							Dysprosium lamp	
	313 nm	365 nm			365 nm				Glass filter
Patient		Trioxsalen pretreatment			Methoxsalen pretreatment				Trioxsalen
no.		0.05%	0.005%	0.0005%	0.1%	0.01%	0.001%		0.05%
36	0.2	2	4	15	3	15	>30	2.0	4.0
37	0.4	3	8	>15	4	15	>30	3.0	5.0
38	0.3	1.5	2	20	3	7	30	2.5	2.0
39	0.4	0.7	1	7	1.5	10	>30	3.0	3.0
40	0.2	0.4	1	7	1.5	10	30	2.0	1.5
Mean log	0.3	1.2	2.9	15	2.4	10	>30	2.5	3.0

Table III. *Exposure times (in seconds) with dysprosium solarium for patients given psoralen baths*

Treatment	No. of pat.	1–7 days Mean	1–7 days Range	8–15 days Mean	8–15 days Range	15–22 days Mean	15–22 days Range	22–29 days Mean	22–29 days Range	29+ days Mean	29+ days Range
Trioxsalen baths. Patient not recently light exposed	10	15	10–30	30	10–60	55	20–120	120	20–180	135	30–180
Trioxsalen baths. Patient recently light exposed	8	50	20–60	100	10–180	160	60–300	210	90–420	300	120–480
Methoxsalen bath. Patient not recently light exposed	8	30	10–90	60	20–150	90	40–210	180	60–300	240	90–420

could be increased more quickly. With methoxsalen bathing, the irritation was usually scarcely noticeable and the light doses could be increased more quickly.

Only local treatment with white petrolatum was allowed on the psoralen-treated skin. The coal-tar bathed arm received approximately twice as much light as the psoralen-bathed skin but the same light doses were given after 1 to 2 weeks. After irradiation, the skin was here treated with 0.1 or 0.4% dithranol paste. The treatment was followed until all skin areas were healed—or for 6 weeks.

The patients were checked 2 to 3 times a week and a judgement was made of the healing, irritation of the skin, and degree and evenness of pigmentation. Photographs were taken at least once a week of all psoriatic areas of each patient.

RESULTS

Healing

Details of the results are shown in Table IV. The trioxsalen baths gave a faster healing than the Ingram regimen in 9 of 17 patients, a comparable healing in 7, and a slower in one. During the first week of treatment with trioxsalen there often occurred a more or less strong irritation of the skin and signs of healing were observed in only a few cases. During the second week, the psoriasis healed considerably and the plaques stopped peeling and became thinner. The patients began to develop a pigmentation that was most accentuated in earlier irritated areas. At the end of 3 weeks, the psoriasis was nearly or completely healed in most cases but remains of very thick, therapy-resistent plaques could still be found on the elbows or lower legs. After 4–6 weeks, the trioxsalen-treated patients had completely healed with the exception of the patient with pustular psoriasis. This patient had improved but still had widespread plaques with infiltrated psoriasis. He had used methotrexate for 8 years and, during the bath therapy, his dose could be reduced from 15 to 7.5 mg a week. No other patient had had any internal medication during the treatment series. Four patients were forced to stop treatment with the Ingram regimen as irritation occurred.

Methoxsalen treatment was superior to the Ingram regimen in one of 8 cases, comparable in 4, and inferior in 3. One patient did not improve with either the Ingram or the methoxsalen treatment. Two patients became rather irritated after methoxsalen but healed rapidly. The other 2 in the group who healed were less irritated and the healing was slower. In 4 cases, the methoxsalen baths were discontinued after 4 weeks because of resistance to therapy.

Irritation

A generalized erythema occurred in half of the patients after 5–8 days of treatment. The irritation was most noticeable in the areas with thin skin and, in 2 cases, even blisters were seen around the axilla and between the breasts.

A 1–2 cm wide zone of inflamed skin often occurred around the psoriatic plaque but the lesion itself was usually unaffected. Sometimes similar, well-delineated and circumscribed irritated areas could be seen in normal-appearing skin. Three patients, who could tolerate 3–5 min of light treatment after 3–4 weeks of treatment with trioxsalen baths, developed sharply erythematous, 0.5 to 2 cm diameter plaques on the trunk and legs. The plaques increased in size during the following days, sometimes with small, thin-walled blisters on them. They all disappeared in 4–5 days despite continued treatment, leaving areas of increased pigmentation.

Two patients who, despite careful instructions, were out in the daylight for more than 5–10 min

Table IV. *Healing of patients treated with psoralen baths plus UV-light, vs. the Ingram regimen*

The figures indicate the following grading scale of healing: 0=healed, 1=nearly healed, 2=obvious healing, 3=some healing, 4=unchanged, 5=worsening

	Week											
Pat. no. ...	1	2	3	4	5	6	1	2	3	4	5	6
No previous UV-light treatment												
	Trioxsalen baths						*Ingram treatment*					
4	2	2	1	0	0	0	3	3	2	1	0	0
5	2	1	0	0	0	0	3	2	1	0	0	0
6	3	2	1	1	1	0	3	2	1	1	1	0
10	3	3	2	1	0	0	4	4	4	3	2	1
11	4	3	4	2	0	0	4	4	5[a]	–	–	–
13	3	2	0	0	0	0	3	2	0	0	0	0
15	4	3	1	0	0	0	4	2	0	0	0	0
19	4	3	1	0	0	0	3	3	2	1	0	0
20	4	3	2	2	1	0	4	5	5[a]	–	–	–
25	2	1	0	0	0	0	3	1	0	0	0	0
Mean	3.1	2.3	1.2	0.6	0.2	0.1	3.4	2.8	2.0	0.8[d]	0.4[d]	0.1[d]
Previous UV-light treatment												
	Trioxsalen baths						*Ingram treatment*					
1	3	3	2	1	0	0	4	3	2	1	0	0
8	4	2	1	0	0	0	3	2	1	0	0	0
9	3	2	1	0	0	0	3	3	2	1	0	0
12	3	2	2	1	0	0	4	5[a]	–	–	–	–
18	3	2	1	0	0	0	4	5[a]	–	–	–	–
22	3	3	3	2	1	0	4	3	3	2	2	1
24[b]	3	2	2	2	1	1	3	2	2	2	2	1
26[c]	3	2	1	1	0	0	–	–	–	–	–	–
Mean	3.1	2.3	1.7	0.9	0.3	0.1	3.6	3.3	2.0[d]	1.2[d]	0.8[d]	0.4[d]
No previous UV-light treatment												
	Methoxsalen baths						*Ingram treatment*					
2	4	3	2	1	0	0	4	3	2	1	0	0
3	2	1	0	0	0	0	3	1	0	0	0	0
7	4	4	3	3	–	–	4	3	2	1	0	0
14	4	4	4	3	–	–	4	4	4	3	–	–
16	3	2	1	0	0	0	3	2	2	1	0	0
17	3	2	1	1	0	0	3	2	1	1	0	0
21	4	4	4	4	–	–	3	2	1	0	0	0
23	4	4	4	4	–	–	4	4	3	1	0	0
Mean	3.5	3.0	2.4	2.0	–	–	3.5	2.6	1.9	1.0	–	–

[a] Treatment interrupted because of intolerance.
[b] Pustular psoriasis.
[c] Control Ingram treatment missing—excluded from the mean.
[d] The mean is not representative as interrupted patients have been excluded.

without skin protection during the first week of treatment developed severe swelling, redness, and blisters on the hands and lower legs. Women must be instructed to wear slacks and also to protect the ankles. Gloves should be worn during the first week. After the first treatment week, the danger of burns is over and patients can be outdoors. After the second week, moderate sunbathing can be allowed if the irritation has subsided; however, a certain amount of care is still advisable.

Two patients complained of itching after methoxsalen baths and light treatment. One patient developed contact dermatitis to both trioxsalen and methoxsalen after 5 days. He had been treated some weeks earlier with daily local application of 0.05% trioxsalen in an alcohol solution.

Pigmentation

Pigmentation began to develop in the patients during the first week. Those who had light treatment prior to the present experiment usually had a more even pigmentation than those with winter pallor. The pigmentation was uneven at 2 weeks but became even and dark at 4 weeks. The former spots of psoriasis then consisted of somewhat less pigmented areas surrounded by dark skin. If the treatment was continued 1–2 weeks after healing, this pigment variation evened out.

If too much light was given during the last part of the treatment series, a reteiform reddening occurred and was followed by peeling after a couple of days.

DISCUSSION

Psoriasis has been treated successfully for 20 years using the Ingram regimen. In Europe, it is considered one of the best methods.

The result of treatment with trioxsalen baths and dysprosium lamplight was found to be equal or superior to the Ingram method in all but one case. Healing results seem to be good as the earlier described treatments with psoralens and UV-light (10, 15, 19, 20, 23, 24, 25, 26).

The baths have some advantages over application of ointments or painting solutions containing psoralens. Light sensitisation with bathing is maximal immediately after the bath and greater than after application or lubrication. The light sensitisation that occurs is also not as long-lasting as that after painting or lubrication with psoralens.

Furthermore, with the bath treatment, two essential disadvantages with the previous types of local psoralen treatment have been overcome, the time-consuming pretreatment and the cosmetically unsatisfactory uneven pigmentation. The cosmetic end results with both lubrication and painting are most often less satisfactory because an extreme hyperpigmentation occurs in the treated areas, in contrast to the untreated skin (10, 24). Even when there was an initial hyperpigmentation in some areas with the trioxsalen bath treatment, it evened out during the continued treatment.

There may be an interplay of several factors which gives the strong immediate light sensitisation of the trioxsalen bath. Pathak et al. (16) found that 90 min after painting trioxsalen on shaved guinea pig skin, only 1 % of that substance had reached the living epidermal cells. Painting gives a high surface concentration of trioxsalen and this may act as a filter to UV-light. Not only does the bathing probably give a better penetration of trioxsalen, but the heating and hydration of the skin that occurs in the bath can also improve the penetration of UV-light and increase the sensitivity to it (14).

Peroral methoxsalen treatment and longwave UV-light has recently been used with good effect in psoriasis (15, 26). The most important objection to such treatment is that the toxic risks are not completely resolved (16), despite the fact that psoralens have been used for more than 25 years in treating vitiligo.

There are also other disadvantages with peroral methoxsalen treatment. About 30% of the patients receiving an adequate dose (20–50 mg) feel nausea 2 hours later. Antihistamines reduce this discomfort but not completely (15, 26). With long-term peroral methoxsalen treatment, some patients experience an irritation of the eyes when outdoors. Light sensitisation with peroral treatment is considerably weaker than with local treatment but this requires quite strong lamps or long irradiation times in order to obtain a therapeutic effect from a solarium. However, the patient can tolerate sunlight better and seldom becomes sunburned outdoors.

The strong light sensitisation of the skin with psoralen baths requires that the patient avoid light exposure during the hours immediately following the bath, especially during the first and second treatment weeks. Although a troublesome irritation occurred in sensitive skin areas in a couple of cases, the treatment never needed to be discontinued, and a certain amount of irritation is required in order to obtain rapid healing. The patient must be well-informed about this reaction. It is also very important to complete the treatment and that it is not stopped during the irritation stage as there is a high risk of an isomorphic reaction. Experiments with small skin areas, both in obviously healthy and also in psoriatic skin, have shown that single, irritating exposures can cause an isomorphic reaction, while a longer period of repeated exposures at the irritation threshold affords healing in psoriasis (5).

Three types of inexplicable irritation have occurred:

1. A strong initial irritation around the psoriasis plaques. 2. A similar irritation may occur in certain skin areas that appear healthy at the beginning of the treatment. 3. Small irritated areas, sometimes

with blisters, can develop later during the treatment, but they heal quickly. All of these types of irritation leave a more or less noticeable pigmentation. These reactions may be signs of subclinical psoriasis or areas where the body tries to combat the disease. The increased UV-light sensitivity may be due either to a greater binding of trioxsalen or an increased sensitivity to photochemotherapeutic treatment.

Contact dermatitis is an obvious risk, as one case has already shown. However, this patient had been painted with a strong trioxsalen solution some weeks before the baths and it is hoped that the very diluted bath treatment will not have the same sensitizing potential as painting.

Persistent light allergy after psoralen treatment has been predicted (3) and even prolonged swelling after long-term peroral psoralen treatment has been described (17). No such reactions have occurred in this investigation. Psoralen treatment has also been suspected of causing an increased frequency of skin cancer in man, although no case has yet been reported. Experimental animals exposed to local or intraperitoneally supplied psoralen and high doses of UV-light show a higher skin cancer frequency than animals exposed to UV irradiation alone. Although experients with local coal tar treatment have a much higher cancer risk than psoralen (7, 22), few clinicians hesitate to treat psoriatic patients with coal tar. The frequency of skin cancer in psoriatic patients is no higher than in a normal population (18). Thus, the risk of skin cancer connected with psoralen treatment does not appear great enough to warrant refraining from using this new treatment possibility.

It has been difficult to develop a UV-A light source of sufficient intensity for practical use in combination with psoralen activation. Recently, a new construction with black light tubes giving an intensity of 9 mW/cm^2 has been described (9, 15). These light tubes are not easily available at present and the dysprosium lamps give approximately the same UV-A output. The UV-A light intensity of these two sources is sufficient for psoralen activation using either baths or tablets. The use of dysprosium lamps is completely acceptable to the patients.

The erythema effect with psoralen and UV-A is about three times that of UV-B and both wavelengths help to heal the patient's psoriasis. Dysprosium lamps can be fitted with a glass filter only for UV-A emission. Recently Osram has developed a new lamp (Uvistra) that is similar to HQI-TS but having a higher emission in the UV range. We are now investigating this lamp in light therapy.

The results of this investigation show that treatment of psoriasis with trioxsalen and a dysprosium light solarium is practical and easily managed, giving a good cosmetic result, and avoids the risk of toxic side effects that can be connected with peroral treatment.

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