

# PHOTOCHEMOTHERAPY (PUVA) OF PSORIASIS IN SINGAPORE A PRELIMINARY STUDY

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## SYNOPSIS

**PUVA (Psoralen and Ultraviolet light A) used for the first time in Singapore was found to be highly effective in the treatment of 12 patients with chronic psoriasis having completely cleared all the lesions in 9 and achieving 70 to 75% clearance in the rest.**

**This confirms the reports from American and European studies involving more than three thousand patients extending over the past five years.**

**By combining PUVA with topical corticosteroids (Clobetasol propionate or Fluocinolone acetonide), a more rapid clearance of psoriatic lesions was observed than with PUVA alone. Even with our more pigmented skin, we found that the mean number of days for clearance, the number of UVA exposures and the average total Joules per square centimeter required for clearance were 16.2, 4.1, and 1.6 respectively. Compared with western results, ours are 7 to 50 time less than those employing PUVA alone and 5 to 15 time less than those who also employed the combined therapy of PUVA and topical corticosteroids.**

**The reason for this marked sensitivity to PUVA and topical corticosteroids in our subjects is not known and further evaluation is necessary. However the reduced UVA radiation time and total dosage will help to reduce the longterm potential immunological, degenerative and oncogenic hazards. Short-term side-effects were rare. Maintenance therapy was given to those in remission and 2 patients (16.6%) had mild relapse during the 2 months of followup.**

## INTRODUCTION

Psoriasis, a common skin disease of unknown aetiology, affects 1 to 3 per cent of world's population (Baker & Wilkinson 1972).

Though rarely a life-threatening disorder, this skin condition brings untold sufferings to its victims because of the chronicity, intractability, discomfort and disfigurement. Besides physical restriction, many have mental anguish and embarrassment from social ostracism and many illiterates give them the "lepra" reception. Financial loss through hospitalisation and medical care amounts to more than a billion dollars annually in the United States (Parrish et al., 1974) and thus a vigorous search was carried out to find a rapid cure for the disease in many parts of the world.

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In the past and even at the present moment, psoriasis has been successfully treated with the coal tar preparations, the dithranol, the corticosteroids and the cytotoxic drugs, either alone or in combination with conventional ultraviolet light (UVL) or sunlight. Many major drawbacks have now emerged with these treatment. Tar and dithranol are both messy, irritating, unpleasant, required hospitalisation and several weeks to clear and they are not easily acceptable to many patients. Topical corticosteroids, though highly effective initially, frequently relapse on withdrawal or become resistant with prolonged use. Moreover longterm treatment especially with occlusion, invariably produces numerous local or systemic side-effects, thus limiting its administration. Topical cytotoxics had been abandoned because of their toxic and allergic properties. Systemic cytotoxics such as methotrexate, hydroxyurea and azaribine are very effective anti-psyoriatic agents but they carry a very high risk of toxicity to the bone marrow, liver, kidney, gut, nervous tissue and the skin.

The discovery of PUVA (Psoralen + Ultraviolet A light) in the treatment of generalised and resistant psoriasis reported by Parrish and his American workers (1974) ushered in a new era of treatment which is not only extremely effective but is also very simple to use and most importantly, it is totally devoid of major side-effects.

The treatment known as Photochemotherapy, is based on the combined effect of an orally administered photosensitive substance, 8-methoxypsoralen and irradiation with longwave ultraviolet light (UVA 320-400 nm, maximum 365 nm). Combined action by these two, inhibits DNA-synthesis at the epidermis and upper dermis, thus reduces the psoriatic hyper-proliferative epithelial process and leads to a clinical remission. (Figure 1).

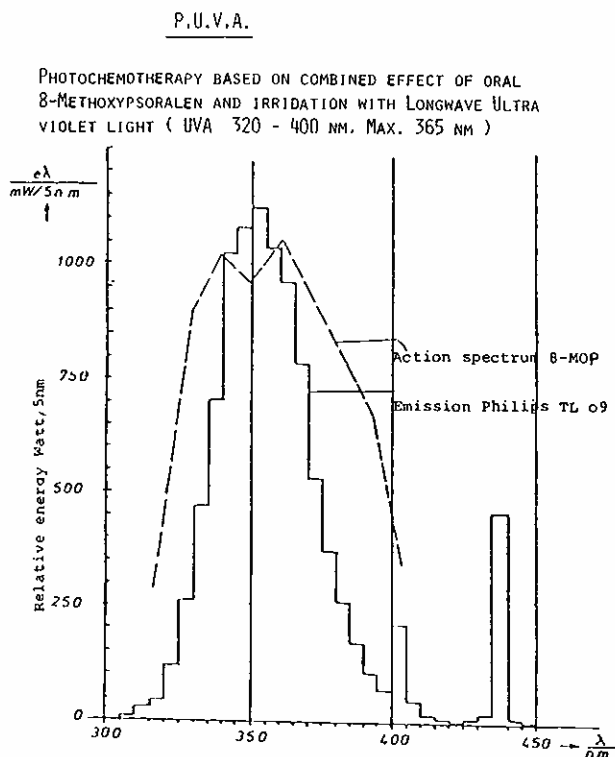


Figure 1. Action spectrum of oral 8-Methoxypsoralen and the UVA irradiation of Philips TL 09 light.

Numerous centres in United States and Europe have confirmed the efficacy of PUVA after treating several thousands of their patients with this combination (Wolff et al., 1976; Swanbeck et al., 1975; Melski et al., 1977; Roenigk et al., 1978; Lakshmi pathi et al., 1977; Morison et al., 1978; Nietzsche 1978; Siddiqui & Cormane 1978; Roenigk et al., 1979).

Though the methods used in each study were slightly different from one another, the results obtained ranged from 85 to 100% of the patients having cleared completely after an average of about 21 irradiations which delivered a mean UVA dose of 15.5 to 22 Joules/cm<sup>2</sup> and take an average of 9 to 16 weeks to clear. Maintenance irradiations given at weekly or fortnightly intervals resulted in a relapse rate of between 15 to 35%.

The great concern regarding the longterm cumulative effect of PUVA, especially the potential skin carcinogenesis and other degenerative changes, have prompted many studies to reduce the length and total dosage of UVA exposures without losing its therapeutic efficacy.

Thus PUVA has been combined with various topical steroids and other topical agents, or with oral administration of Retinoic acid derivative (Retinoid) and the results obtained were encouraging (Morison 1978; Gould 1978; Schmoll et al., 1978; Fritsch et al., 1978). Another method of treatment is the PUVA bath with or without systemic Psoralen or Retinoid (Hannuksela 1978; Fischer & Alsin 1976; Michalsson 1978).

In Singapore and indeed, in many parts of Asia, there is as yet, no reported experience of the using PUVA in the treatment of psoriasis. Perhaps this is due to the non-availability of the UVA-light system in these regions.

Recently, for the first time in Singapore, a UVA-light source was acquired (Skin-O-Clast) which made the study of local patients feasible. The aim of this preliminary study is to confirm the effectiveness of PUVA in Asian psoriatics; to assess whether the darker pigmented Asians require more treatment than the Caucasians (Melki et al., 1977); the efficacy of combination of PUVA with different steroid creams and with oral Retinoid, and finally, how the results compared with those already reported in the literature.

## MATERIALS AND METHODS

**PATIENTS:** 12 patients were admitted into the study after obtaining their informed consent. All had more than 40% of total body involvement of psoriasis. All had previous unsuccessful therapy with tar preparations, dithranol or various types of corticosteroids. Three even had previous oral Methotrexate therapy. Excluded were patients below the age of 15, pregnancy and those with heart, lung, liver and kidney diseases. Those with a history of light sensitivity or light-induced diseases and those with clinical findings of skin cancer, melanoma, aphakia, cataracts, connective tissue diseases and photodermatitis were also excluded. Systemic cytotoxic agents had to be discontinued one month prior to PUVA. Besides a full physical examination on the first visit, all the patients had full blood and urine examination.

## METHODS

**DRUG:** Oral psoralen used in this study was 8 methoxypsoralen (Paul B Elder) or Meladinine (Promedica). Ten

milligram of the table were taken 2 hours prior to irradiation on the first treatment and the dose was increased every 10 mg each subsequent treatment until a maximum of 40 mg or 0.6 mg/Kg was reached. When nausea developed, the dose was reduced.

**ULTRAVIOLET LIGHT SYSTEM:** The fluorescent lamp system used in this study was manufactured by ATMOS and called "SKIN-O-CLAST". This is a radiation unit on a fixed stand consisting 8 Philips TL 09-120cm-40W tubes. The spectral distribution was from 320 to 390 nm, with maximum UVA emission at 360 nm. At the distance of 30 cm, the radiation intensity was 2.2mW/sec/cm<sup>2</sup> and the UVA dose per minute was 0.132 Joules per cm<sup>2</sup>.

**RADIATION:** Two hours before treatment, the patients took the prescribed oral psoralen and wore protective Polaroid sunglasses which was worn 5 hours after UVA irradiation. During treatment, the patients usually stood nude 30 cm in front of the lights with UVA protective goggles. During half time, they were turned to expose the other half of the body to the light.

Initial light exposure time was 4 minutes and the exposure time was increased one minute per subsequent treatment with the maximum of 30 minutes. All were treated twice a week except for two. One with severe lesions was treated thrice a week and another, who stayed in Johore, was able to come for treatment once a week.

Between PUVA, they were allowed to use topical corticosteroids twice a day. Thus seven patients received topical Clobetasol propionate ointment (Dermovate); four had Fluocinolone acetonide cream (Synalar), and one patient was treated with Dermovate plus oral Retinoid (Tigasone) 30 mg a day.

Therapeutic response was assessed every visit with particular emphasis on the degree of scaling, palpability, erythema and the percentage of clearance was calculated when the lesions were compared with the original condition. Side-effects were noted, if any. Pruritus was treated with oral antihistamines. Scalp and nail lesions were treated symptomatically. Polytar shampoo and sometimes, corticosteroid scalp lotion were prescribed to the former.

**TABLE 2 RESULTS OF TREATMENT**

METHODS	No. Part cleared	Tt per wk	TO CLEAR LESION			REMARKS
			No. Exp.	No. days	Av. J/cm <sup>2</sup>	
PUVA+ SYNALAR CREAM	4/4 (100%)	Twice	5.5	22 days	2.4 J	1 relapse after 46 days. 3 in remission 50 — 60 days.
PUVA + DERMOVATE OINTMENT	7/7 (100%)	Twice (6) Once (1)	3.3	14.3 days	1.15 J	1 relapse after 38 days, Rest in remission for 25-45 days
PUVA + DERMOVATE RETINOID	+1/1 (100%)	Thrice	4.0	10 days	1.45 J	Rapid clearance
WHOLE SERIES	12/12 (100%)		4.1	16.5 days	1.60 J	2/12 (16.6%) relapsed 25 — 60 days

**MAINTENANCE SCHEDULE:** When the patients appeared to clear of psoriasis (ie. at least 95% improvement compared with the original extent of the disease), they were placed on maintenance schedule: one treatment a week for one month, then one treatment every 2 weeks for another month and then no treatment until new lesions appeared. The maintenance dose of methoxsalen and UVA (Joule/cm<sup>2</sup>) was the dose of the last treatment of clearing. If flare-up occurred, the dose and the exposure time were stepped up as for clearing.

If no improvement was recorded after 30 irradiations, a failure was recorded and other methods could be substituted.

## RESULTS

Table 1 shows the relevant medical data of the 12 patients in this study. All were chronic psoriatics not responding to conventional therapy.

**TABLE 1  
MEDICAL DATA OF THE 12 PATIENTS ON PUVA**

SEX: 7 females, 5 males.

AGE: Mean — 40.9 years, Range 25 to 68 years

RACE: Chinese 9, Indian 2, Malay 1.

DURATION OF DISEASE: Mean 10 years, Range 1 to 25 yrs

BODY INVOLVEMENT: Mean 65%, range 40 to 100%

TYPES OF PSORIASIS: Guttate 3, Plaque 4, Plaque and Guttate 4, Erythroderma 1.

PREVIOUS TREATMENT: Tar & steroid — 12, Methotrexate 3

As summarised in Table 2, all 12 patients (100%) were cleared of their psoriasis — three-quarter of them (9 patients) having 85 — 100% clearance while the remainder had 70 — 75% improvement of their original lesions. Guttate lesions cleared faster than large plaques and lesions on the trunk responded faster than those on the limbs. Patients treated with the combined PUVA and Dermovate ointment cleared more rapidly than PUVA with Synalar cream. The former required 3.3 light exposures averaging 1.15 Joules/cm<sup>2</sup> and an average of 14.3 days while the latter recorded an average of 5.5 light exposures, 2.4 Joules/cm<sup>2</sup> and the mean period of clearance of 22 days.

One patient with very severe and extensive psoriasis was treated with PUVA, Dermovate ointment and oral Retinoid 30 mg a day. She achieved complete clearance after 4 irradiations receiving only 1.6 Joules/cm<sup>2</sup> and was free from psoriasis on the 10th day (Figures 2A to 2F). Dramatic results were also observed with those treated with PUVA plus Dermovate (Figures 3A to Figure 3C) as well as those treated with the combined PUVA and

Synalar cream (Figures 4A to 4C). The patient with the weekly treatment responded slower and with partial improvement (Figures 5A to 5C) and the lesions relapsed when he failed to come for regular irradiation.

The series as a whole recorded 4.1 PUVA treatment for complete clearance, requiring 1.6 Joules per cm<sup>2</sup> and achieved this on the average of 16.5 days.

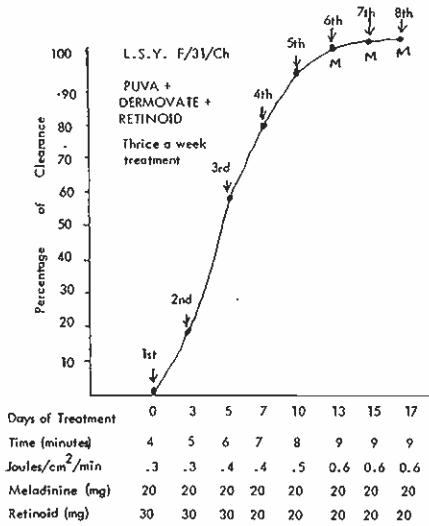


Figure 2A. Triple combination of PUVA, Dermovate and oral Retinoid therapy in one patient.

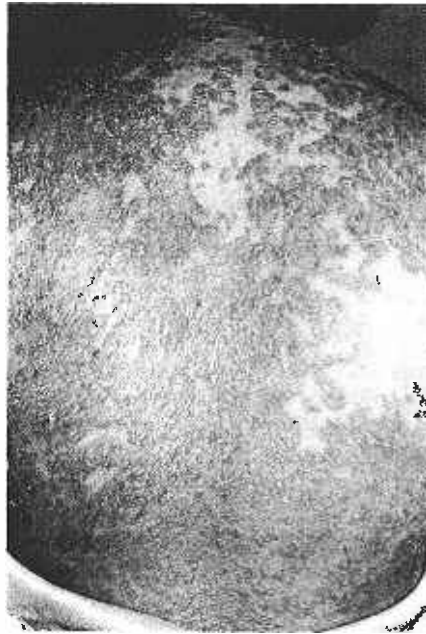


Figure 2B. Patient's back before treatment — note the extent and severity of the lesions.



Figure 2C. Patient's back after 3rd treatment showing 80% clearance.



Figure 2D: Patient's back after 6th treatment showing complete clearance.

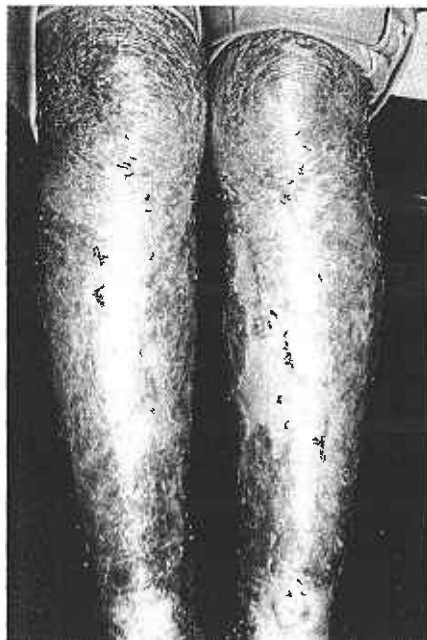


Figure 2E: Patient's legs before treatment.



Figure 2F: Patient's legs after 6th treatment, showing complete clearance.

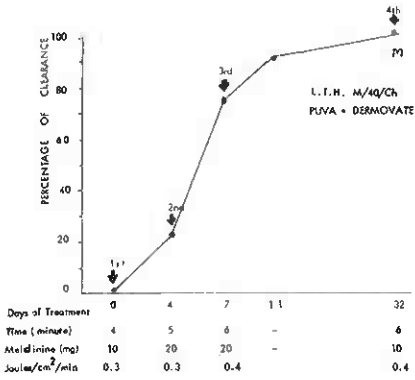


Figure 3A. Patient treated with PUVA and topical Dermovate ointment.



Figure 3B. Patient's legs before treatment — note erythrodermic plaques.

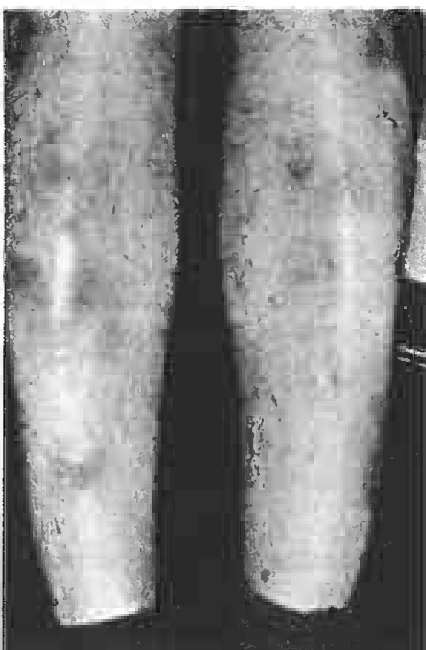


Figure 3C. Patient's legs after 3rd treatment — complete clearance.

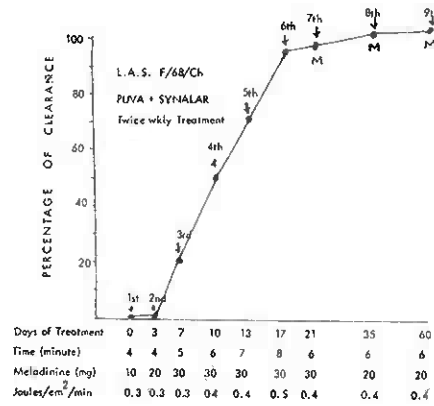


Figure 4A. Patient treated with PUVA and Synalar cream.



Figure 4B Patient's abdomen before treatment.



Figure 4C. Patient's abdomen after 5th treatment-note 70% clearance.

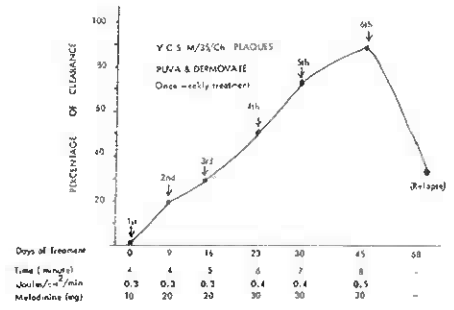


Figure 5A Patient on weekly treatment of PUVA and topical Dermovate ointment.

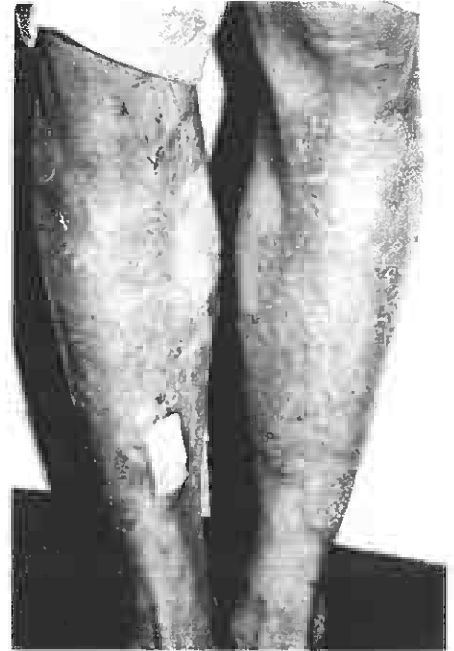


Figure 5B. Patient's legs before treatment.

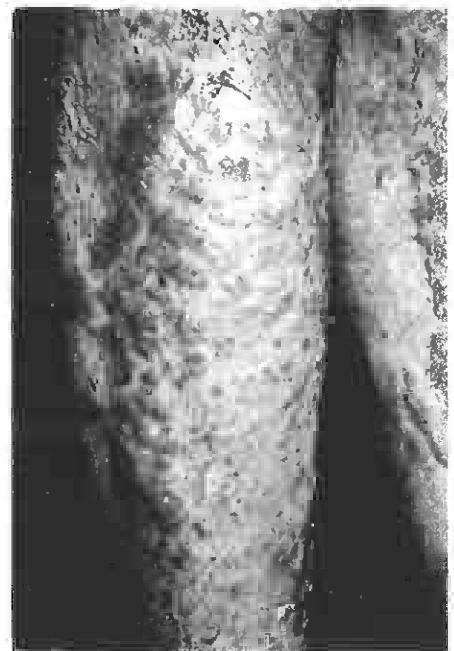


Figure 5C. Patient's legs after 5th treatment showing partial clearance of the plaque.

**SIDE-EFFECTS:** Five patients complained of mild pruritus and they responded to oral anti-histamines. Nausea in one patient subsided when the oral dose was reduced. One Sikh woman had temporary shedding of scalp hair after the 4th treatment. Marked exfoliation and desquamation was observed in one with psoriatic erythroderma whose lesions cleared 85% on the 46th day. Two had transient exacerbation during treatment, but cleared with subsequent irradiations. No blood or urinary abnormalities were detected during the PUVA therapy.

**FOLLOW UP:** As shown in Table 2, most patients were followed up for less than 2 months and 2 patients (16.6%) had mild relapse requiring a further course of clearance.

**DISCUSSION**

Since its first introduction in 1974 (Parrish et al., 1974), PUVA therapy for psoriasis has been extensively used throughout America and Europe with excellent to good results (Wolff et al., 1976; Melski et al., 1977; Swanbeck et al., 1975; Nietsche 1978; Michaelsson & Vahlquist 1978; Fritsch et al., 1978; Tronnier & Loehning 1974) Experience

with this treatment in Asia has not been documented and it is not known whether our Asian psoriatics will react to this new therapy as they generally have heavier pigmentation, lived in a more sunny climate and their environment is different from that of the westerners.

This study therefore is of great interest as it is perhaps the first study in this part of the world to provide some information regarding the response and reaction of our patients to this miraculous "magic light" which has been hailed as a major breakthrough in the treatment of psoriasis.

In this preliminary study of a small series of 12 patients, we confirm the effectiveness of PUVA treatment in Asians as all our patients (100%) had their skin lesions cleared within 2 weeks of therapy.

When comparing our results that those reported from America and Europe amongst the caucasians, we were surprised that we had achieved a faster rate of clearance and recovery with a smaller UVA dose and within a much shorter period of time in spite of the fact that we were using a small light unit with lower UVA intensity and that the Asian skin, being darker (Type 4) could require much more irradiations (Melski et al., 1977). Table 3 shows that

**ABLE 3 P.U.V.A. STUDIES**

METHODS	AUTHORS	% Patients cleared (No. Pat)	No. days to clear	No. PUVA exposure	Final clearance UVA Joules		Relapse
					Mean	Range	
. PUVA & Emollients	Parrish 1974 (US)	100% (21)	1 — 2 wks	12 — 18	18	9 — 24	10% in 6 mos
i. PUVA	Melaki 1977 (US)	88% (1308)	9 — 16 wks	17 — 21	15.5	10 — 21	35% in 18 mos
i. PUVA + Lubricant	Morison 1978 (US)	100% (18)	13.8 wks	23	17.0	7 — 36	17% in 4 mos
. PUVA + Dithranol	Morison 1978 (US)	95% (20)	8.5 wks	15	12.0	4 — 35	10% in 4 mos
. *PUVA + Steroid ("SYNALAR")	Morison 1978 (US)	100% (19)	8.4 wks	14	11.0	3 — 25	42% in 4 mos
i. PUVA + Tar	Morison 1978 (US)	84% (19)	9.8 wks	18	16.0	6 — 29	15% in 4 mos
* PUVA + "Dermovate"	Gould 1978 (UK)	100% (16)	1 — 4 wks	7.2			25% in 2 mos
i. PUVA + Retinoid	Fritsch 1978 (US)	100%	11 — 12 d	6.3	22.0	11 — 31	
i. PUVA only	Fritsch 1978 (US)	100%	15 — 27 d	14.3	93.2	13 — 173	
i.* PUVA + Tramcinolone	Schmoll 1978 (Germany)	100%	27 d	12.5	30.2	24 — 37	
. PUVA only	Schmoll 1978 (Germany)	100%	4 wks	16.2	74.1	40 — 108	
i.* PUVA + "Dermovate/Synalar"	Tay 1979 (Singapore)	100%	16.5 d	4.1	1.6	0.6 — 3.9	17% in 2 mos

= PUVA PLUS A CORTICOSTEROID

our patients with the majority using PUVA combined with topical Dermovate ointment, cleared rapidly in 16.5 days after undergoing 4.1 exposures and receiving only 1.6 Joules/cm<sup>2</sup>. This is four to fifty times less than the western series treating with PUVA alone or with lubricants (Melaki et al., 1978; Morison 1978; Schmoll 1978; Fritsch 1978) which required between 14 to 23 exposures to a higher intensity light source and requiring 15 to 93 Joules/cm<sup>2</sup>.

Even compared to 3 other series using PUVA plus topical corticosteroids (Morison 1977; Gould 1978; Schmoll 1978) the local result is still more favourable with 2 to 3 time less exposures and with much saving of the total Joules/cm<sup>2</sup> delivered (1.6 compared to between 11 and 30 Joules/cm<sup>2</sup>). Our patient with the triple combination of PUVA, topical Dermovate and Oral Retinoid showed an improvement in result than the study by Fritsch et al. 1978, who employed PUVA and Oral Retinoid. Although they found that this combination reduced the PUVA dosage and exposure time by more than 50%, our triple treatment cleared the lesions with only 1.45 Joules in 10 days after 4 exposures.

Although treatment with PUVA alone is extremely effective, simple, convenient, safe and acceptable to all patients, one of the main concern is the cumulative effect on longterm treatment. The potential hazards related to the total cumulative dose of UVA energy include oncogenic and degenerative changes of the skin and the eyes (Wolff et al., 1977; Fitzpatrick et al., 1977). The reported incidence of these however, is extremely rare, but efforts have been directed to diminish these possibilities by reducing exposure time and dosage such as the augmentation with oral Retinoid (retinoic acid derivative) or in combination with corticosteroids or indeed, combining PUVA with Corticosteroids, coal tar and cytotoxics. This form of multiple drugs treatment is similar to that being used for leukaemia as the combination will reduce the side-effects of each one of them, but the effects of antipsoriatic action are synergistically improved. Not only the combined therapy clears fast, but the relapse rate too is reduced when compared with single drug therapy. In Morison's study (1978), PUVA plus topical steroids appears to relapse more frequent than PUVA plus dithranol or PUVA with tar. However, in Gould's series using PUVA and Dermovate, Schmoll's series using PUVA and Triamcinolone cream and our series using PUVA plus Dermovate and/or synalar, the relapse rate of 17 to 25% was recorded and this is comparable to the rate found with PUVA alone. Certain patients not responsive to PUVA and topical steroids can be treated with addition of oral Retinoid which is in itself a potent antipsoriatic agent but with many side-effects (Viglioglia & Barclay, 1978; D. Soto 1978). Similarly, PUVA has been combined with Trioxsalen bath with good results (Hannuksela & Karvonen 1978). However, both these methods carries marked local or systemic side-effects and they should be reserved for patients who failed to respond to PUVA or who cannot use PUVA for other reasons.

Short-term side-effects were minimum as in other series but we had one with temporary shedding of hair, one with miliaria rubra and another with extensive skin exfoliation after receiving several treatment. These were transient. Pruritus usually required antihistamines. No systemic complications were noted. Thus it appears we have now a very effective, simple and safe treatment for psoriasis in this country—a long way from the ancient

treatment with the messy, dirty irritating crude coal tar which required weeks of hospitalisation and with uncertain results.

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