

## IS UVB TREATMENT OF PSORIASIS SAFE? A STUDY OF EXTENSIVELY UVB-TREATED PSORIASIS PATIENTS COMPARED WITH A MATCHED CONTROL GROUP

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**Abstract.** The aim of the study was to investigate whether or not extensively UVB-treated psoriatics ran a greater risk of developing skin cancer than did controls. The 85 most extensively UVB-treated psoriasis patients during recent decades have been investigated with regard to premalignant and malignant skin lesions and compared with a population matched for age, sex, and geographic region. The prevalence of persons who had or had had premalignant/malignant skin lesions was 5.9% ( $n=85$ ) in the psoriasis group, vs. 10.1% in the control group ( $n=338$ ). This difference is not statistically significant and the confidence limits are such that it is unlikely that the psoriasis patients treated in the past have an increased prevalence of premalignant and malignant skin lesions. A multiple regression analysis has been conducted among the controls, showing a correlation between premalignant/malignant skin changes and advanced age and outdoor occupations. No such correlation was found for the factors: sex, skin type, or travel to southern latitudes.

**Key words:** UVB, Safety; Psoriasis; Risk factors

UVB treatment for skin diseases has a long tradition in Scandinavia. It started with Niels Finsen who received the Nobel price in medicine in 1903 for introducing UV treatment of lupus vulgaris. In the city of Gothenburg UVB treatment for psoriasis has been used for several decades. In our clinic, which is the only one for dermatology in the city, we have accurate records of UVB treatments for more than 20 years. During this period mainly carbon arc (but lately only fluorescent sunlamps) have been used and, generally speaking, minimal erythema doses have been given. Both these types of treatment lamp emit mainly UVB and UVA radiation.

The development of PUVA therapy gave us a more effective treatment. At that time, controlled studies on the effectiveness of UVB treatment for psoriasis also started, although the treatment had been in use for many decades (2, 4, 7, 9, 14). The discussion about carcinogenic effect of PUVA

treatment started practically at the same time as the new treatment was introduced. Later on, UVB treatment was also discussed with respect to carcinogenicity, although we have known for many years that sunlight is the major carcinogenic factor with regard to squamous cell skin cancer and most probably some types of malignant melanoma (1, 13). Even in Sweden sunlight is the dominant cause of skin cancer (11).

We know that the induction period for skin cancer in the human is a long one. Studies on humans therefore should be based on a material that has received a relatively well-defined quality and amount of UVB irradiation for several years and preferably also include premalignancies. In the present study we have compared the prevalence of patients who had or had had premalignancies and malignancies in the skin among the most frequently treated psoriatic patients during recent decades, contrasted with a control population matched for sex, age, and geographical residence.

### MATERIAL AND METHODS

Psoriasis patients who had received more than 100 UVB treatments during a long period were selected for the present investigation. Of the 120 patients who fulfilled this criterion, 85 could take part in the present study. The rest had either moved from Gothenburg, died, or otherwise been impossible to get in contact with. None had died of a skin malignancy.

The control population was extracted from the city's official birth and address register. The control population was matched for sex and age. For every psoriasis patient, 6 controls were selected, giving 510 altogether. 338 showed up after two calls. Of the remaining 172, 21 had moved from the city, 54 did not wish to come, 33 could not come due to illness, etc. We have no information about the other 64 persons. Of the 87 we got in contact with but who did not wish to come to the investigation, none had a history of skin cancer. Those persons who showed up at the first call were compared with those who showed up at

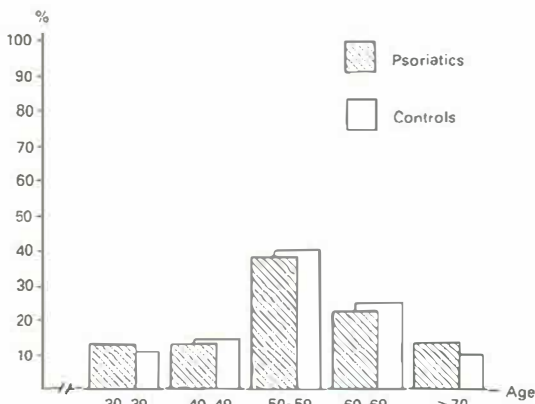


Fig. 1. Diagram showing relative distribution of psoriasis patients and controls in different age groups.

the second call, and with those who did not come at all, with regard to age, sex, and occupation. No relevant differences were found between these groups.

Both the psoriasis patients and the controls were investigated in the same way. All individuals were investigated by the same doctor. An ocular inspection of the whole body surface was made, to look for premalignant and malignant lesions. Suspected lesions were biopsied for verification. For every psoriasis patient and randomly every sixth control, a punch biopsy on the buttocks and trunk was carried out in order to evaluate the degree of actinic elastosis. Both the psoriatics and the controls were questioned about sunbathing habits, tolerance to sunlight, history of skin cancer or other diseases, and type of occupation.

### RESULTS

The age distributions for both groups are given in Fig. 1. There were 69% males in both groups. The

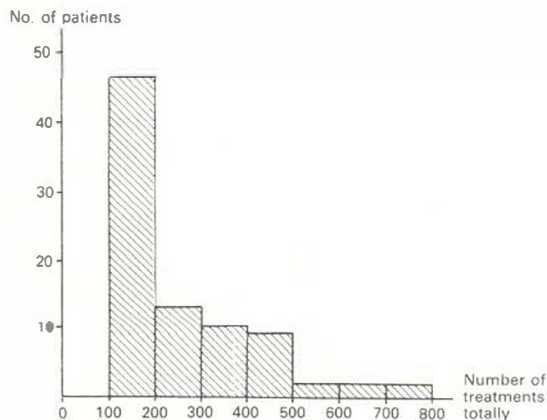


Fig. 2. Diagram showing total number of UVB treatments for the psoriasis patients.

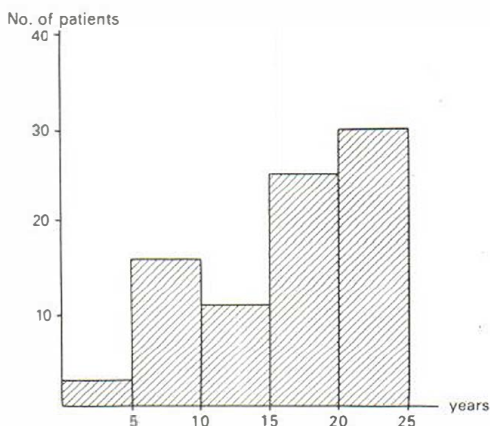


Fig. 3. Time between first UVB treatment and start of the present study: psoriasis patients.

total number of UVB treatments for the psoriatic patients is given in Fig. 2. The average number of UVB treatments was 249, ranging from 101 to 785. The intervals between the first UVB treatment of the psoriatic patients and the investigation are shown in Fig. 3. Apart from UVB treatment, most patients had at some occasion received other types of antipsoriatic treatment for short periods of time. Of the 85 patients, 69 had used anthraline, 80 tar, 80 steroids, and 30 had been treated with arsenic. The distribution of weeks spent in southern latitudes during the last 20 years for the two groups is shown in Fig. 4.

When selecting the control group, no matching was made with respect to occupation. However, only small differences with respect to outdoor vs. indoor work were found in the two groups, as seen

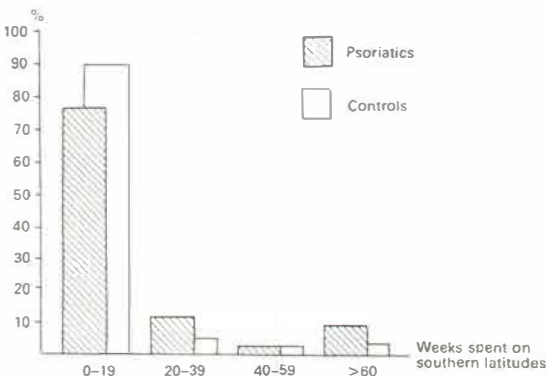


Fig. 4. Time (in weeks) spent in southern latitudes during the last 20 years: psoriasis patients and controls.

Table I. Relative frequency of indoor, mixed and outdoor occupations for psoriasis and control groups

Occupation	Psoriasis patients (%)	Controls (%)
Indoor	69.4	71.3
Mixed	20.0	16.9
Outdoor	10.6	11.8

in Table I. The same holds true for skin type (see Table II).

Regarding the prevalence of patients who had or had had premalignancies/malignancies in the skin, we found 4/85 actinic keratoses and 2/85 basalomas in the psoriasis group. One patient had both. No squamous cell skin cancer or melanoma was found. One patient had a history of a previous basaloma.

In the control group the prevalence as described above was 25/338 actinic keratoses, 7/338 basalomas, and 3/338 squamous cell skin cancers. One patient had both an actinic keratosis and a basaloma. As far as earlier premalignancies or malignancies in the skin in the control group are concerned, 2 persons had a history of previous basaloma, one a history of previous malignant melanoma, and one had a history of both basaloma and actinic keratosis. The patient with the previous melanoma was found at the investigation to have a basaloma.

All premalignant and malignant changes in both groups were seen on the face, except one actinic keratosis which was located on the hand in one of the control patients. The melanoma discovered before the investigation was located on the trunk.

The prevalence of persons who had or had had premalignant and malignant lesions in the psoriasis group is 5.9% and in the control group 10.1%, as shown in Fig. 5. The difference is not statistically

Table II. Relative frequency of skin types for psoriasis and control groups

Skin type	Psoriasis patients (%)	Controls (%)
I	2.4	7.7
II	61.2	63.6
III	35.3	27.2
IV	1.1	1.5

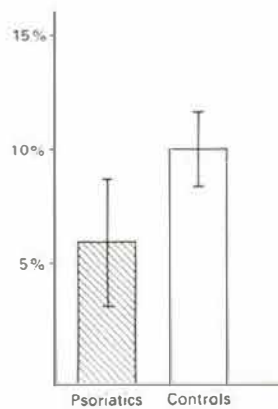


Fig. 5. Percentage of premalignancies and malignancies in the psoriasis and control groups. Standard errors indicated.

significant between the psoriatic group and the control group with respect to total number of premalignant and malignant lesions. The 95% confidence limits for the difference between the percentage of controls and psoriatics with premalignant and malignant lesions are 10.1% and -1.8%. If one assumes that none of the 172 in the control group who did not wish to attend had premalignant or malignant lesions, the percentage would still be 6.7%.

No sign of actinic elastosis was found in any of the biopsies from buttocks or trunk in any of the groups.

In the control group the number of individuals has been high enough to allow a study of the relationship between the prevalence of premalignant/malignant changes and some background factors. The importance of age is evident, as is seen in Table III. As far as skin type is concerned there seems to be no relationship with premalignant/malignant lesions. Sex seems to be of no significance in this respect either. The effect of occupation is significant, as is seen in table IV, but the outdoor workers are older than indoor workers. Crosstabelling reveals that the significance is not due to the higher age among outdoor workers. As far as travel to southern latitudes is concerned, there is a tendency to decreasing prevalence among people who travel a lot, but those who travel the most are the youngest. Using multiple regression analysis, a correlation was found between the factors age and outdoor work with the prevalence of premalignant and malignant lesions. No such correlation was

Table III. Table showing age distribution in the control group with premalignancies/malignancies indicated

	30-39	40-49	50-59	60-69	70-79	>80	Total
Healthy controls							
No.	35	48	118	77	20	6	304
%	94.6	100.0	87.4	92.8	76.9	66.7	
Controls with premalignant/ malignant changes							
No.	2	0	17	6	6	3	34
%	5.4	0.0	12.6	7.2	23.1	33.3	
Total	37	48	135	83	26	9	338

found for the factors sex, skin type or travel to southern latitudes.

According to the Swedish Cancer Registry the expected number of melanomas and non-melanoma skin cancers is 1.3, as computed from the average incidence figures for 1965-73. In the Swedish Cancer Registry, basalionas are generally not reported, i.e. the figure 1.3 stands for the combined sum of melanomas and squamous cell skin cancers.

#### DISCUSSION

It is well documented that UVB is an important etiological factor for skin malignancies (1, 10, 11, 13). It is therefore evident that UVB treatment of psoriasis increases the risk of cutaneous malignancies. However, this statement in itself is not relevant. One has to get a quantitative comparison between the risk of the treatment, sun exposure in daily life, and other hazards, in order to evaluate the significance of the increased risk.

The city of Gothenburg is situated at a latitude of 58° N and the inhabitants of the city get a relatively small amount of UVB radiation, compared with people in Australia, USA, and southern Europe, for example. This, together with the fact that we, in our clinic, have records of UVB-treated patients extending more than 20 years back, makes it possible to get an idea of the magnitude of the risk involved in UVB treatment.

The most extensively UVB-treated psoriasis patients during recent decades have been investigated. The time from the first treatment is, for the majority of patients, more than 15 years. We do not know the exact induction time for skin malignancies. As in the present study we have included premalignancies as well, the data obtained are more

relevant to the problem of the present study than if only malignancies had been registered. Accurate records have been kept as far as number of treatments and light sources are concerned. However, the total UV dose is not expressed in terms of definable energy units, but in minimal erythema exposures. This could be even more relevant as, in a sense, it compensates for differences in skin pigmentation.

The trend may be to give higher annual UVB doses in psoriasis treatment now than earlier. However, even by today's standards the typical psoriasis patient has to be on UVB treatment for 5-10 years to reach the average level of treatments recorded in this study. The annual dosage received nowadays lies somewhere in the region of outdoor work (8).

Most patients have had many other forms of antipsoriatic treatment, some of which are also suspected to be carcinogenic. A substantial number of

Table IV. Table showing occupations in the control group and with premalignancies/malignancies indicated

	Indoor/ outdoor	Indoor	Outdoor	Total
Healthy controls				
No.	51	223	30	304
%	89.5	92.5	75.0	
Controls with pre-malignant/ malignant lesions				
No.	6	18	10	34
%	10.5	7.5	25.0	
Total	57	241	40	338

the psoriasis patients have also received short-term arsenic treatment. The psoriasis patients in this study have made many trips to southern latitudes in order to treat their skin disease with climate therapy. Thus, the psoriasis patients in this study have probably been more exposed to other known or suspected carcinogenic factors than have the control group. To be able to evaluate the results it is essential to have a properly designed control group. Merely comparing with a cancer register may introduce a systematic error hard to evaluate.

In the control group 3 malignancies of squamous cell type were found and one patient had earlier had a melanoma. On the basis of Swedish Cancer Registry data we have calculated the accumulated expected number of squamous cell skin cancers and melanomas in the control group and obtained a value of 1.3. This should be compared with the 4 cases observed. However, it is important to keep in mind that we have calculated the expected number of average incidence figures during the period 1965-73, and that these figures show an increasing tendency. This means that the expected figure might be higher than 1.3. Still, it seems likely that especially with regard to squamous cell skin cancers, national registries give an underestimation of the incidence. Even such a reliable cancer register as the Swedish one cannot be used as a control in an investigation of this type. It is therefore important that the psoriasis group and the controls be examined by the same doctor in a similar manner. The two groups have furthermore been matched with regard to sex, age, and geographical residence. It has not been possible to match skin type and occupation actively, but there seems to be no difference in this respect between the two groups. There is a possibility that psoriasis patients are more resistant to skin malignancies than are other people. However, there are no data proving such a difference, although it has been suggested (5, 6).

In this study the difference between the prevalence of subjects who had or had had premalignant and malignant skin lesions in the psoriasis and control group is not statistically significant. Furthermore, the confidence limits are such that it is unlikely that the psoriatics have an increased prevalence of premalignancies and malignancies in the skin in spite of extensive UVB treatment for many years.

In the control group we have looked at the various 'risk factors' for the development of skin

cancer such as advanced age, light-sensitive skin type, type of occupation, and travel to southern latitudes. Studying the factors one at a time reveals that advanced age is an obvious risk factor. Skin type does not seem to be of any significance in this study, nor is sex of any significance in this respect. Outdoor workers seem to be at greater risk, but then they are older than indoor workers. As far as travel is concerned, there is a tendency to decreasing prevalence with more travel to the south, but the people who travel most are the youngest. Both crosstabelling and multiple regression analysis reveal that the pattern of advanced age and outdoor occupation as risk factors persists. According to the Swedish Cancer Registry, the incidence of non-melanoma malignant skin tumours (mainly squamous cell skin cancers) is about 2.6 times as high in farmers as in workers in the metal and engineering industry (12). No such difference is present for malignant melanoma. Skin type, sex, and travel to southern latitudes do not seem to be important, according to the present study. Regarding skin type, however, it is conceivable that people with light-sensitive skin type do not stay as many hours per day in the sun as others do, as they burn more easily.

A comparison was made in an earlier study between the amount of UVB received in psoriasis treatment and various outdoor vocational activities. The results indicate that the therapeutic doses are not appreciably higher than may be received by active sunbathing for the same period during the summer months in Sweden (3).

A study is in progress to compare the erythema-producing UVB doses received in indoor and outdoor work. The results indicate substantial differences. It might be that travel to southern latitudes and UVB treatment add only a small percentage of the total UVB energy received among people working outdoors (8).

In both the psoriatic group and the control group all premalignant and malignant lesions were on sun-exposed areas. As the hands and feet receive the highest UVB exposure in daily life and most often are not affected by psoriasis, one may shield these areas during UVB therapy.

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