

Indications of a Considerable Decrease in the Death Rate in Mycosis Fungoides by PUVA Treatment

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PUVA therapy has its roots in ancient India and Egypt and began to come into general use in the highly developed countries in the middle of the 1970's (1). The first reports of PUVA treatment of mycosis fungoides were published in 1976 (2); these were followed by several other studies in the two following years (3-7). Some of the early work on PUVA therapy was carried out in Sweden (8, 9), and the modality was in general use in most major clinics by 1977.

The dramatic effect on mycosis fungoides of PUVA therapy is well known, but whether the death rate is influenced is not known. For ethical reasons no controlled clinical studies have been performed.

Sweden is a highly organized country with reliable death statistics at least for diseases as conspicuous as mycosis fungoides. The purpose of the present study was to provide data on the death rate in mycosis fungoides in Sweden from 1961 to 1990, which we think is relevant to the question whether PUVA treatment decreases the death rate in mycosis fungoides.

(Accepted May 24, 1994.)

Acta Derm Venereol (Stockh) 1994; 74: 465-466.

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MATERIAL AND METHODS

Annual reports of death causes have been published in Sweden since 1911. They are now published by the National Central Bureau of Statistics in Stockholm and are regarded as very reliable. The National Central Bureau of Statistics has on request sent us yearly death rate data for mycosis fungoides for the period 1961-1990.

The number of deaths per year of mycosis fungoides for the period 1961-1978 has been compared with the corresponding data for the period 1979-1990. Both a *t*-test and the Kolmogorov-Smirnov two-sample test have been used with the help of the data program Statgraphics (STCS). In order for us to obtain a better visualization of the data, smoothing out statistical variation, a moving average (7-year period) was used.

RESULTS

The data are given in Fig. 1. The average number of people dying from mycosis fungoides yearly between 1961 and 1978 is 7.33 and between 1979 and 1990 2.83. This difference is statistically significant ($p < 0.001$) both with the *t*-test and the non-parametric test.

DISCUSSION

Sweden has a population of about 8 million people and a well-developed dermatological service. The death statistics of dermatological diseases are regarded as very reliable. Before 1977-1978 mycosis fungoides was mainly treated with radio-

therapy in the tumor stage. When PUVA was introduced, the patients were treated at a very early stage of the disease. Many patients had very long remissions. Radiotherapy has then been used only for tumors appearing in spite of PUVA treatment. Our experience of the clinical effect of PUVA therapy on mycosis fungoides is in accordance with earlier reports (2, 7). The quality of life of the patients has certainly increased.

In the period 15 to 20 years before the introduction of PUVA treatment for mycosis fungoides, the death rate seems to have been constant, with only statistical fluctuations. We have no reason to believe that the incidence of mycosis fungoides has changed. The death rate dropped significantly, however, after the introduction of PUVA treatment towards the end of the 1970's. After then, the death rate seems to have remained constant again.

Could other factors than PUVA treatment have influenced the death rate? In Sweden electron beam therapy has not been used against mycosis fungoides. The efforts of the Scandinavian mycosis fungoides study group with combinations of cytostatic agents systemically (10) were simultaneous with the introduction of PUVA therapy. Retinoids have been used after 1984 in Sweden. The effect of retinoids on mycosis fungoides was studied considerably later (11). PUVA was introduced slightly before the drop in the death rate of mycosis fungoides and has since then been the dominating treatment for this disease in Sweden.

It is difficult to know how soon after the introduction of PUVA therapy in mycosis fungoides one could expect an effect on the death rate. We have chosen to regard the period till 1978 as the prePUVA era and from 1979 as the PUVA era in the treatment of mycosis fungoides. Both the average death rate per year and the smoothing out of the death rate curve indicate that the death rate has decreased by more than 50 percent after the introduction of PUVA therapy.

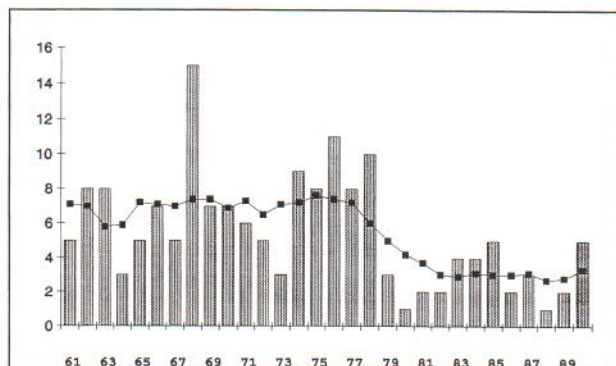


Fig. 1. The bars give the number of patients that died from mycosis fungoides in Sweden yearly during the period 1961-1990. The line shows the moving average for 7-year periods in the same time interval.

An apparent decrease in the death rate, as indicated by this study, may in fact only be a prolongation of life. It is thus possible that the apparent death rate starts to increase again. The present data, however, indicate that the prolongation of life for patients with mycosis fungoides by means of PUVA therapy is over 10 years in most cases.

What could be the mechanism of the decrease in death rate or prolongation of life in mycosis fungoides by PUVA therapy? The effect of PUVA is restricted to the upper few millimeters of the skin. In mycosis fungoides the malignant cells certainly have an epidermotropism. When they harbor in the skin they are also accessible to the effect of PUVA therapy. Treating early stages of mycosis fungoides with PUVA may thus contribute to a draining of malignant lymphocytes from the skin, decreasing the tumor burden. In a number of cases this may be enough to keep pace with the production of malignant cells.

Another possibility is that malignant lymphocytes are affected in the superficial capillaries of the skin by PUVA therapy. We find this explanation less likely, however. Already in 1974 we were concerned about the cytogenetic effects of PUVA treatment (8). Extensive follow-up did not however, show any significant damage to circulating lymphocytes (12).

Even if the data presented in this report do not prove PUVA treatment to be the cause of the decrease in death rate in mycosis fungoides in Sweden, they certainly give a strong indication of this. More work is now in progress to further strengthen this hypothesis.

It is our opinion that aggressive PUVA therapy in the very early stages of mycosis fungoides is recommendable. We might even decrease the death rate further by early treatment, before a reliable diagnosis has been established, even at the parapsoriasis stage.

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