CONCISE REPORT

# Seasonal variation of disease activity of systemic lupus erythematosus in Finland: a 1 year follow up study

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**Objectives:** To study the role of different seasons in the disease activity of patients with systemic lupus erythematosus (SLE). Additionally, to evaluate whether the outdoor behaviour during the summer or a photoprovocation test affects disease activity.

**Methods:** 33 patients with SLE were examined by a rheumatologist and a dermatologist at a university hospital in winter, spring, and summer. The activity of SLE was assessed by the ECLAM index. Their outdoor behaviour was recorded by a questionnaire during the summer. In the winter, 12 patients were photoprovoked by ultraviolet A and B radiation on a small skin area.

**Results:** The ECLAM scores were higher in spring and tended to be higher in summer than in winter ($p = 0.006$ and $p = 0.051$). This finding, as well as the outdoor behaviour, were independent of the patients' own impression of their photosensitivity. Overall, the sun protection actions were inadequate. The photoprovocation had no statistical effect on disease activity, but one patient had a violent exacerbation of SLE manifestations shortly after the photoprovocation.

**Conclusions:** In the northern climate SLE may be activated during the sunny season. Therefore, more effort should be focused on sun protection of patients with SLE.

It is widely known that sunlight can aggravate skin symptoms in systemic lupus erythematosus (SLE). However, the data on aggravation of systemic LE symptoms by ultraviolet (UV) radiation[1] are conflicting.[2–6] These data will be even more important if the preliminary good effect of UVA1 phototherapy leads to its more extended use in patients with SLE.[7]

One reason for this study was our previous observation of a violent exacerbation of systemic manifestations in a female patient with SLE shortly after photoprovocation on a small skin area.[8] Previously, such a photoprovocation test in patients with SLE has been regarded as safe.[9]

The modern western lifestyle favours outdoor activities. If a patient notices that sun exposure worsens the skin symptoms, he/she is motivated to use sun protection. However, systemic symptoms are more difficult to link with a specific lifestyle. A relevant question is whether all patients with SLE should strictly avoid sunlight, regardless of the photosensitivity of their skin.

In this study we prospectively investigated the disease activity of patients with SLE during different seasons and compared it with the patients' own impression of their photosensitivity and with their outdoor behaviour during three summer months. We also examined whether the outdoor behaviour is affected by the patients' own impression of the photosensitivity. Furthermore, the disease activity was determined after a photoprovocation test.

## METHODS

The study was conducted at the Departments of Internal Medicine and Dermatology, Tampere University Hospital. Of all the 52 patients with SLE of Finnish origin treated at the Department of Internal Medicine during 1996–98 and fulfilling at least four of the American College of Rheumatology (ACR) criteria for SLE,[10] 30 women and 3 men (63%) volunteered for the study after signing an informed consent. The study was approved by the ethics committee of the hospital.

The study protocol included three clinical and laboratory examinations in 1999 by a rheumatologist and a dermatologist: in January-February, May-early June, and August-early September. When major changes in drugs occurred during the study, the data of the subsequent visits were not evaluated. Of the 33 participating patients, 12 volunteered for a photoprovocation test. In this test, two small (5×8 cm) areas of intact upper back skin were irradiated in the winter with maximally two minimal erythemal doses of UVA (UVASUN 3000 equipment, emission spectrum 340–400 nm) and 1–2 minimal erythemal doses of UVB (Philips TL 20W/12 light bulbs, main emission spectrum 280–370 nm) on three consecutive days, as described previously.[8] The mean total doses of UVA and UVB were 283 J/cm$^2$ and 511 mJ/cm$^2$, respectively. An additional examination was performed for the photoprovoked patients 12–15 days after the photoprovocation and for another 12 non-photoprovoked patients 13–43 days after their first examination.

Blood cell counts, erythrocyte sedimentation rate (ESR), serum creatinine, creatinine clearance, 24 hour urinary protein excretion, urine analysis, creatine kinase, indirect Coombs test, components of complement (C3, C4, and $CH_{50}$), and antibodies to double stranded DNA antigens (anti-dsDNA) were examined on each visit. On the first visit, antinuclear antibodies, antibodies against extractable nuclear antigens, anticardiolipin antibodies, anti-$\beta_2$-glycoprotein antibodies, electrocardiography, and a chest *x* ray examination were also carried out.

The ECLAM (European Consensus Lupus Activity Measurement) score, a combination of 15 clinical and laboratory variables, was used as the disease activity index.[11] The clinical signs included articular, mucocutaneous, pleuropulmonary, intestinal, and neuropsychiatric manifestations, pericarditis, myositis, fever, and fatigue. Laboratory measures included tests of renal functions, blood cell counts, ESR, C3, C4, and $CH_{50}$. The theoretical maximal ECLAM score was 17.5, of which mucocutaneous manifestations included 1.5 points.

Each patient was asked to complete a previously introduced questionnaire[12] on their daily outdoor behaviour in June, July, and August 1999. The following questions were

**Abbreviations:** ECLAM, European Consensus Lupus Activity Measurement; ESR, erythrocyte sedimentation rate; SLE, systemic lupus erythematosus

**Table 1** Characteristics of patients with SLE

| | |
|---|---|
| *Patient characteristics* | |
| Male | 3 (9) |
| Female | 30 (91) |
| Indoor workers | 31 (94) |
| Age (years), mean (SD) | 47 (12) |
| Duration of SLE (years), mean (SD) | 17 (10) |
| *Previous or present clinical features* | |
| Haematological manifestations | 29 (88) |
| Musculoskeletal symptoms | 28 (85) |
| Skin/mucosal manifestations | 25 (76) |
| Peripheral vascular disease | 22 (67) |
| Cardiopulmonary disease | 12 (36) |
| Renal disease | 11 (33) |
| Neuropsychological manifestations | 10 (30) |
| Keratoconjunctivitis sicca | 6 (18) |
| *Antibodies present at the start of the study* | |
| ANA | 28 (85) |
| DNA | 16 (48) |
| ENA | 21 (64) |
| aCL | 26 (79) |
| Anti-$\beta_2$GPI | 2 (6) |
| *Treatment for SLE at the start of the study* | |
| Corticosteroids | 18 (55) |
| Chloroquine/hydroxychloroquine | 8 (24) |
| Cytotoxic drugs | 5 (15) |
| Ciclosporin | 1 (3) |
| No treatment | 12 (36) |

Results are given as No (%) unless otherwise stated.
ANA, antinuclear antibodies; ENA, extractable nuclear antigens; aCL, anticardiolipin antibodies; anti-$\beta_2$GPI, anti-$\beta_2$-glycoprotein I.
Skin/mucosal manifestations, includes butterfly rash/erythema (22 patients), photosensitivity (21 patients), alopecia/defluvium (14 patients), mucosal ulcers (11 patients), extended rash (7 patients), discoid lupus erythematosus (3 patients), subacute cutaneous lupus erythematosus (SCLE; 2 patients); peripheral vascular disease, includes also Raynaud's phenomenon; extractable nuclear antigens, antibodies against Ro/SSA (16 patients), La/SSB (6 patients), Sm (5 patients), RNP (3 patients), centromere (2 patients); cytotoxic drugs. includes azathioprine and methotrexate.

included: (*a*) How long did you spend outdoors today? (*b*) How long did you spend outdoors between 11 00 am and 3 00 pm? (*c*) Did you keep your arms covered? (*d*) Did you use a hat or a scarf? (*e*) Did you apply a sunscreen and, if you did, what was the sun protection factor?

For comparison between two groups or paired differences, the Mann-Whitney, Wilcoxon signed ranks, or sign test was used. $\chi^2$ Analysis was used for testing associations, and correlations were calculated by Spearman's rank correlation coefficient. The analyses were performed with SPSS 11.5 for Windows (SPSS Inc, Chicago, USA). A significance level of $p<0.05$ was considered significant.

## RESULTS

Table 1 gives the characteristics of the patients. Two patients discontinued the study after one or two visits. Their data were included in the analysis whenever possible. As the drug treatment was intensified in one photoprovoked patient, his ECLAM scores after the provocation were not analysed. In another patient, glucocorticosteroid treatment was withdrawn and her summer values were not analysed either.

Of the 52 eligible patients 19 did not volunteer for this study. Their age, sex, and previous SLE symptoms, such as skin, neurological, pulmonary, or cardiovascular symptoms, did not differ significantly from those of the participants.

The ECLAM scores were significantly higher in spring (median 2.0, range 0–6.5, $p = 0.006$) and tended to be higher in summer (median 2.0, range 0–6.5, $p = 0.051$) than in winter (median 1.5, range 0–4.0). The scores did not differ between spring and summer. In spring, 86% of the increases in the ECLAM scores were due to activation of renal disease, impaired values of components of complement, or blood counts; in summer 73%. The proportion of skin symptoms in the case of raised scores was only 6% in spring and 4% in summer. The use of chloroquine/hydroxychloroquine or a history of photosensitivity did not affect the ECLAM scores.

The ECLAM scores did not increase more in the UV provoked than in the non-provoked patients. However, in one male patient SLE deteriorated seriously 11 days after the photoprovocation, manifesting as high fever, muscular pain, peroneal paresis, butterfly rash, and mucous ulcers. In addition, leucopenia, reduced levels of C3, C4, and $CH_{50}$, and a raised level of anti-dsDNA antibodies were found.

Twenty nine of the 31 patients (94%) completing the study answered the questionnaire. Information was received for 87% of the summer days. The ECLAM scores in summer did not correlate with any aspects of the outdoor behaviour. Forty two per cent of the patients spent less than 1 hour outdoors during mid-day. A sunscreen was used by 20% and the arms or the head were covered by 21% and 30% of the patients, respectively, more often than 50% of the outdoor days.

Seven (27%) of the 26 patients used a sunscreen with a sun protection factor <15. The median total and daily consumption of sunscreen were 50 g and 0.6 g, respectively. There were no differences in any aspects of the outdoor behaviour between the patients who regarded their skin as photosensitive ($n = 12$) and those who did not ($n = 17$).

## DISCUSSION

The main observation of our study was the aggravation of the disease activity in patients with SLE during the sunny season. It is noteworthy that the activation of SLE was mostly due to non-cutaneous reasons and was measurable. However, seasonal worsening of the disease was not pronounced in any of the patients. The results of previous investigations on seasonal variation in SLE activity are contradictory.[2–6] Owing to the methodological differences and/or major differences in climate, exact comparisons between these studies are difficult.

We emphasise that the activation of SLE did not depend on the patients' opinion of their photosensitivity. This would imply that all patients with SLE should avoid sun exposure. Interestingly, activation of the disease was already found in spring with no further worsening during the summer. Unfortunately, we did not record the outdoor behaviour in spring. However, it is tempting to suggest that a non-UV exposed patient is vulnerable already to moderate UV exposure, whereas a somewhat UV hardened patient is protected against even more extensive UV exposure. The UV hardening is a well known concept in photodermatology and exploited in the treatment of various photodermatoses by phototherapy.[12] It may also explain the efficacy of the UVA1 phototherapy in patients with SLE.[7]

No serious side effects in LE patients have been reported from the photoprovocation protocol used in the present study.[9] As one of our previous patients with SLE[8] and in this study another patient had a violent exacerbation of SLE shortly after the photoprovocation, we question the safety of such a provocation in the systemic form of LE.

Our cohort of patients with SLE protected themselves less efficiently from the sun than patients with pure dermatological photodermatitis,[13] evaluated by a similar, although not validated, questionnaire in a recent study. The amount of sunscreen used was at least 10-fold less than recommended.[14] The sun protection of patients with SLE has also previously shown to be inadequate.[15] Interestingly, there was no difference in the outdoor behaviour of those patients who regarded themselves as photosensitive and those who did not, although this finding has to be interpreted with caution

owing to the small number of the patients in these two groups.

We conclude that in our cohort of patients with mild or moderate symptoms of SLE, the disease was activated during the sunny season most probably owing to UV exposure. Because the sun protection of the patients was inadequate, we should focus on better patient guidance.

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