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Soluble E-selectin correlates with disease activity in cyclosporin A-treated patients with atopic dermatitis

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Key words: adhesion molecules; soluble; atopic dermatitis; cyclosporin A treatment; ELAM-1; soluble; E-selectin; soluble.

Background: The expression of adhesion molecules on endothelial cells regulates leukocyte migration. The level of soluble adhesion molecules which are shed into the circulation is known to reflect the degree of inflammation, and this level can therefore be used as an indicator of disease activity.

The objective of this study was first to investigate the relationship between sE-selectin levels and disease activity parameters (scores of extent, severity, itch, and sleep) in atopic dermatitis (AD) patients, and second to determine the effect of therapy with an immunosuppressive drug (cyclosporin A) on sE-selectin levels.

Methods: Fourteen patients with severe AD and 41 healthy controls were studied. sE-selectin was measured by ELISA both 2 weeks before therapy with cyclosporin A and after 16 weeks of treatment.

Results: At baseline, the level of sE-selectin was significantly higher in patients with AD than in healthy control subjects ($P < 0.0001$). After treatment of AD with cyclosporin A, there was a significant reduction of the sE-selectin levels ($P < 0.0001$). In addition, changes in sE-selectin levels significantly correlated with changes in disease activity parameters such as severity ($P < 0.002$) and extent of disease ($P < 0.049$).

Conclusions: Soluble E-selectin is a new serologic marker in AD which reflects disease activity. Therefore, soluble E-selectin may be a useful parameter in the monitoring of this disease.

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Abbreviations: AD: atopic dermatitis; sE-selectin: soluble E-selectin; CsA: cyclosporin A; SEM: standard error of mean; ELISA: enzyme-linked immunosorbent assay; VCAM: vascular adhesion molecule; ICAM: intercellular adhesion molecule; ELAM: endothelial cell-leukocyte adhesion molecule; LEC-CAM: leukocyte-endothelial cell – cellular adhesion molecule.

Atopic dermatitis (AD) is an inflammatory skin disease which is characterized by a distinct pattern of serum parameters that reflect the ongoing inflammation. Besides the well-known elevation of total serum IgE, which correlates with the severity of the course of the disease (1), the measurement of soluble interleukin-2 receptor (sIL-2R), soluble intercellular adhesion molecule-1 (sICAM-1), eosinophilic cationic protein (ECP), and CD14 in the sera of patients with AD can be used to monitor the activity of the disease (2–4). E-selectin – the membrane-bound form of soluble E-selectin (sE-selectin) – is a cell-surface adhesion molecule which is expressed on endothelial cells during inflammatory processes. It is a member of the LEC-CAM adhesion molecule family and a glycoprotein of 115 kDa molecular mass (5, 6). E-selectin is involved in leukocyte recruitment into inflamed tissue and plays a crucial role in determining the degree of an inflammatory infiltrate (7). Therefore, its expression is restricted to sites of inflammation. Sialyl-Lewis^x and other carbohydrate ligands have been shown to mediate the initial attachment of polymorphonuclear granulocytes and monocytes to E-selectin in activated endothelium. Human memory T cells, which do not express sialyl-Lewis^x, can bind to E-selectin via the cutaneous lymphocyte antigen (CLA) (8–12). Cytokines such as interleukin (IL)-1, tumor necrosis factor- α , and bacterial endotoxin may, in addition to substance P, UVB irradiation, stimulation by haptens, and mast-cell degranulation, induce the expression of E-selectin in endothelial cells (6, 13–17). Thus, the expression of E-selectin on endothelial cells correlates well with endothelial cell activation. The distribution of E-selectin in inflammatory skin diseases, such as allergic contact dermatitis, AD, psoriasis, and several malignant skin tumors, has been investigated by immunohistologic methods (18, 19). Recombinant E-selectin acts as a neutrophil chemoattractant, suggesting functional activity also for the soluble form (20). sE-selectin – which is shed by cytokine-activated endothelial cells – has been studied recently by ELISA (21).

For evaluation of sE-selectin during a clinical trial with cyclosporin A (CsA) in patients with severe AD resistant to

conventional therapy, levels of sE-selectin were measured in the serum at the baseline and at the end of treatment, compared to healthy controls, and correlated with disease activity.

Material and methods

Patients and study design

Fourteen patients with severe AD who fulfilled the clinical and morphologic criteria as defined by Hanifin & Rajka (22), as well as the criteria for atopy according to Diepgen et al. (23), were included in the study. None of the patients had been treated with immunosuppressives, retinoids, interferon (IFN), phototherapy with Psoralen plus UVA (PUVA), and oral steroids for at least 4 weeks before receiving the first dose of CsA. Use of topical emollients, steroid preparations, and antihistamines was not restricted, but the frequency of their application was monitored. Patients received CsA either in the old formulation (Sandimmun) or in the new formulation (Neoral microemulsion). Sandimmun and Neoral were administered in identical gelatin capsules. The daily dose to be administered b.i.d. was fixed at 4–4.5 mg/kg body weight. The medication was to be taken together with meals to ensure good and stable absorption of CsA from the Sandimmun formulation. The treatment period lasted 16 weeks. Baseline laboratory values and blood pressure were well within normal range in all patients. Since the clinical outcome and the comparison of the old with the new CsA formulation (Neoral) has been published elsewhere (24) and showed no significant differences in clinical disease activity parameters after 16 weeks of treatment with either medication, it was not determined whether the patients received Sandimmun or Neoral with regard to their sE-selectin levels. During the study, one patient had to be excluded for violation of the study protocol.

The patient sera were compared with the sera of 41 consecutive, healthy blood donors (Table 1).

Table 1. Characteristics of patients and controls

Group	n	Sex	Age (years; median)	Age (years; range)	Multidisk sx1
Atopic dermatitis	14	9 M/5 F	35	20–64	10+/3–
Controls	41	27 M/14 F	51	26–71	17+/24–
+: positive; –: negative.					

The study was approved by the hospital ethics committee and was performed according to the guidelines of the Declaration of Helsinki. Informed consent was obtained from each patient.

Disease activity parameters

The efficacy of the CsA treatment in patients with AD and disease activity was determined by a scoring system consisting of four parameters at baseline and after 16 weeks of treatment (25).

Extent

The area affected by AD was estimated according to the rule of nines (maximum score value: 100).

Severity

Disease severity was assessed according to a total body disease activity score. Six clinical features (erythema, purulence, excoriation/crusting, dryness/scaling, cracking/fissuring, and lichenification) were graded at six defined body sites on a scale of 0 (none) to 3 (severe), resulting in a total body activity score (maximum: 108).

Itch and sleep

The symptoms of itching and sleep disturbance were rated on a scale of 0 (no itching, sleep not disturbed, respectively) to 10 (unbearable itching, no sleep at all).

Collection of serum samples, and determination of specific immunoglobulin E (Multidisk) and sE-selectin

After 10 ml of venous blood was drawn, serum was separated and stored at -20°C until use. The presence of specific IgE was screened by the CAP FEIA multidisk sx1 system (Pharmacia, Upjohn, Dübendorf, Switzerland).

sE-selectin was measured with a commercially available ELISA kit (R+D Systems, Minneapolis, MN, USA). According to the manufacturer, the ± 1 SD range for sE-selectin is 29–63 ng/ml.

Statistical evaluation

Clinical efficacy parameters (disease activity, extent of disease, itching, sleep quality) were compared with the sE-selectin levels with the Wilcoxon signed-rank test. Differences between patients with AD and controls were analyzed by the Mann-Whitney U-test. The correlation between the clinical scores and sE-selectin in the sera was calculated by

Table 2. Soluble E-selectin in sera of patients with atopic dermatitis and healthy controls

sE-selectin (ng/ml)	Atopic dermatitis (n=13)	Controls (n=41)
Mean*	95.1**	36.81
SEM	25.4	3.9
Median	87.2	36.6
Range	31.2–376.6	14.7–123.2
*Geometric mean; ** $P < 0.001$ as compared to normal controls.		

Spearman's rank correlation and tested for statistical significance.

Results

Elevated levels of sE-selectin in patients with AD

Patients with severe AD showed significantly elevated serum levels of sE-selectin before treatment as compared to healthy controls ($P < 0.0001$) (Table 2). Although the geometric mean of sE-selectin in patients with AD was significantly elevated when compared to normal controls, sE-selectin was well within the normal range in three of the 14 AD patients (Fig. 1). Two of these three patients had the intrinsic type of AD.

CsA treatment decreases sE-selectin levels in patients with AD

The level of sE-selectin in the sera of CsA-treated patients with AD was found to be significantly reduced after 16 weeks of treatment with CsA ($P < 0.0001$; Fig. 1). However, sE-selectin levels were still significantly elevated in CsA-treated patients with AD when compared with healthy controls ($P < 0.02$) (data not shown).

Correlation between sE-selectin levels and disease activity

Extent

After establishing therapy, we observed an initial rapid decrease of the average extent of the disease. At the end of week 8, the difference from baseline reached significance for all patients treated with CsA.

Severity

The average severity of disease at inclusion time was rather high. There was a rapid initial decrease after initiation of

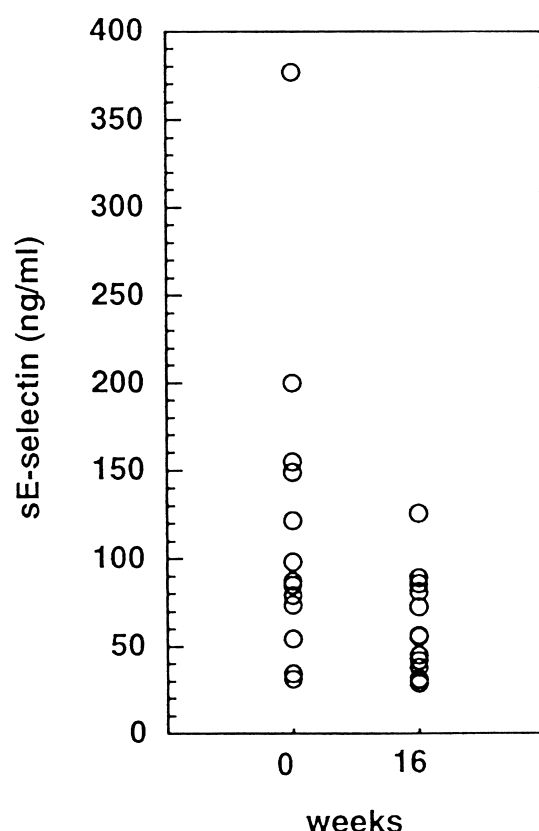


Figure 1. Levels of sE-selectin in patients with atopic dermatitis treated with CsA. sE-selectin levels were initially increased (mean: 95.1 ± 25.4 SEM ng/ml, $n=14$) and decreased during 16 weeks of CsA treatment (mean: 54.2 ± 8.1 SEM ng/ml, $n=13$). Difference was highly significant ($P<0.0001$).

therapy. The improvement of the severity score was statistically significant at week 8 of the treatment.

Itch

Average itch score was high at inclusion time and dropped during the first 2 weeks of treatment with continued improvement until the end of week 8. After week 8, average itch scores remained unchanged until the end of week 16.

Sleep

The sleep score decreased between inclusion and therapy initiation, as did the itch score. The sleep parameters improved clearly during the first 2 weeks of treatment. After week 8, the sleep score remained more or less similar until the end of week 16.

Twenty-eight assessments in 14 AD patients treated with CsA were examined. The clinical outcome in these patients has been published elsewhere (24). There was a significant correlation between changes in sE-selectin levels and the changes in scores for the severity ($P<0.002$) and extent of

disease ($P<0.049$). However, no significant correlation was found for itch and sleep scores (Fig. 2).

Discussion

Our findings indicate that sE-selectin is useful in monitoring AD. Clinical improvement in CsA-treated patients with AD was associated with a significant decrease in sE-selectin levels. In addition, we could demonstrate that there is a significant correlation between changes in sE-selectin levels and those in disease activity scores. To the best of our knowledge, this is the first study on sE-selectin levels in patients with AD treated with CsA.

In our opinion, AD is a heterogeneous disease with different subtypes characterized by distinct skin cytokine profiles, as we were able to demonstrate for the so-called extrinsic (allergic) and intrinsic (nonallergic) type (26). Indeed, two of the three AD patients with sE-selectin levels within the normal range (Fig. 1) were of the intrinsic type. In the pathogenesis, both type I and type IV mechanisms play an important role in the induction (acute) and maintenance (chronic) phase of the eczematous lesions. Whereas Th2 type cytokines such as IL-4, IL-5, and IL-13 play a crucial role in mediating local inflammation in the acute phase, Th1 type cytokines such as IL-2 and IFN- γ are required to support the ongoing inflammation in the chronic phase (27, 28). Elevated IgE levels are often observed in AD, but are not a prerequisite, indicating that not only IL-4 (and probably IL-13) but also other cytokines are relevant to this disease. The skin lesions in AD are infiltrated by eosinophils, demonstrating the importance of IL-5 – a key cytokine for eosinophil recruitment to sites of inflammation and an important factor in eosinophil survival (26).

The clinical assessment of inflammatory skin diseases is complicated not only by the individual variability between investigators but also by the numerous time-consuming scoring systems. Therefore, a simple serologic laboratory test might give a more precise basis for the monitoring of disease activity. It is well established that serum levels of sIL-2R, sCD14 (a marker for human monocytes), and ECP (a marker for eosinophil activation) correlate with the clinical activity of AD and can be used to monitor the disease (3, 4, 29, 30). However, neither of these parameters is specific for AD.

Recently, soluble adhesion molecules have been found to be markers of inflammation, too. In contrast to the already mentioned parameters, each soluble adhesion molecule may

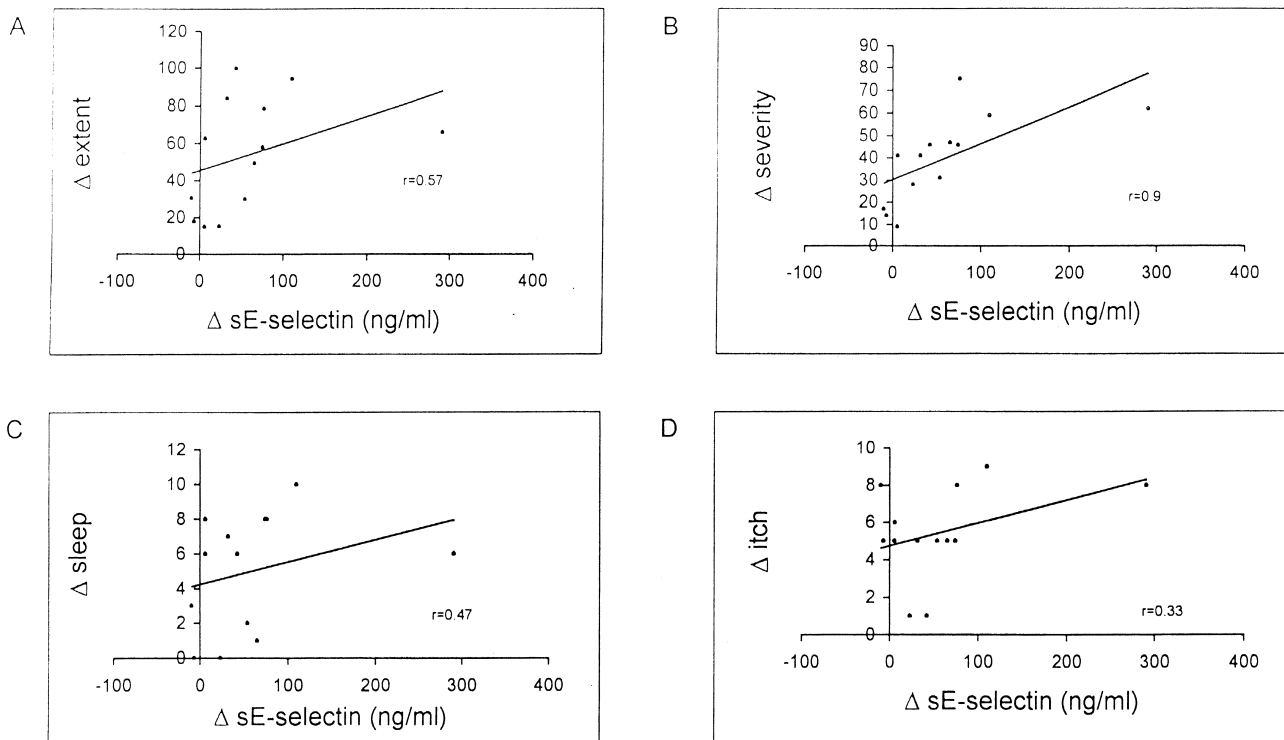


Figure 2. Correlation between changes in sE-selectin and disease activity scores. There was significant correlation between changes in sE-selectin levels and changes in score for severity ($P<0.002$) and extent of disease ($P<0.049$). However, no significant correlation was found for itch and sleep score.

reflect a particular component of the cellular infiltrate in a certain disease and may, therefore, be disease-specific. For example, sVCAM-1 shows an excellent correlation with the activity of systemic lupus erythematosus, whereas sE-selectin and sICAM-1 do not (31). Moreover, sE-selectin levels were significantly elevated in patients with discoid lupus erythematosus and widespread active cutaneous disease, suggesting different patterns of soluble adhesion molecules in different forms of lupus erythematosus correlating with the extent of cutaneous disease (32).

However, in other inflammatory skin diseases such as psoriasis and AD, data on sE-selectin as a novel serologic marker for endothelial cell activation are conflicting. Whereas Bonifati et al. (33) reported a direct correlation of sE-selectin and PASI scores in psoriasis patients, Czech et al. (34) were not able to demonstrate a significant correlation between the PASI scores and the levels of sE-selectin in 16 patients with psoriasis. This difference may be explained by different therapeutic approaches. The reduction of sE-selectin levels – reflecting only activated vascular endothelial cells – may be due to the anti-inflammatory effect of glucocorticosteroids, whereas the lack of reduction of sE-selectin in some psoriasis patients may be due to the fact that dithranol or tar treatment specifically reduces epidermal cell proliferation but has little effect on vascular

endothelial cells. This may also be the case in patients with AD treated with different regimens. Several studies demonstrated elevated levels of sE-selectin in AD, as compared to controls, and an association of the clinical improvement with the decrease in sE-selectin levels (34–37). In our study, a significant decrease of the sE-selectin levels could also be demonstrated. However, the levels of sE-selectin in patients with AD were still significantly higher after 16 weeks of CsA treatment than in healthy controls. In addition, according to Kowalick et al. (38), clinical improvement did not result in a significant drop of sE-selectin levels in AD patients after UVA1-treatment. Other possible explanations for these discrepancies may be differences in patients studied and different grading systems. In addition, sE-selectin levels may reflect only certain aspects of a given disease. As shown in Fig. 2, sE-selectin levels correlated with disease activity scores such as extent and severity, as manifested as erythema, papules, vesicles, and edema. However, and importantly enough, sE-selectin did not correlate with itch and sleep scores. Our findings are in agreement with a recent report which suggests that itching is reflected best by sICAM-1 levels (37).

In our study, we could demonstrate elevated sE-selectin levels in the sera of AD patients. Treatment of severe AD with CsA resulted in impressive improvements of the

patients' clinical condition already after 2–4 weeks of treatment (average dose of CsA was fixed at 4–4.5 mg/kg body weight). Moreover, treatment of AD with CsA was associated with a significant decrease of sE-selectin levels, and a significant correlation of the changes of the disease activity scores with the changes in the sE-selectin levels was found. Further studies should focus on the question of

whether sE-selectin, which seems to be a useful marker for monitoring disease activity in AD, can also serve as a marker for prognosis and prevention measures.

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References

1. Wüthrich B, Kopper E, Virchow C. IgE-Bestimmung bei Neurodermitis und anderen Dermatosen. *Hautarzt* 1973;**24**:381–386.
2. Wüthrich B, Joller-Jemelka H, Kägi MK. Levels of soluble ICAM-1 in atopic dermatitis. A new marker for monitoring the clinical activity? *Allergy* 1994;**50**:88–89.
3. Kägi MK, Joller-Jemelka H, Wüthrich B. Correlation of eosinophils, eosinophil cationic protein and soluble interleukin-2 receptor with the clinical activity of atopic dermatitis. *Dermatology* 1992;**185**:88–92.
4. Wüthrich B, Kägi MK, Joller-Jemelka H. Soluble CD14 but not interleukin-6 is a new marker for clinical activity in atopic dermatitis. *Arch Dermatol Res* 1992;**284**:339–342.
5. Siegelman MH, van der Rijn M, Weissmann IL. Mouse lymph node homing receptor cDNA clone encodes a glycoprotein revealing tandem interaction domains. *Science* 1989;**243**:1165–1172.
6. Bevilacqua MP, Pober JS, Mendrick DL, et al. Identification of an inducible endothelial-leucocyte adhesion molecule. *Proc Natl Acad Sci U S A* 1987;**84**:9238–9242.
7. Osborn L. Leucocyte adhesion to endothelium in inflammation. *Cell* 1990;**62**:3–6.
8. Philips ML, Nudelman E, Gaeta FCA, et al. ELAM-1 mediates cell adhesion by recognition of a carbohydrate ligand, sialyl-Le^x. *Science* 1990;**250**:1130–1132.
9. Polley MJ, Philips ML, Wayner E, et al. CD62 and endothelial cell-leucocyte adhesion molecule 1 (ELAM-1) recognize the same carbohydrate ligand, sialyl-Le^x. *Proc Natl Acad Sci U S A* 1991;**88**:6224–6228.
10. Picker LJ, Kishimoto TK, Smith CW, et al. ELAM-1 is an adhesion molecule for skin homing T cells. *Nature* 1991;**349**:796–798.
11. Shimizu Y, Shaw S, Graber N, et al. Activation-independent binding of human memory T-cells to adhesion molecule ELAM-1. *Nature* 1991;**349**:799–800.
12. Berg EL, Yoshino T, Rott LS, et al. The cutaneous lymphocyte antigen is a skin lymphocyte homing receptor for the vascular lectin endothelial cell-leucocyte adhesion molecule-1. *J Exp Med* 1991;**174**:1461–1466.
13. Messadi DV, Pober JS, Wheeler ME, et al. Induction of an activation antigen on post-capillary venular endothelium in human skin organ culture. *J Immunol* 1987;**13**:1557–1562.
14. Matis WL, Lavker RM, Murphy GF. Substance P induces the expression of an endothelial-leucocyte adhesion molecule by microvascular endothelium. *J Invest Dermatol* 1990;**94**:493–495.
15. Norris P, Poston RN, Thomas S, et al. The expression of endothelial leucocyte adhesion molecule-1 (ELAM-1), intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in experimental cutaneous inflammation: a comparison of ultraviolet B erythema and delayed hypersensitivity. *J Invest Dermatol* 1991;**96**:763–770.
16. Goebeler M, Meinardus-Hager G, Roth J, et al. Nickel chloride and cobalt chloride, two common contact sensitizers, directly induce expression of intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and endothelial leucocyte adhesion molecule-1 (ELAM-1) by endothelial cells. *J Invest Dermatol* 1993;**100**:759–765.
17. Klein LM, Lavker RM, Matis WL, et al. Degranulation of mast cells induces an endothelial antigen central to leucocyte adhesion. *Proc Natl Acad Sci U S A* 1990;**86**:8972–8976.
18. Rhode D, Schlüter-Wigger W, Mielke V, et al. Infiltration of both T cells and neutrophils in the skin is accompanied by the expression of endothelial leucocyte adhesion molecule-1 (ELAM-1): an immunohistochemical and ultrastructural study. *J Invest Dermatol* 1992;**98**:794–799.
19. Groves RW, Allen MH, Barker JN, et al. Endothelial leucocyte adhesion molecule-1 (ELAM-1) expression in cutaneous inflammation. *Br J Dermatol* 1991;**124**:117–123.
20. Lo SK, Lee S, Ramos RA, et al. ELAM-1 stimulates the adhesive activity of leucocyte integrin CR3 on human neutrophils. *J Exp Med* 1991;**173**:1493–1500.
21. Gearing AJ, Hemingway IK, Piggot R. Soluble forms of vascular adhesion molecules, E-selectin, ICAM-1 and VCAM-1: pathological significance. *Ann N Y Acad Sci* 1992;**667**:324–331.
22. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol (Stockh)* 1989;**69**:41–45.
23. Diepgen TL, Fartasch M, Hornstein OP. Evaluation and relevance of atopic basic and minor features in patients with atopic dermatitis and the general population. *Acta Derm Venereol Suppl (Stockh)* 1989;**144**:50–54.
24. Zurbriggen B, Wüthrich B, Cachelin AB, Wili PB, Kägi MK. Comparison of two galenical formulations of cyclosporin A in the treatment of severe atopic dermatitis. *Dermatology* 1999 (in press).
25. Swoden JM, Berth-Jones J, Ross JS, et al. A multicenter, double-blind, placebo-controlled crossover study to assess the efficacy and safety of cyclosporin A in adult patients with severe refractory atopic dermatitis. *Lancet* 1991;**338**:137–140.
26. Kägi MK, Wüthrich B, Montano E, et al. Differential cytokine profiles in peripheral blood lymphocyte supernatants and skin biopsies from patients with different forms of atopic dermatitis, psoriasis and normal individuals. *Int Arch Allergy Immunol* 1994;**103**:332–340.
27. Hamid Q, Boguinewicz M, Leung DY. Differential *in situ* cytokine gene expression in acute versus chronic atopic dermatitis. *J Clin Invest* 1994;**94**:870–876.
28. Grewe M, Walther S, Gyufko K, Czech W, Schöpf E, Krutmann J. Analysis of the cytokine pattern expressed *in situ* in inhalant allergen patch test reactions of atopic dermatitis patients. *J Invest Dermatol* 1995;**105**:407–410.
29. Kapp A, Czech W, Krutmann J, Schöpf E. Eosinophil cationic protein in sera of patients with atopic dermatitis. *J Am Acad Dermatol* 1991;**24**:555–558.
30. Wüthrich B, Kägi MK, Joller-Jemelka H, Helfenstein H, Grob PJ. Levels of soluble interleukin-2 receptors correlate with the severity of atopic dermatitis. *Dermatologica* 1990;**181**:92–97.

31. Spronk PE, Bootsma H, Huitema MG, Limburg PC, Kallenberg CGM. Level of soluble VCAM-1, soluble ICAM-1 and soluble E-selectin during disease exacerbation in patients with systemic lupus erythematosus (SLE): a long term prospective study. *Clin Exp Immunol* 1994;**97**:439–444.
32. Nyberg F, Acevedo F, Stephansson E. Different patterns of soluble adhesion molecules in systemic and cutaneous lupus erythematosus. *Exp Dermatol* 1997;**6**:230–235.
33. Bonifati C, Trento E, Carducci M, et al. Soluble E-selectin and soluble tumor necrosis factor receptor (60 kD) serum levels in patients with psoriasis. *Dermatology* 1995;**190**:128–131.
34. Czech W, Schöpf E, Kapp A. Soluble E-selectin in sera of patients with atopic dermatitis and psoriasis – correlation with disease activity. *Br J Dermatol* 1996;**134**:17–21.
35. Morita H, Kitano Y, Kawasaki N. Elevation of serum-soluble E-selectin in atopic dermatitis. *J Dermatol Sci* 1995;**10**:145–150.
36. Yamashita N, Kaneko S, Kouro O, Furue M, Yamamoto S, Sakane T. Soluble E-selectin as a marker of disease activity in atopic dermatitis. *J Allergy Clin Immunol* 1997;**99**:410–416.
37. Hirai S, Kageshita T, Kimura T, et al. Soluble intercellular adhesion molecule-1 and soluble E-selectin levels in patients with atopic dermatitis. *Br J Dermatol* 1996;**134**:657–661.
38. Kowalzik L, Kleinheintz A, Neuber K, Weichenthal M, Kohler F, Ring J. Elevated serum levels of soluble adhesion molecules ICAM-1 and ELAM-1 in patients with severe atopic eczema and influence of UVA1 treatment. *Dermatology* 1995;**190**:14–18.