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An immunological study in patients with seborrhoeic dermatitis

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Summary

The humoral and cellular immune-status was studied in 30 patients with seborrhoeic dermatititis. Increased frequencies of natural killer cells were found in 46% of patients. Furthermore, subnormal mitogen stimulation responses were demonstrated in 13 patients, whereas two individuals were found to have very high numbers of activated T lymphocytes in peripheral blood. Higher-than-normal total serum IgG and IgA was observed in 14 and 11 patients, respectively. For nine of 12 patients with skin lesions, dermal perivascular cell infiltrates were seen. The majority of the infiltrating cells reacted with anti-CD4 antibodies. HLA-DR-expressing keratinocytes were found in two biopsies. The study suggests that patients with seborrhoeic dermatitis may have depressed T-cell function. This could have a bearing on their susceptibility to the *Pityrosporum ovale*-associated dermatitis. The very high frequencies of activated T cells observed in the peripheral blood of two otherwise healthy seborrhoeic individuals suggests that intermittent systemic immune activation may occur.

Seborrhoeic dermatitis is a common skin disease.[1] It can be diagnosed by its characteristic red to yellow–brown lesions covered with greasy scales distributed in areas with a high number of sebaceous glands, such as the scalp, face and upper trunk.[1] There is an association between seborrhoeic dermatitis and the lipophilic yeast *Pityrosporum ovale* but its exact aetiological role is not known.[2] The yeast is a member of the normal cutaneous flora[3] but also the aetiological agent of pityriasis versicolor[4] and *Pityrosporum* folliculitis.[5] *P. ovale* can activate complement via the direct and alternative pathways.[6,7] This may play some part in the induction of inflammation. Serum antibodies against *P. ovale* have been found in normal individuals.[8–11] In seborrhoeic dermatitis, both normal[11,12] and high[13] serum antibody levels have been demonstrated. A cell-mediated immune reponse to *P.ovale* has been found in normal human adults using *P. ovale* extracts in lymphocyte-transformation studies.[14]

In the present investigation, the humoral and cellular immune status of patients with seborrhoeic dermatitis was analysed. Blood samples and skin biopsies, from lesions and normal skin, were studied.

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Methods

Characteristics of the patients

Thirty patients, 24 males and six females, with a mean age of 46 years (range 19–81), with seborrhoeic dermatitis were included in the study (Table 1). A typical clinical picture was seen in all patients and all had positive cultures of *P. ovale* from the chest. No patient had received systemic antifungal drugs. Concomitant diseases were seen in six patients; ankylosing spondylitis (Patient 9), diabetes mellitus (Patient 29), rosacea (Patient 5), *Pityrosporum* folliculitis (Patients 25 and 29) and pityriasis versicolor (Patients 1 and 23). Besides the 30 patients, seven age- (range 64–83 years) and sex-matched healthy individuals were included as controls for the oldest patients in the study population.

Lymphocyte surface markers on peripheral blood lymphocytes

The surface expression of antigens on peripheral blood lymphocytes was determined by quantitative two-colour analysis with a FACS-star (Becton Dickinson, Sunnyvale, CA, USA). Ten-thousand events were counted in each case. Forward and right-angle scatter gates were set on lymphocytes, excluding other leucocytes, erythrocytes and debris. Analysis was performed on unseparated heparinized blood using fluorescein isothiocyanate (FITC) or R-Phycoerythrin-conjugated monoclonal antibodies (see Table 2). There were no clinical signs of acute infection at the time of blood sampling.

Table 1. Characteristics of patients with seborrhoeic dermatitis

Patient	Sex	Age	Years of duration	Severity score*		Skin biopsies obtained
				scalp	skin	
1	M	30	<5	3	3	x
2	M	76	6–10	2	2	x
3	M	35	6–10	3	2	x
4	F	55	6–10	3	2	x
5	M	65	6–10	3	2	x
6	M	75	6–10	2	3	x
7	F	67	6–10	3	2	
8	M	81	6–10	2	2	x
9	M	48	6–10	3	2	x
10	M	40	<5	3	3	
11	F	42	>10	3	2	
12	M	41	6–10	3	3	x
13	M	21	<5	3	3	
14	M	64	>10	3	3	
15	F	21	<5	1	2	
16	F	26	<5	2	2	
17	M	63	>10	2	2	x
18	M	54	>10	3	2	x
19	M	27	6–10	3	1	
20	M	48	<5	2	3	
21	M	38	>10	3	3	
22	M	30	>10	2	3	
23	M	50	<5	3	3	
24	F	38	<5	3	3	
25	M	37	<5	3	3	
26	M	19	<5	3	3	x
27	M	36	<5	2	1	
28	M	30	>10	2	2	
29	M	44	6–10	2	2	
30	M	66	6–10	3	2	

* 0=no lesions; 1=mild (erythema); 2=moderate (erythema+scaling+papules); 3=severe (erythema+scaling+papules+yellow-brown crusts).

Table 2. Monoclonal antibodies used in the study

Antibody* (cluster determinant)		
Peripheral blood	Skin	Cellular distribution
Leu 4 (CD3)	Leu-4	Pan T-cells
Leu-2a (CD8)	Leu-2a	'Suppressor/cytotoxic' T-cells
Leu-3a (CD4)	Leu-3a	'Helper/inducer' T-cells
Leu-7 (CD57)		Natural killer-cells, T- and B-cells
Leu-11 (CD16)		Fc IgG receptor
Leu-12 (CD19)		B-cells
Leu-6 (CD1a)	Leu-6	Langerhans' cell, thymocytes
HLA-DR		HLA-DR antigens
Leu-10		HLA-DQ antigens

* Becton Dickinson, CA, USA.

The normal ranges for CD3, CD4, CD8 and CD19 levels and CD4/CD8 ratios were determined in a recent multicentre study including 319 healthy individuals up to the age of 70 years using the same monoclonal antibodies as in the present study.[15] Normal values for DR expressing CD4 and CD8 cells were obtained from the clinical immunology laboratory, University of Gothenburg, and the CD57/CD16 levels were compared with previously published levels.[16]

Lymphocyte stimulation by mitogens

Mononuclear cells were prepared from heparinized venous blood by centrifugation on Ficoll–sodium-metrizoate lymphoprep (Nyegard, Denmark). The cells were diluted to a concentration of 5×10^5 cells/ml in Iscoves modified Dulbecco's medium (Gibco Europe, Paisley, UK), supplemented with 10% pooled heat-inactivated human AB serum, 2-mmol/l L-glutamine and 100-μg/ml gentamicin. The mitogens were Concanavalin-A (Con-A, Miles Yeda, Rehovat, Israel) and phytohaemagglutinin (PHA, Difco Laboratories, MI, USA). Triplicate cultures containing 0·2 ml of the lymphocyte suspension and 10 μl of 100-μg/ml mitogen were prepared on Linbro Tissue Culture grade microtitre plates and incubated at 37°C in 5% CO_2 in air for 3 days before 1 μCi of H^3-thymidine (Amersham International, UK) was added to each well. After overnight incubation, the incorporation of ^{3}H-thymidine was determined by liquid scintillation as described previously.[17] The results were expressed as ratios between the counts of the patient sample and the mean count of three healthy blood donors analysed simultaneously (stimulation index). A normal stimulation index >0·7 was established in the clinical immunology laboratory, University of Gothenburg.

Antibodies against P. ovale

Serum samples were taken from 29 patients and stored frozen at −70°C until used. IgG antibodies against *P. ovale* were estimated as described[8] using FITC-labelled antihuman IgG (DAKO, Copenhagen, Denmark, lot 034, F202). *P. ovale* (ATCC 42132) cells were used as the antigen. The prepared cells were examined under a Zeiss fluorescence microscope and the serum dilution, where a fluorescent ring surrounding the majority of the cells still was seen, was recorded as the end-point titre.

Quantification of immunoglobulin classes and subclasses

Immunoglobulin isotype quantification was performed by the Mancini technique. To measure IgG, IgA and IgM, heavy-chain-specific rabbit polyclonal antibodies (DAKO-immunoglobulins, Copenhagen, Denmark) were applied, and as reference sera the Behringwerke (AG, Marburg Lahn, Germany) standard human serum was used as well as the WHO serum 67/97. IgE antibodies were determined by RAST using commercially available

Phadebas RAST kits (Pharmacia Diagnostics AB, Uppsala, Sweden). For determination of IgG subclass levels we used subclass-specific monoclonal antibodies (clones JL512, GOM1, ZG4, RJ4, Unipath, Bedford, UK) as previously described.[18] The WHO serum 67/97 was the reference serum, and age- related normal ranges for IgG subclasses were determined on 227 healthy adults using the same method.[18] Previously published normal ranges were used for IgG, IgA, IgM[19] and IgE.[20]

Immunohistochemical staining of skin sections

Three-millimetre punch biopsies were taken under local anaesthesia from lesions and normal-looking skin on the chest from 12 patients (Table 1). The biopsies were snap-frozen in liquid nitrogen and stored at −70°. Acetone-fixed cryostat sections (6 μm thick) were processed for the avidin–biotinylated-peroxidase complex (ABC, Vector laboratories, Burlingame, CA, USA) technique.[21] The monoclonal antibodies (Table 2) Leu 4, Leu 3a and Leu 2a were diluted 1/32, Leu 6 was diluted 1/64 and anti-HLA-DR was diluted 1/128. The sections were counter-stained with Mayer's haematoxylin. Omission of the primary antibodies gave no staining. Keratinocytes were considered to be positively stained when the full circumference of the cells was labelled. Routine haematoxylin-and-eosin staining was also carried out for each biopsy.

Results

Detection of surface markers on peripheral blood lymphocytes and lymphocyte stimulation by mitogens

The leucocyte counts as well as the results of the surface-marker analysis on peripheral lymphocytes are shown in Table 3. All patients but two (Patients 3 and 29) had normal total lymphocyte counts, and four (Patients 11, 14, 17 and 30) showed a decrease in relative total T cells as measured by CD3 antibodies. CD8-expressing cells were found in lower-than-normal numbers in two patients (Patients 2 and 4). The CD4/CD8 ratios were >0·6 in all patients, but 1·0 or lower in 10 (Fig. 1). Four patients, on the other hand, had higher-than-normal ratios. Low B-cell (CD19) frequencies were seen in eight patients (Patients 3, 4, 5, 6, 8, 9, 10 and 11) (Table 3).

The frequencies of HLA-DR-expressing cells were more than 35% of the lymphocytes in three individuals (Patients 18, 24 and 29), one with a high B-cell count (Table 4). The HLA-DQ expression was lower than the HLA-DR in most patients. Of the three individuals with HLA-DR expression >35%, one (Patient 24) had a similarly high DQ number whereas the other two showed lower DQ than DR expression. Two patients had very high frequencies of activated CD8-positive lymphocytes and two patients showed a high proportion of activated CD4-positive cells.

Table 3. Observations on peripheral-blood-lymphocyte findings in patients with seborrhoeic dermatitis. Values lying outside the normal range are indicated with an asterisk

Patient	Lymph 10^9/l	Percentage of lymphoid cells			
		CD19	CD3	CD4	CD8
1	3·4	11·0	61·0	39·0	39·0
2	2·8	14·0	68·0	62·0*	14·0*
3	3·6*	1·1*	61·0	50·0	26·0
4	2·5	3·0*	70·0	62·0*	13·0*
5	2·9	1·0*	79·0	69·0*	19·0
6	1·5	3·0*	69·0	32·0	39·0
7	2·8	10·0	73·0	61·0*	26·0
8	2.1	2·0*	66·0	35·0	29·0
9	2·0	1·0*	77·0	46·0	30·0
10	ND	1·0*	74·0	54·0	21·0
11	ND	6·5*	59·6*	37·2	36·4
12	1·6	14·7	75·0	54·7	22·2
13	1·4	9·0	ND	36·0	36·0
14	2·6	16·3	56·7*	35·4	38·8
15	3·0	12·8	76·1	38·9	32·1
16	1·7	23·3*	67·7	36·1	35·0
17	1·4	11·1	46·5*	43·4	33·8
18	1·8	14·1	65·7	39·0	35·0
19	2·1	8·0	64·0	42·0	27·0
20	2·1	9·0	72·0	60·0*	19·0
21	3·1	17·0	68·0	38·0	34·0
22	2·0	7·0	76·0	49·0	39·0
23	3·2	7·4	78·8	29·9	46·9
24	1·9	28·0*	80·0	47·0	51·0*
25	1·9	14·0	62·0	39·0	38·0
26	2·7	12·0	80·0	37·0	51·0*
27	2·6	14·0	70·0	41·0	34·0
28	2·8	11·5	67·9	47·4	29·3
29	3·7*	10·0	80·7	31·9	48·3*
30	1·2	ND	59·0*	44·0	27·0
Normal range†	1·2–3·5	7 23	60 85	29 59	19–48

ND = no data; NA = not available.

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Cells associated with natural-killer-cell activity (NK cells) were seen in high frequencies in 14 of 29 patients as measured by Leu 7 and Leu 11 (Table 5). $CD57^+16^+$ cells were also seen.

Low Con-A stimulation was seen in 11 patients. In six of these, and in two additional patients, a low PHA stimulation was detected (Figs 2 and 3). The low stimulations were confirmed in a second test.

Immunoglobulins in serum and IgG subclass levels

Total IgG levels were high in 14 of the 29 patients, and IgA was higher than normal in 11 (Table 6). Twelve

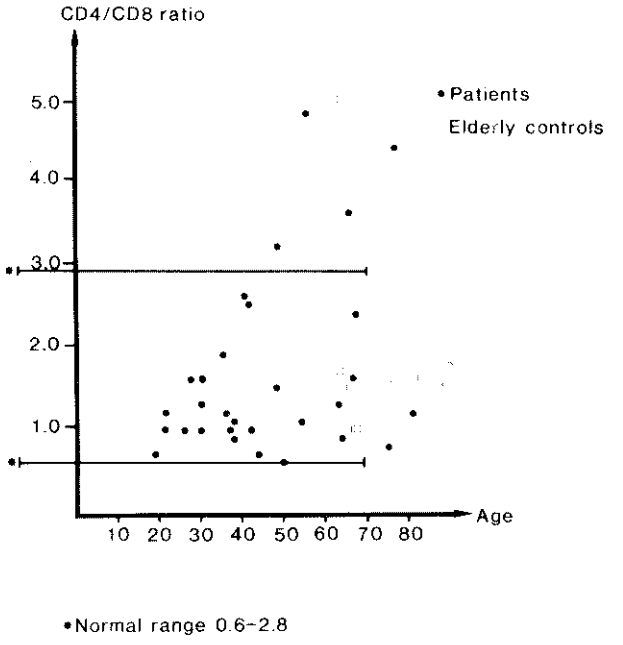

Figure 1. Lymphocyte surface makers on peripheral blood lymphocytes in patients with seborrhoeic dermatitis and elderly controls.

patients showed high IgG subclass levels, and two individuals were low in IgG4. Three patients had elevated levels of IgE.

Antibodies against P. ovale

The mean (±s.d.) serum IgG antibody titre against *P. ovale* was 349±333 (Table 6). In an earlier study, the mean serum IgG antibody titre from 57 healthy individuals was 113±136.[22] The difference is not significant ($P > 0.05$; multiple-regression analysis).

Immunohistochemical and PAS staining

In lesional skin from two of 12 patients (Patients 6 and 26) large perivascular dermal-cell infiltrates were observed. Seven patients (1, 3, 8, 9, 12, 17 and 18) had small to moderate dermal-cell infiltrates and in three the appearances did not differ between lesional and from the individual clinically normal skin. The majority of the infiltrating cells reacted with anti-CD4 antibodies, whereas CD8-expressing cells were few and scattered. There was a similar number and distribution of epidermal anti-CD1a reactive cells in normal and lesional skin. In the two biopsies with large (Patients 6 and 26) and in one biopsy (Patient 17) with moderate dermal-cell infiltrates, a few epidermal dendritic cells were CD4 positive. Patchy areas of HLA-DR-expressing keratinocytes were found in two of the biopsies (Patients 17 and 18) with moderate dermal-cell infiltrates.

Table 4. Percentage of HLA class II expression of peripheral blood lymphocytes in patients with seborrhoeic dermatitis. Values lying outside the normal range are indicated with an asterisk

Patient	HLA-DR	HLA-DQ	CD4;DR	CD8;DR	CD8;DQ
1	7	ND	ND	ND	ND
2	7	ND	ND	ND	ND
3	8	ND	ND	ND	ND
4	6	ND	ND	ND	ND
5	8	ND	ND	ND	ND
6	6	ND	ND	ND	ND
7	17	ND	ND	ND	ND
8	15	ND	ND	ND	ND
9	6	ND	ND	ND	ND
10	6	ND	ND	ND	ND
11	8·3	8·6	0·7	0·7*	0·6
12	17·6	13·5	2·3	0·7*	0·2
13	ND	ND	ND	ND	ND
14	12·8	8·8	1·5	0·4*	0
15	15·3	9·5	1·0	1·0	0·2
16	21·3	19·8	0·8	0·5*	0·1
17	18·2	13·2	8·2	4·6	0·8
18	35·4*	16·3	5·2	6·0	1·6
19	12·0	10·0	3·0	0·6*	0·1
20	11·0	9·0	2·0	0·2*	0
21	19·0	16·0	2·0	0·6*	0·2
22	13·0	7·0	2·0	3·7	0·7
23	17·3	9·0	2·6	4·5	0·2
24	47·0*	49·0*	7·0	43·0*	ND
25	20·0	1·1	1·4	2·8	ND
26	15·0	5·0	ND	ND	ND
27	26·0	9·0	4·0	4·0	1·8
28	28·7	17·0	23·0*	6·3	2·1
29	43·5*	10·8	3·2	27·3*	0·2
30	24·0	9·0	24·0*	6·0	0
Normal range†	NA	NA	1·0 9·0	1·0–8·0	NA

ND=no data; NA=not available.

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Discussion

Seborrhoeic dermatitis is a common skin disease seen in generally healthy individuals. Many studies now indicate an association between *P. ovale* and seborrhoeic dermatitis.[2] The majority of these are treatment studies showing a good response to anti-fungals.[2] Clearance of lesions is often paralleled by a reduction in number of *P. ovale*, and recurrence of the disease with an increase in the number of yeast cells.[2] However, no difference in number of *P. ovale* on the skin has been described in healthy individuals compared to patients with seborrhoeic dermatitis.[11,23]

How *P. ovale* induces inflammation and desquamation is unclear. The distribution of seborrhoeic dermatitis is parallel to the distribution of *P. ovale* and the sebaceous glands. We have found higher sebum levels in patients

Table 5. Percentage of natural killer cells in peripheral blood in patients with seborrhoeic dermatitis. Values lying outside the normal range are indicated with an asterisk

Patient	CD57	CD16	CD57+ CD16+
1	27·0	7·0	ND
2	27·0	ND	ND
3	14·0	ND	ND
4	10·0	ND	ND
5	5·0*	8·0	ND
6	49·0*	11·0*	ND
7	22·0	14·0*	ND
8	41·0*	15·0*	ND
9	45·0*	9·0	ND
10	22·0	18·0*	ND
11	6·0	17·2*	2·5
12	2·8*	3·8*	1·1*
13	2·0*	ND	ND
14	21·7	13·5*	4·5
15	7·2	6·2	2·3
16	3·4*	5·0	0·6*
17	8·8	19·2*	5·1
18	52·0*	8·0	1·8
19	9·0	15·0*	2·3
20	4·0*	10·0*	2·0
21	9·0	7·0	3·0
22	8·0	10·0*	3·0
23	20·6	5·8	2·3
24	20·0	3·0*	ND
25	17·0	11·0*	3·7
26	ND	9·0	ND
27	15·0	8·0	4·0
28	9·6	9·4	4·0
29	16·5	2·2*	1·0*
30	18·0	16·0*	6·0
Normal range[16]	6–29	4·7–9·9	1·6–9·6

ND = not done.

with seborrhoeic dermatitis compared to controls[11] but others have found normal sebum levels[24] and sebum excretion rates.[25] Minor abnormalities in the composition of sebum, e.g. increased cholesterol levels and decreased concentrations of squalene and unsaturated fatty acids, have been reported.[24,26] *P. ovale* can be found in the sebaceous glands. As humans have about 100 900 sebaceous glands per cm^2 skin, there are theoretically many possibilities for *P. ovale* and degradation products derived from *P. ovale* lipase activity[27,28] to come into contact with the blood vessels surrounding the sebaceous glands. This could be a possible way for predisposed patients to activate the immune system. A twin study indicates a genetic disposition for seborrhoeic dermatitis.[29] Experimental infections have demonstrated that some individuals are predisposed to develop *Pityrosporum* folliculitis, a disease closely related to seborrhoeic dermatitis.[30]

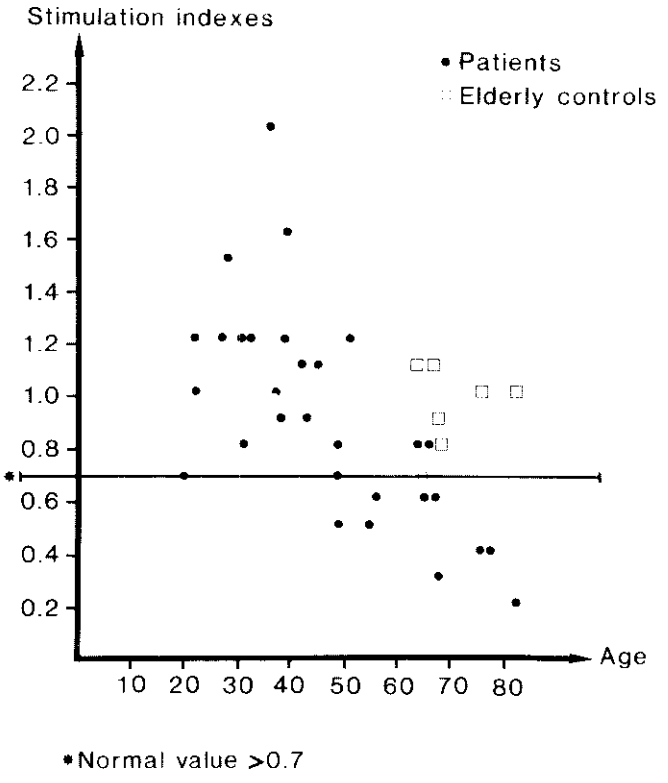

Figure 2. Lymphocyte stimulation by Con-A in patients with seborrhoeic dermatitis and elderly controls.

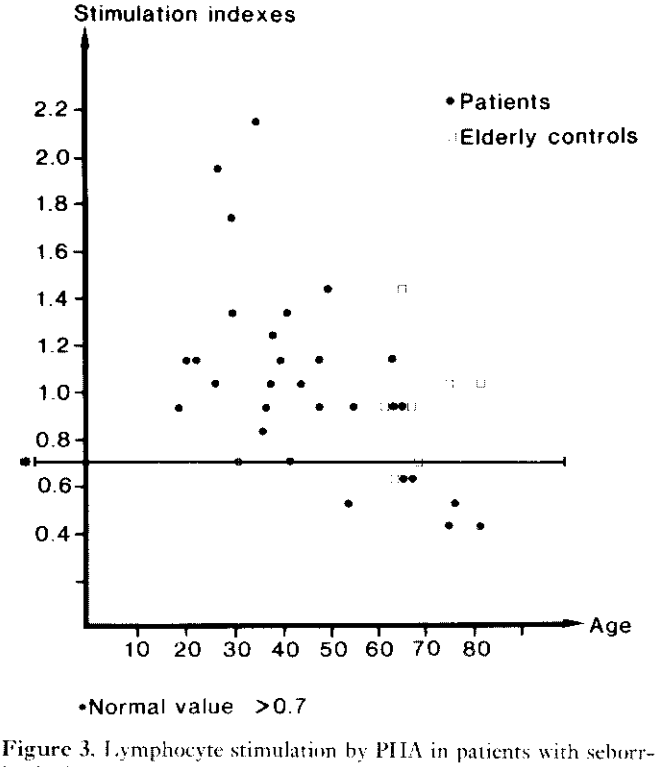

Figure 3. Lymphocyte stimulation by PHA in patients with seborrhoeic dermatitis and elderly controls.

Table 6. Serum immunoglobulins and anti *P. ovale* antibody titres in patients with seborrhoeic dermatitis. Values lying outside the normal range are indicated with an asterisk

Patient	IgG (g/l)	IgA (g/l)	IgM (g/l)	IgE (kU/l)	IgG1 (g/l)	IgG2 (g/l)	IgG3 (g/l)	IgG4 (g/l)	*Anti-P. ovale* serum IgG titres
1.	11·1	1·5	2·5	40	6·95	4·10	0·60	0·43	80
2.	10·4	4·1*	1·5	14	5·44	5·67	0·67	0·59	320*
3.	14·2*	3·0	2·8	16	9·98	4·99	0·94	0·46	40
4.	12·1	3·0	2·1	45	7·46	4·10	0·53	0·43	320*
5.	10·4	2·2	1·1	102	6·45	3·08	0·33	0·81	1280*
6.	13·2	2·6	2·6	40	9·98	4·86	1·08*	0·46	1280*
7.	15·2*	4·6*	2·0	22	11·99*	4·10	0·70	0·34	160
8.	15·6*	3·1	2·6	5	9·98	6·76*	1·30*	2·26*	40
9.	12·8	3·4*	2·0	9	8·97	3·34	0·70	0·09	640*
10.	16·7*	3·1	2·9	20	13·50*	4·86	1·08*	2·41*	80
11.	9·7	1·8	1·7	23	6·18	2·69	0·93	0·02*	80
12.	11·1	3·7*	2·0	230*	6·18	3·16	0·59	0·34	640*
13.	15·1*	2·4	1·2	45	11·59	2·46	0·72	0·43	ND
14.	8·3	0·7	1·1	55	4·71	2·93	0·53	0·69	80
15.	16·3*	1·7	3·7*	15	11·59	3·86	1·03*	0·52	160
16.	11·4	3·0	1·2	10	8·64	2·46	0·68	0·54	320*
17.	13·4	3·0	1·6	110	10·31	7·24*	0·78	0·58	160
18.	16·4*	2·8	1·9	ND	11·24	4·32	0·93	0·52	160
19.	18·5*	3·4*	1·6	90	9·62	6·81*	0·65	0·82	80
20.	10·2	3·4*	0·8	8	7·17	1·88	0·68	0·03*	640*
21.	13·9*	2·0	2·8	50	10·61	3·39	0·93	0·39	320*
22.	9·3	3·1	1·5	75	9·62	2·23	0·96	0·21	160
23.	13·2	3·0	1·9	20	8·64	4·32	1·33*	0·43	320*
24.	21·2*	5·3*	2·3	130*	15·17*	7·12*	1·50*	0·65	160
25.	12·1	3·0	2·4	280*	8·15	3·74	0·72	0·21	640*
26.	11·4	1·5	0·9	8	5·20	4·79	0·65	1·29	640*
27.	20·0*	3·4*	3·2	ND	16·74*	5·02	1·15*	0·41	320*
28.	15·6*	3·2*	0·9	65	9·12	4·06	0·78	1·10	320*
29.	15·6*	5·1*	1·5	40	8·65	6·67*	0·35	0·43	640*
30.	19·1*	5·1*	2·0	90	13·60*	5·37	1·75*	0·34	40
Normal range†	6·39–13·49[19]	0·70–3·12[19]	0·56–3·52[19]	0–115[20]	4·33–11·3[18]	1·33–6·08[18]	0·14–1·01[18]	0·07–1·85[18]	113±136[22]

ND = no data; NA = not available.

An explanation for the fact that some individuals develop *Pityrosporum* folliculitis could be a tendency to occlusion of the sebaceous glands.

In this study, dermal perivascular-cell infiltrates were observed in lesional skin in nine of 12 patients. In agreement with previous studies of patients with pityriasis versicolor, *Pityrosporum* folliculitis, candida intertrigo and dermatophytosis, there was a dominance of CD4-positive cells in the cell infiltrates.[31,33] An increase in anti-CD1a-reactive Langerhans cells in lesional skin has been described in patients with fungal infections.[32,34] In this study, we have not found any increase of CD1a-positive cells but have observed CD4 expression on dendritic epidermal cells, presumably Langerhans cells. This seems to indicate an 'activation' of such cells, which has been described in other inflammatory skin conditions.[35] The expression of HLA-DR antigens on keratinocytes in two of the biopsies from lesional skin is in accordance with our observations in patients with *Pityrosporum* folliculitis, candida intertrigo and dermatophytosis.[32,33] The mechanism of induction may be the same although the biopsies from the patients with seborrhoeic dermatitis showed only moderate dermal-cell infiltrates.

High serum IgG antibody titres against *P. ovale* have been reported in patients with seborrhoeic dermatitis compared to controls.[13] We, however, have not been able to confirm this finding using a slide immunofluorescence method with whole *P. ovale* cells,[11] or using three methods for antibody detection.[36] In fact, we found that seborrhoeic patients had significantly lower serum antibody titres against a *P. ovale* cell-wall protein than non-seborrhoeic controls. This surprising observation may be partly explained by the finding in the present study that patients with seborrhoeic dermatitis can show a low levels of T-cell function, as it is likely that the antibody response to the protein is T-cell dependent. In contrast, total

serum IgG and IgA levels were high in 14 and 11 individuals, respectively. This could be the result of polyclonal activation in connection with inflammation mediated by degradation products derived from *P. ovale* lipase activity. The frequent finding of a high IgA levels might indicate exposure of the mucosal immune system to *P. ovale* antigens, for instance along the gastrointestinal tract. High IgG subclass levels were found in 12 patients and only two individuals showed a low subclass level (Patients 11 and 20). The clinical significance of the low IgG4 is unclear.

Thirteen patients showed low PHA and/or Con-A responses in studies of lymphocyte transformation in comparison with healthy blood donors. It should be noted, however, that the six patients with low responses to both mitogens had a mean age close to 70 years, as compared to 46 years for the total series. These patients also had a longer duration of disease. In the control group of seven healthy individuals over 63 years of age, two showed low mitogen stimulation. This may suggest that the low response observed among the older seborrhoeic patients may partly be related to age.

Normal numbers of HLA-DR-expressing activated T cells were seen in the circulation of most individuals. Two of 18 patients, however, showed very high numbers of activated T cells without any known clinical cause. This finding suggests that intermittent systemic immune responses may occur in seborrhoeic dermatitis. In some patients, we found a differential expression of HLA-DR and DQ on the lymphocytes. A distinct role for HLA-DR and DQ in immune regulation has been suggested.[37] HLA-DR was shown to upregulate the immune response whereas it was suggested that HLA-DQ may be associated with immune suppression. No information is available about a specific interaction between *P. ovale* degradation fragments and HLA-DR or DQ. A high incidence of seborrhoeic dermatitis has been found in patients with acquired immunodeficiency syndrome (AIDS) (83%) and in patients with AIDS-related complex (42%).[38] The severity of seborrhoeic dermatitis appeared to correlate to the patients immune status and staging. These findings suggest a relation between the T-cell function and the development of seborrhoeic dermatitis.

In our study high frequencies of circulating NK cells (CD16) were found in 12 of 26 patients. Further studies are required to determine whether the T-cell and NK-cell aberrations are due to a primary immune dysfunction or represent events secondary to episodes of recurrent seborrhoeic dermatitis.

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