DEFECTIVE FUNCTION OF T LYMPHOCYTES IN PSORIASIS

WIESŁAW GLINSKI, M.D., SŁAWOMIR OBĄZEK, M.D., ANDRZEJ LANGNER, M.D., STEFANIA JABŁONSKA, M.D., AND MAREK HAFTEK, M.D.

Department of Dermatology, Academy of Medicine, Warsaw, Poland

The distribution of thymus-derived (T) and bone marrow-derived (B) lymphocytes in 100 patients with psoriasis was studied by the rosetting techniques. Depression of the number of T lymphocytes forming spontaneous rosettes with sheep erythrocytes (E rosettes) occurred in 66% of patients, whereas no difference in B lymphocytes bearing C3 receptor (EAC rosettes) was observed between psoriatics and normals.

The decrease in E rosettes was associated with the active phase of the disease. This disappeared 4-6 wk after onset of remission, which suggested that the abnormality in T-cell marker distribution is transitional.

Lymphocytes forming neither E nor EAC rosettes, which were found to be significantly increased in active psoriasis, were identified as T lymphocytes since they reacquired normal E rosette function during short-term preincubation with concanavalin A (Con A).

A serum factor was also demonstrated which inhibited E rosette formation by normal peripheral blood lymphocytes. Its activity increased linearly within 2 mo from the onset of skin lesions.

The data suggest that in active psoriasis serum factors may be coated on the lymphocyte surface membrane which may be responsible for blocking of specific receptor for sheep erythrocytes and/or interfere with T lymphocyte function.

Immunological studies have been undertaken recently in psoriasis to clarify the concept of the autoimmune immunogenetic of the disorder.

Rimbaud et al [1] have demonstrated anti-IgG activity on the surface membrane of peripheral blood lymphocytes. Furthermore, rheumatoidlike factors were identified in IgA and IgG classes of serum immunoglobulins [2-4].

Cormane et al [5,6] have studied the eluates from lymphocytes and polymorphonuclear leukocytes of psoriatic patients. Using the immunofluorescence method, antinuclear antibodies (ANA) have been encountered which reacted with the nuclei of the basal cell layer of uninvolved skin, but not with basal cell nuclei of the skin lesions. This raised the possibility that ANA may be bound in vivo in psoriatic lesions.

Antistatrum corneum (anti-SC) antibodies were found to be deposited with complement (C3 and C4) in the uppermost layer of psoriatic scales, but not in clinically uninvolved skin of patients with psoriasis [7-10]. The psoriatic scales also contain an extractable substance(s) which shows chemotactic activity for peripheral blood leukocytes [11].

The mechanism of anti-SC antibodies binding in psoriatic lesions is not clear. These autoantibodies are normally present in the sera of normal individuals as well as in patients with psoriasis. However, they are not bound with SC antigens in uninvolved skin. It is presumed that SC antigens have no contact with immune system or that alteration of their antigenicity is necessary for immune complex formation [12].

Studies on experimental DNCB sensitivity in psoriasis revealed that the patients were marginally immunodeficient. Epstein and Maibach [13] noted that only 42% of psoriatic patients could be sensitized to DNCB compared with 69% of normal controls. This defect was more evident in patients receiving immunosuppressive drugs, only 15% of such patients developed delayed hypersensitivity to DNCB, though control subjects similarly treated showed no decrease in the frequency of allergic reactions to DNCB.

A marked decrease in E rosette forming cells in patients with psoriasis has been found by several investigators [5,14], while other authors have observed no alterations in E rosette formation [15,16].

A slight depression of mitogen-induced lymphocyte transformation was demonstrated in psoriatic patients [14,15]. Leventine and Brostoff [15] have observed a significant inverse relationship between the extent of skin lesions and lymphocyte transformation to PHA. These data were not confirmed by Guilhou et al, who reported on reduced concanavalin A (Con A) and PWM lymphocyte response [14].

The purpose of our work was to determine the distribution of T and B lymphocytes in psoriasis in relation to the extent and activity of the disease. Further investigations were undertaken to determine if the decrease in E rosette forming cells is a permanent and primary abnormality in patients with psoriasis, and whether serum factors have effects on E rosette formation. An attempt was also made to reverse in vitro the suppression of E rosette formation.

MATERIAL AND METHODS

Selection of Patients

One hundred patients with psoriasis vulgaris and 27 healthy volunteers of both sexes were studied. The clinical state of the patients was evaluated according to the activity of the disease and the extent of skin lesions. Activity was determined by 2 observers and was graded as: + if skin lesions, mostly small papules and pin-point lesions, were spreading in the manner which occurs following streptococcal infection, + if skin lesions were active, and spreading peripherally (usually plaques, only occasionally small papules), and ++ if skin lesions were stationary for a long period of time.

The extent of skin lesions was graded +, ++, ++++, with + representing less than 10%, ++ 10-40%, and +++ more than 40% of the skin involved.

Onset of the last relapse was noted as well as the time of clearing of skin lesions after treatment.

Isolation of Lymphocytes [17]

Peripheral blood was drawn into preservative-free heparin (25 USP units/ml). The heparinized blood was diluted 1:1 with isotonic Hanks' medium, and layered onto an equal volume of a Ficoll-Ronpacon gradient (specific gravity-1.078). Lymphocytes, separated at the inter-
face following centrifugation at 400 × g for 40 min, were removed with a Pasteur pipette and washed 3 times with Hanks’ solution. Cells were counted using a hemocytometer. Cell viability was more than 98%, as demonstrated by trypan blue exclusion. Lymphocyte recovery averaged 91%. Resultant cell preparations contained more than 94% lymphocytes.

E Rosettes

A modification of the method of Wybran, Carr, and Fudenberg [18] was used for rosette formation. Briefly, sheep red blood cells (SRBC) were washed 3 times with Hanks’ medium at a concentration of 4 × 10^7/ml. A total of 0.2 ml of this cell preparation was added to 0.2 ml of 0.5% washed sheep erythrocytes in Hanks’ medium (4 × 10^7 SRBC) and 0.2 ml of heat-inactivated, SRBC-absorbed fetal calf serum. The mixture (SRBC:lymphocyte ratio of 10:1) was incubated at 37°C for 30 min, followed by centrifugation at 300 × g for 5 min and incubation at 4°C overnight. A rosette was defined as a lymphocyte surrounded by 3 or more adherent SRBC. Four hundred lymphocytes were counted in duplicate assays for each patient and the mean percentage of E rosettes accepted if the difference was less than 5%. When the difference was more than 5% the result has been interpreted as an error of the method. This sample was not discarded, but test was repeated next day in the same patient and data included into the examined group.

EAC Rosettes

The EAC rosette test was used as a marker for B lymphocytes. The percentage of lymphocytes bearing complement (C3) receptors was determined by measuring the number of lymphocytes binding 3 or more SRBC which have been sensitized with rabbit-anti-SRBC IgM antibody plus murine complement. IgM fraction of rabbit antiserum to SRBC was used in a subaglutinating dilution (1-640). Equal volumes of antibody and 2% SRBC in veronal buffered saline (VBS) were incubated at 37°C for 45 min, washed 3 times in VBS, containing 1% bovine serum albumin, and resuspended in 2 ml of medium. Complement, 0.2 ml fresh murine serum, was added to each 2 ml of antibody-coated SRBC, incubated at 37°C for 45 min, washed 3 times in VBS, and diluted to a SRBC concentration of 0.5%. To 0.2 ml of this suspension 8 × 10^7 lymphocytes in 0.2 ml VBS were added, incubated at 37°C for 45 min, and vigorously resuspended by rotation of the test tube. The test was done in duplicate, 400 cells were enumerated for each tube, and the mean percentage of lymphocytes forming EAC rosettes recorded when the results differed not more than 5% (see above in E rosette paragraph).

Preincubation of Lymphocytes

Normal lymphocytes or lymphocytes from patients with psoriasis were suspended at a concentration 1 × 10^9/ml in Hanks’ medium in separate tubes. Concanavalin A was added at different times to a final concentration of 10 µg/ml. The short-term cultures incubated for 1/2, 1, 2, 4, and 8 hr at 37°C with Con A or without mitogen were centrifuged and washed 3 times with PBS. Then, the rosette assay was performed, as described above.

The effects of sera from patients with psoriasis on the E rosette formation by normal lymphocytes were next studied. Sera from psoriatic patients were inactivated at 56°C for 30 min. Typically, 5 × 10^6 normal peripheral blood lymphocytes were suspended in 1 ml of Hanks’ medium. To this was added 0.25 ml of psoriatic serum, which represents dilution of 1:5. Controls consisted of normal human serum previously inactivated. The lymphocytes were incubated at 37°C for 1 hr, washed 3 times in PBS, and then their ability to form E rosettes was studied, as above.

Skin Test with DNCB

Patients were sensitized with 2000 µg of DNCB using the method of Eibler and Morton [19]. The patients were challenged with 100 µg of DNCB on the day of sensitization and with doses of 12.5, 25, 50, and 100 µg 14 days after sensitization. The skin reactions were examined 24 and 48 hr later, and reported as positive if over at least one half of the test site was involved by erythema and induration. The quantitative DNCB reactivity was presented as the lowest dose of DNCB which induces positive measurable skin reaction. A flare reaction was reported, if erythema and induration appeared spontaneously within 10–14 days after sensitization at the site of the first challenge with 2000 µg of DNCB.

RESULTS

T- and B-Lymphocyte Distribution in Patients with Psoriasis and Control Subjects

The cell type in peripheral blood lymphocytes of 100 patients and 22 controls was identified by determining the percent of cells forming E and EAC rosettes (Table I). “Null” cells were designed as lymphocytes forming neither E nor EAC rosettes by calculating the percent remaining cells for each individual studied. In normal controls T lymphocytes identified as E rosette forming cells accounted for 68.4 ± 5.1% of the total lymphocyte population, whereas 21.4 ± 4.0% of the lymphocytes were found to be B cells on the basis of EAC rosette test. In contrast, two-thirds of psoriatic cases had a significant reduction in the relative number of E rosette forming T lymphocytes (i.e., more than 2 SD below the mean of E rosettes in normal controls). The mean percent E rosettes in patients with psoriasis was 50.6 ± 14.7%. However, psoriasis resembled normal individuals in the distribution of B lymphocytes (20.9 ± 5.5%).

The sum of E and EAC rosette forming cells in psoriasis cases accounted for 46–97% of the total lymphocyte population. This resulted in the appearance of a third population of cells deficient in respect of both surface markers. The relative number of “null” cells was significantly greater in patients with psoriasis (28.5 ± 12.6%) when compared to control subjects (10.2 ± 5.8%).

Defective T-Lymphocyte E Rosette Function During the Active State of Psoriasis

Distribution of E rosette forming lymphocytes in respect of the extent of skin lesions and the activity of the disease is summarized in Table II. The patients could be classified into 3 categories on the basis of extent of skin lesions. These 3 groups of patients did not differ from each other in the relative number of E rosette forming cells and percent of cases with decrease in E rosettes. Mean percentage of E rosettes in all groups of patients with various extent of psoriasis was significantly reduced as compared with normals.

However, when the results of E rosette assay were analyzed in relation to activity of the disease, a marked reduction in E rosettes was found only in active psoriasis. Almost all the patients with active and spreading skin lesions, 81.5% and 90% of cases respectively, had evident abnormalities of E rosette function.

In patients with active popular skin lesions T lymphocytes were as low as 42.5%. Those with active plaque lesions were found to have 46.6% of E rosette forming cells. The majority of cases with stationary skin lesions had normal E rosette formation. A slight reduction in percent of E rosettes was observed only in 33.3% of patients with inactive psoriasis, but

<p>| Table I. Tests for E rosettes (T lymphocytes) and EAC rosettes (B lymphocytes) in 100 blood sample of psoriasis cases and in 22 controls |
|----------------------------------|----------------|----------------|----------------|----------------|
|                                   | Percentage of lymphocytes |               |               |               |
|                                   | Psoriasis (100) | Normal (22) | Statistical comparison* |</p>
<table>
<thead>
<tr>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>Mean</th>
<th>Range</th>
<th>SD</th>
<th>p</th>
<th>&lt; 0.001</th>
<th>p</th>
<th>&lt; 0.8</th>
<th>p</th>
<th>&lt; 0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>E rosette</td>
<td>50.6</td>
<td>12–81</td>
<td>14.7</td>
<td>68.4</td>
<td>60.5–79.5</td>
<td>5.1</td>
<td>p</td>
<td>&lt; 0.001</td>
<td>p</td>
<td>&lt; 0.8</td>
<td>p</td>
</tr>
<tr>
<td>EAC rosette</td>
<td>20.9</td>
<td>8–30</td>
<td>5.5</td>
<td>21.4</td>
<td>14–30</td>
<td>4.0</td>
<td>p</td>
<td>&lt; 0.001</td>
<td>p</td>
<td>&lt; 0.8</td>
<td>p</td>
</tr>
<tr>
<td>&quot;Null&quot; cell</td>
<td>28.5</td>
<td>3–54</td>
<td>12.6</td>
<td>10.2</td>
<td>(−4)–20.5</td>
<td>5.8</td>
<td>p</td>
<td>&lt; 0.001</td>
<td>p</td>
<td>&lt; 0.8</td>
<td>p</td>
</tr>
</tbody>
</table>

*Statistical significance of difference from controls (t-test).
TABLE II. E rosette function in psoriasis cases with various disease activity and extent of skin lesions

<table>
<thead>
<tr>
<th>Skin lesions</th>
<th>No. of cases</th>
<th>Percentage of E rosette forming cells</th>
<th>% Patients with decrease in E rosettes*</th>
<th>Statistical comparison b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>Range</td>
<td>SD</td>
</tr>
<tr>
<td>Extention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>16</td>
<td>54.6</td>
<td>31.5–73</td>
<td>12.3</td>
</tr>
<tr>
<td>++</td>
<td>44</td>
<td>50.7</td>
<td>20–81</td>
<td>14.5</td>
</tr>
<tr>
<td>+++</td>
<td>32</td>
<td>48.4</td>
<td>12–79</td>
<td>16.5</td>
</tr>
<tr>
<td>Activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Stationary</td>
<td>30</td>
<td>63.0</td>
<td>34.5–81</td>
<td>10.5</td>
</tr>
<tr>
<td>+ Active, peripherally spreading</td>
<td>32</td>
<td>46.0</td>
<td>12-68</td>
<td>13.9</td>
</tr>
<tr>
<td>++ Small papules spreading</td>
<td>30</td>
<td>42.5</td>
<td>26-66</td>
<td>11.6</td>
</tr>
<tr>
<td>Control</td>
<td>22</td>
<td>68.4</td>
<td>60.5–79.5</td>
<td>5.1</td>
</tr>
</tbody>
</table>

* More than 2 SD below the mean of normal controls.

b Significantly decreased in comparison with normal controls (t-test).

the mean percent of E rosette forming cells was not significantly lower than in controls (p < 0.1).

**Reversal of Defect in E Rosette Function by Concanavalin A**

Lymphocytes of 7 patients with active psoriasis which appeared deficient for T cell surface marker were preincubated with Con A at concentration of 10 μg/ml for increasing times. Figure 1 presents mean results of 2 individual experiments using the lymphocytes of 7 patients with psoriasis and 5 normal controls. The patients were selected for these experiments with regard to extremely low percent of E rosette forming cells (range 26–51.5%) which resulted in the relative increase in “null” cells.

Psoriatic lymphocytes preincubated with Con A recovered their E rosette formation function. The phenomenon was found to be a time-dependent, the longer the preincubation the greater the percentage of E rosette forming lymphocytes; so that the normal value was reached after 6–8 hr contact with mitogen. The lower concentration of Con A (1 μg/ml) had only a slight effect on E rosette function of lymphocytes of patients with psoriasis (data not shown). No inhibition or increase of E rosettes was observed when normal lymphocytes were cultured in the presence of Con A before they assayed for T cell surface marker.

**Relation of the Defect in E Rosette Function to the Course of Psoriasis**

The patients with extreme decrease in percent of E rosettes before treatment were reexamined at the time of clearing of skin lesions following treatment. The kind of therapy and the results of serial experiments on 14 patients are presented in Table III. In those in whom E rosette function was depressed in the first assay performed after the onset of remission, the test was repeated later during remission. Ten patients were examined within 2 wk after treatment, 6 of these cases (No. 4, 7, 9, 10, 11, and 13) were found to have normal percent of E rosettes, while No. 5, 6, 12, and 14 showed the decrease in E rosettes, which disappeared within 4–6 wk of the remission. The percent of E rosette forming lymphocytes was found to be normal in at least the third examination in all of 14 patients with psoriasis in the remission. The regeneration of E rosette function in all these cases, suggests that T lymphocyte E rosette formation becomes normal within about 6 wk of clearing of skin lesions.

**Serum Inhibitors of E Rosette Function in Psoriasis**

Psoriatic sera were found to inhibit E rosette formation by normal lymphocytes when preincubated for 1 hr at 37°C before E rosette test was performed. Table IV presents the mean percentages of E rosette forming cells in 37 patients with psoriasis (46.6 ± 13.9%) compared to E rosette function of normal lymphocytes previously exposed to individual patient sera (50.2 ± 12.0%). The sera of patients with decrease in E rosettes (72.2% of cases) usually inhibited normal lymphocyte E rosette formation which was found with 62.2% of sera tested.

Only 4 of such a serum from patients with psoriasis did not induce a marked inhibition of E rosette function. Sera of 3 patients in remission showed no inhibiting activity for E rosette function.

Percent reduction in E rosettes when normal peripheral blood lymphocytes were cultured in the serum from psoriasis cases were plotted against the time of the onset of recent relapse (Fig 2). The linear increase of inhibiting serum activity was observed by 2 mo of the last relapse. In the next months no further increase of the serum mediated inhibition of E rosette function was found. Three patients with psoriasis who were free of skin lesions for several months appeared to have no serum inhibitors.

**DNCB Sensitivity in Patients with Psoriasis**

The frequency of positive skin reactions after secondary challenge with DNCB was similar in patients with psoriasis (85.3%) and in normals (100%). Only 5 out of 34 patients were anergic to DNCB (Table 5). In contrast, the intensity of developed DNCB sensitization was much lower in patients with psoriasis; only 38.3% of cases showed strong positive reaction to DNCB (12.5 and 25 μg) in comparison to 81.8% of healthy subjects.

A total of 14 out of 34 (41.2%) patients were found to exhibit spontaneous flare reactions at the site of primary challenge with DNCB, in contrast to 90.9% of controls.

In patients with no flare reaction the higher dose of DNCB was required to provoke positive reaction after secondary challenge.

The patients with psoriasis who appeared to be anergic,
TABLE III. E rosette function of peripheral blood lymphocytes during the active phase of psoriasis and in remission (repeated examinations in 14 patients with psoriasis)

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Skin lesions</th>
<th>Extent</th>
<th>Activity</th>
<th>% E rosettes</th>
<th>Kind of treatment</th>
<th>Test repeated after</th>
<th>Free of lesions for</th>
<th>% E rosettes</th>
<th>Test repeated after</th>
<th>Free of lesions for</th>
<th>% E rosettes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>J.F.</td>
<td></td>
<td>+++</td>
<td>++</td>
<td>37</td>
<td>PUVA</td>
<td>2.5 mo</td>
<td>1.5 mo</td>
<td>72</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>H.N.</td>
<td></td>
<td>++</td>
<td>+</td>
<td>39</td>
<td>Tars</td>
<td>3 mo</td>
<td>2 mo</td>
<td>69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>B.I.</td>
<td></td>
<td>+++</td>
<td>+</td>
<td>39</td>
<td>Tars</td>
<td>7 mo</td>
<td>5.5 mo</td>
<td>65.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>H.G.</td>
<td></td>
<td>+</td>
<td>-</td>
<td>60</td>
<td>Tars</td>
<td>6 mo</td>
<td>2 wk</td>
<td>58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>T.R.</td>
<td></td>
<td>++</td>
<td>+</td>
<td>42.5</td>
<td>Tars</td>
<td>3 wk</td>
<td>1 wk</td>
<td>28.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>K.T.</td>
<td></td>
<td>+++</td>
<td>++</td>
<td>43</td>
<td>PUVA</td>
<td>7 wk</td>
<td>1 wk</td>
<td>34</td>
<td>2 mo</td>
<td>6 wk</td>
<td>62</td>
</tr>
<tr>
<td>7</td>
<td>K.B.</td>
<td></td>
<td>+++</td>
<td>++</td>
<td>30.5</td>
<td>PUVA</td>
<td>4 wk</td>
<td>2 wk</td>
<td>61</td>
<td>3 mo</td>
<td>6 wk</td>
<td>58</td>
</tr>
<tr>
<td>8</td>
<td>P.F.</td>
<td></td>
<td>++</td>
<td>+</td>
<td>20</td>
<td>Tars</td>
<td>4.5 mo</td>
<td>3 mo</td>
<td>52</td>
<td>7 mo</td>
<td>5.5 mo</td>
<td>60</td>
</tr>
<tr>
<td>9</td>
<td>S.D.</td>
<td></td>
<td>++</td>
<td>++</td>
<td>28</td>
<td>PUVA</td>
<td>5 wk</td>
<td>1 wk</td>
<td>64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>E.E.</td>
<td></td>
<td>++</td>
<td>+</td>
<td>39</td>
<td>Tars</td>
<td>5 wk</td>
<td>2 wk</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>H.P.</td>
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<td>+</td>
<td>++</td>
<td>50</td>
<td>Tars</td>
<td>4 wk</td>
<td>1 wk</td>
<td>65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>W.S.</td>
<td></td>
<td>+++</td>
<td>-</td>
<td>50</td>
<td>Tars</td>
<td>4 wk</td>
<td>1 wk</td>
<td>51.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>J.Z.</td>
<td></td>
<td>+++</td>
<td>++</td>
<td>35.5</td>
<td>Tars</td>
<td>4 wk</td>
<td>1-2 wk</td>
<td>65.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>J.S.</td>
<td></td>
<td>+++</td>
<td>+</td>
<td>41.5</td>
<td>Tars</td>
<td>5 wk</td>
<td>2 wk</td>
<td>56</td>
<td></td>
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<td></td>
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</table>

Table IV. The inhibition of normal lymphocyte E rosette formation by sera from 37 patients with psoriasis

<table>
<thead>
<tr>
<th>Procedure</th>
<th>% E rosettes</th>
<th>% cases with decrease in E rosettes*</th>
<th>Statistical comparison (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients lymphocytes (37)</td>
<td>46.6</td>
<td>72.2</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Normal lymphocytes preincubated for 1 hr at 37°C with</td>
<td>50.2</td>
<td>62.2</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>psoriatic serum (37)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal lymphocytes preincubated for 1 hr at 37°C with</td>
<td>66.9</td>
<td>8.3</td>
<td>NS</td>
</tr>
<tr>
<td>normal serum (12)</td>
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<td></td>
</tr>
<tr>
<td>Normal lymphocytes (12)</td>
<td>69.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

During the active phase of psoriasis when the skin lesions were spreading, reduced numbers of E rosette forming lymphocytes were found in the majority of patients, whereas the number of EAC rosette forming (B) cells remained relatively normal. This resulted in significantly increased numbers of lymphocytes deficient for both, T and B cell surface markers. Decreased E rosette function was not related to extent of skin lesions, but correlated with disease activity. The abnormalities were found to be transient since the lymphocytes reacquired normal T lymphocyte E rosette function by 4–6 wk after recovery. Suppression of E rosette formation could be reversed by short-term in vitro preincubation of patient lymphocytes with Con A, suggesting that the functionally deficient cells are T lymphocytes.

The lymphocyte receptor sites for Con A react with surface glycopeptides, whereas the E receptor appears to be of different nature [23]. It is possible that Con A, which has a high affinity to thymus-dependent lymphocytes, induces the restoration of specific surface receptors to sheep erythrocytes or stimulates the shedding of blocking factor from surface membrane.

E rosette formation has been found to parallel certain other parameters of T lymphocyte function including PHA responsiveness and delayed cutaneous hypersensitivity responses [24–27].

The studies with a quantitative DNCB method revealed a reduced frequency of spontaneous flare reaction at the site of primary challenge with DNCB which was present in only 41.2% of patients with psoriasis as compared to 90.9% of healthy persons. Furthermore, higher doses of DNCB were required in psoriatics to demonstrate delayed hypersensitivity after secondary challenge with this contact allergen. Our results confirmed the findings of Epstein and Maibach [13] who observed that a considerable number of patients with psoriasis failed to develop contact sensitivity to simple chemicals.

The data provide evidence that E rosette formation may be a sensitive index of the immunological state in certain patho-

**DISCUSSION**

Rosette formation with unsensitized sheep erythrocytes is characteristic of human thymus-dependent lymphocytes. This particular T cell function is related to a specific surface membrane receptor [18,20,21].

The T lymphocyte receptor for sheep erythrocytes has been demonstrated to bind erythrocyte surface glycopeptides. The soluble glycopeptides, such as fetuin glycopeptide, were found to block rosette formation by competition with sheep erythrocytes for specific lymphocyte surface membrane receptors [22].
logical conditions. On the other hand, the relative number of E rosette forming cells indicates the functional efficiency of T lymphocytes, but not their number. Thus, it is of limited value for identification and enumeration of T lymphocytes in many disease states associated with deficient cellular immune responsiveness.

In psoriasis, E rosette function may be more affected than other indicators of T lymphocyte function. Preliminary studies on lymphocyte transformation with T-cell mitogens have shown that response to PHA was only slightly reduced whereas Con A responsiveness appeared to be normal [28]. The differences may be explained on the basis of different receptor sites for mitogens and sheep erythrocytes.

The factors responsible for the defective E rosette function in active psoriasis are not known. A new serum factor, rosette inhibition factor (RIF), which is responsible for an extrinsic defect of E rosette formation by human T lymphocytes was detected in patients with acute viral hepatitis B [27]. The physicochemical properties of RIF clearly distinguished it from immunoglobulins, immunoregulatory α-globulin and other serum glycoproteins, and establish RIF as a bioregulatory lipoprotein.

Anti-T lymphocyte antibodies and/or immune complexes may play an important role in depression of E rosette formation in other diseases, such as systemic lupus erythematosus [29].

Our preliminary data on the effect of sera of patients with psoriasis on E rosette formation by normal lymphocytes suggested the existence of inhibiting substance(s) in the sera at active stage of the disease. The inhibitory activity of sera increased linearly during 2 mo of the recent relapse of psoriasis. We have also observed that the suppression of E rosette function of normal lymphocytes by patient sera correlated with the reduced percentage of E rosettes in the patients. The serum factor in psoriasis is under the study.

The present study provides no evidence for the primary defect of cell-mediated immunity in psoriasis. We were able to demonstrate that diminished E rosette function in active stage of psoriasis was transient and restored to normal in all patients during remission. E rosette formation could also be restored by in vitro incubation of patient lymphocytes with Con A. It is not clear if defective E rosette formation in psoriatic patients is related to inhibiting serum factors or whether they appeared to be distinctive unrelated phenomena responsible for intrinsic and extrinsic functional lymphocyte defect.

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