or local immune mechanisms might play a role in its development. Despite a clinical improvement after each treatment, recurrences of ACA lesions, new LSA patches and pains in the elbow joint occurred.

These new findings enlarge the spectrum of Lyme disease. LSA should also be looked upon as a possible Borrelia infection. The exact infectious mechanism has to be elucidated. For preventing further spreading of the disease a sufficient antibiotic therapy remains to be established.

REFERENCES

Abnormal Vitamin D Metabolism in Patients with Psoriasis

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To elucidate if psoriatic skin involvement induces changes in vitamin D metabolism, the serum concentrations of the major vitamin D metabolites (25-hydroxy-vitamin D$_{3-25}$ (25OHD), 1,25-dihydroxyvitamin D$_{3-25}$ (1,25(OH)$_2$D$_3$), and 24,25-dihydroxyvitamin D$_{3-25}$ (24,25(OH)$_2$D$_3$) were studied in a group of patients with psoriasis, who had not been exposed to ultraviolet radiation at least three months before the investigation. Serum concentrations of 1,25(OH)$_2$D$_3$ were significantly reduced in 17 patients with disseminated psoriasis compared to healthy age and sex matched controls (22.3 pg/ml versus 35.0 pg/ml (p<0.001)) and compared to 15 patients with moderate extended psoriasis (22.3 pg/ml versus 38.3 pg/ml (p<0.005)). Serum concentrations of the two other metabolites were not
significantly decreased. In patients with moderate psoriatic skin manifestations, the values of the three vitamin D metabolites were normal. It is concluded that patients with disseminated psoriasis demonstrate decreased serum concentrations of the vitamin D metabolite 1,25(OH)2D. Since 1,25(OH)2D plays a role in differentiation and proliferation of epidermal cells, the abnormal low serum level of 1,25(OH)2D might be of importance for the abnormalities in cell maturation and proliferation found in psoriatic skin. Key words: Psoriasis; 1,25-dihydroxyvitamin D2-3. (Received April 21, 1986.)

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The main source of vitamin D in man is due to the effect of ultraviolet (UV) radiation on 7-dehydrocholesterol in the skin (1). Biotransformation of vitamin D has been shown to include 25-hydroxylation in the liver (250HD) followed by hydroxylation either at the C1 (1,25(OH)2D) or C24 (24,25(OH)2D) position in the kidney. The biological activity of 1,25(OH)2D, especially the enhancement of intestinal calcium absorption, is at least 100-fold higher than that of 25OHD, whereas the effects of 24,25(OH)2D in man are at present unknown.

Several features of psoriatic skin might influence vitamin D metabolism such as an increased epidermal thickness, a higher skin temperature, or an increased blood flow (2). Furthermore, it has been demonstrated that 1,25(OH)2D has an effect on epidermal cell turnover and differentiation (3). We have therefore in the present study measured the serum concentrations of the three vitamin D metabolites in patients with moderate and disseminated psoriatic skin manifestations.

METHODS

Patients

A selected group of 32 informed patients with psoriasis mean age 44 years (14–77) participated in the study. The extent of the skin involvement was assessed by the "rule of nines". None of the patients had been exposed to UV-radiation on their body three months before the investigation and no one took vitamin pills. All patients had normal renal and hepatic function.

The patients were divided into two groups: group I: 15 patients with psoriasis involving less than 20% of the body surface (mean 8.5%±5.0 SD) and group II: 17 patients with disseminated psoriasis involving more than 20% of the body surface (mean 45%±18 SD). Thirty-seven healthy sex and age matched subjects served as controls.

Assay procedures

Blood samples from the patients and controls were obtained in the morning during the months of November to March.

Vitamin D measurement

Serum concentrations of 25(OH)D, 24,25(OH)2D and 1,25(OH)2D were measured according to a previously described method (4). The method involved combined measurement of the dihydroxylated metabolites of vitamin D3 and D2, therefore named 24,25(OH)2D and 1,25(OH)2D. The method employs specific extraction procedures followed by chromatography on Sephadex LH-20, Lipidex 5000 and high pressure liquid chromatography including known internal standards to determine the recovery of each metabolite (4).

Statistics

For statistical evaluation the Student’s t-test for unpaired data was used (level of significance 5%).

RESULTS

In patients with psoriasis involving less than 20% of the body surface (group I) mean serum concentrations of the three vitamin-D metabolites were virtually similar to those of
### Table 1. Mean serum concentrations of three vitamin D metabolites in 32 patients with psoriasis

Group I is patients with less than 20% of body surface involved. Group II is patients with more than 20% of body surface involved.

<table>
<thead>
<tr>
<th>Vitamin D metabolites</th>
<th>Group I (n=15)</th>
<th>Group II (n=17)</th>
<th>Controls (n=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25(OH)D (ng/ml)</td>
<td>Mean 25.8</td>
<td>20.4</td>
<td>27.8</td>
</tr>
<tr>
<td></td>
<td>±SD 12.1</td>
<td>20.4</td>
<td>12.8</td>
</tr>
<tr>
<td>1,25(OH)_2D (pg/ml)</td>
<td>Mean 38.3</td>
<td>22.3</td>
<td>35.0</td>
</tr>
<tr>
<td></td>
<td>±SD 18.8</td>
<td>11.9</td>
<td>11.3</td>
</tr>
<tr>
<td>24,25(OH)_2D (ng/ml)</td>
<td>Mean 1.13</td>
<td>1.23</td>
<td>1.28</td>
</tr>
<tr>
<td></td>
<td>±SD 1.13</td>
<td>1.95</td>
<td>1.05</td>
</tr>
</tbody>
</table>

healthy, control subjects. In patients with disseminated psoriasis (group II) the levels of 25(OH)D and 1,25(OH)_2D were lower compared to healthy subjects and to patients with moderate extended psoriasis. This difference was significant for 1,25(OH)_2D compared to controls (p<0.001) and compared to patients with more limited psoriasis (p<0.005) (Table I). The serum concentration of 1,25(OH)_2D was negatively correlated to the area of involved skin (r=0.49, p<0.01).

### DISCUSSION

Only one study has previously focused on vitamin D metabolism in untreated patients with psoriasis. Sommer-Tsilenis et al. (5) reported that serum concentrations of 25(OH)D in a group of unexposed psoriatic patients were moderately and not significantly decreased. This finding is in accordance with the result of this study.

The serum concentrations of 1,25(OH)_2D and 24,25(OH)_2D have never been examined in psoriatic patients, and the markedly decreased serum level of 1,25(OH)_2D in patients with disseminated psoriasis found in the present study has never previously been reported. It cannot be settled whether the psoriatic skin abnormalities (such as increased epidermal thickness, higher skin temperature, increased blood flow (2)) or internal abnormalities in patients with disseminated psoriasis cause the demonstrated alterations of the vitamin D metabolism.

The biological activity of 1,25(OH)_2D, especially the enhancement of intestinal calcium absorption and bone resorption, is at least 100 fold higher than that of 25OHD. The formation of this hormone is tightly controlled by plasma concentrations of calcium and phosphate. In untreated patients with psoriasis the serum concentrations of calcium and phosphate has been shown to be within normal range in one study (5). Others have demonstrated that hypoparathyroidism and hypocalcaemia can be associated with severe psoriasis. In these patients the psoriasis improved without local treatment when the serum calcium was restored to normal, emphasizing that fluctuations in serum calcium can affect psoriasis (6, 7). The significance of the decreased serum concentrations of 1,25(OH)_2D is at present unknown, but might be clarified by future studies of the calcium and vitamin D metabolism in patients with psoriasis.

During the last few years it has been shown that the skin is not only a synthetic organ for...
vitamin D but it is also a target organ for its 1,25(OH)2D metabolite (8). Dermal fibroblasts and epidermal keratinocytes have high-affinity receptors for 1,25(OH)2D and a 30-50% inhibition in fibroblast cell division was observed, when normal cultures were incubated with 1,25(OH)2D (9). Furthermore, 1,25(OH)2D caused a dose-dependent increase in the epidermal differentiation of human cultured keratinocytes (10).

In cultured fibroblasts from non-lesional psoriatic skin an inhibition of cell division was observed when incubated with 1,25(OH)2D, but higher concentrations were needed compared to normal cultures (11). The new observations that 1,25(OH)2D can induce morphologic and biochemical differentiation of cultured human keratinocytes, together with the observation that psoriatic dermal fibroblasts and possibly keratinocytes (11) have a partial resistance to the action of this hormone may herald an exciting new role for 1,25(OH)2D in diagnosis and treatment of psoriasis (11, 3). The present demonstrated low serum concentrations of 1,25(OH)2D in patients with severe psoriasis might be of importance for the disruption in cell maturation and hyperproliferation observed in psoriatic skin, and may further indicate that 1,25(OH)2D could play a role in the pathogenesis of psoriasis.

It can be concluded that untreated patients with disseminated psoriasis have decreased serum-values of 1,25(OH)2D. Whether this hormone is of importance for the pathogenesis of psoriasis is at present unknown. However, since the decrease in serum concentration of 1,25(OH)2D is linearly correlated to the area of involved skin, it presumably is due to a secondary effect induced by the disease. The results of this and previous studies (6, 7), indicate that it might be important to determine the serum level of vitamin D metabolites and calcium in patients with severe or disseminated psoriasis.

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