β-HYDROXYACYL-CoA DEHYDROGENASE AND GLUCOSE-6-PHOSPHATE DEHYDROGENASE IN NORMAL HUMAN SKIN AND IN SOME PAPULOSQUAMOUS DISEASES OF THE SKIN

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Abstract. The activity of β-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.35, HOADH) and glucose-6-phosphate dehydrogenase (EC 1.1.1.49, G6PDH) was measured in different epidermal layers in skin from patients with psoriasis, neurodermatitis, lichen planus and pityriasis rosea and from healthy controls. The assays were performed on micro-dissected specimens obtained from cryostat sections according to Lowry's microtechniques. The basal epidermis displayed higher activities of HOADH than obtained in subcorneal epidermis. In psoriasis and neurodermatitis, increased activities of HOADH were found in the non-involved skin when compared with healthy controls and a still higher enzymatic activity was encountered in the psoriatic lesion. HOADH was decreased in the lesions of lichen planus and no change in the enzymatic activity was evident in pityriasis rosea. G6PDH was increased in various degrees in all four lesions studied.

The activity of several enzymes is increased in the psoriatic epidermis (3, 10, 11, 14). This has been interpreted as a sign of augmented metabolism required to satisfy the enhanced epidermal proliferation (2, 18, 19). So far, no conclusive evidence has appeared which relates such data to any metabolic defect of etiological importance. These studies suggest that the availability of energy-rich compounds and metabolites necessary for synthesis should be characterized further in order to delineate the prerequisites for cellular renewal and maturation in psoriasis. Analyses of the epidermal oxygen consumption (8, 13) and of the lipid metabolism (5, 22) infer that, besides glycolysis, other pathways, such as the β-oxidation of fatty acids, also provide substrates for mitochondrial respiration. In the psoriatic lesion changes appear in fatty acids and in their metabolism (7, 9, 17). No enzymes of the β-oxidation of fatty acids have, however, been studied in relation to psoriasis; therefore, in the present study one of the enzymes in this cycle, HOADH, was chosen. For comparison, an enzyme, G6PDH, involved in the oxidation of glucose was also analysed. In order to relate pathological differences to enzymatic activities, neurodermatitis, lichen planus and pityriasis rosea were studied together with psoriasis.

MATERIAL AND METHODS

Punch biopsies were collected without anaesthesia from the extensor aspects of the forearm from patients with psoriasis, neurodermatitis and lichen planus. In patients with pityriasis rosea, biopsies were also taken from the trunk. The material is summarized in Table 1. The psoriatic patients had guttate or nummular lesions. The neurodermatite lesions were of the hypertrophic type described by Hyman & Erger (15). In patients with lichen planus, the characteristic papular lesions were selected. Patients with pityriasis rosea had the macular variant with lesions on the trunk and no lesions of the forearm. The histopathological pictures are summarized in Fig. 1 and are in accordance with others (1, 6, 16, 20).

None of the patients had been treated during the previous month. The patients believed themselves to be healthy except for the skin disease and no concomitant disease was diagnosed. The controls consisted of healthy persons without any dermatological disorders.

The biopsies were taken from the centre of a lesion and from the unaffected skin 40 mm away from the lesion. In pityriasis rosea, biopsies were taken from a guttate lesion on the trunk and from non-involved skin 40 mm away from the lesion and also from unaffected skin on the forearm. The preparations were immediately
frozen in cold isopentane (−86°C) and stored at this
temperature in a Dewar vessel for not more than 2 days.
Subsequently, sectioning, dissection and weighing of the
material were performed as described earlier (14). The
dissected material comprised tissue from the basal part
of the rete ridges and from the adjacent subcorneal
germinat epithelium. Assays of HOADH and G6PDH
activities were performed as recently described (12, 14)
with the exception that the incubation time for the
HOADH was 30 min. The specimens weighed about 100
ng and 75 ng for the two enzymes respectively. Student’s
I-tests were made to confirm differences between the
means given. The experimental error was measured as
coefficients of variation. It was 10% for HOADH and
13% for G6PDH.

RESULTS
The enzymatic activities of HOADH are summa-
rized in Table II. HOADH was higher in the
basal part of the epithelium (Fig. 2). The percent-
ual decrease of the enzymatic activity of HOADH in
subcorneal epithelium as compared with the
basal epidermis was calculated. In the controls the
decrease was 32 ± 4% (mean and its standard
error). In the non-involved and the affected psori-
atic epidermis these figures were 32 ± 5 and
48 ± 3% respectively. The difference was statisti-
cally probable (P < 0.02). In neurodermatitis the
attained values were 40 ± 7 and 51 ± 8%.

An increase of the activity of HOADH was
noted both in the non-involved and in the affected
psoriatic skin, which was evident in both layers
when compared with controls (P < 0.02). The
highest activity was obtained in the basal epithe-
lium from the psoriatic patch. In neurodermatitis a
similar rise of HOADH was evident also in
the non-involved skin (P < 0.01), but in the neu-
rodermatite lesion no further increase occurred.
In the lesion of lichen planus, HOADH was de-
pressed (P < 0.001), as shown in Fig. 2, but in the
non-involved skin no difference was displayed
when compared with controls. In pityriasis rosea
no differences were seen between the non-in-
volved sites and the lesion.

The enzymatic activities of G6PDH are sum-
morized in Table II. In all disorders there was an
increase of G6PDH in affected skin, as shown
in Fig. 3. The subcorneal epidermis displayed
mostly the higher activities when compared with

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Table I. Composition of the patient material

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>Ages of patients Range (Mean)</th>
<th>Duration of illness Range (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>14</td>
<td>23-51 (33)</td>
<td>0.1-33 (8) years</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>24</td>
<td>17-69 (31)</td>
<td></td>
</tr>
<tr>
<td>Neurodermatitis</td>
<td>7</td>
<td>25-70 (55)</td>
<td>2-7 (4) years</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>8</td>
<td>19-70 (46)</td>
<td>1-16 (6) months</td>
</tr>
<tr>
<td>Pityriasis rosea</td>
<td>8</td>
<td>17-42 (28)</td>
<td>4-21 (11) days</td>
</tr>
</tbody>
</table>

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Fig. 1. Summary of the pathological findings in psoriasis, neurodermatitis, lichen planus and pityriasis rosea.
Table II. Activities of β-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.35) and glucose-6-phosphate dehydrogenase (EC 1.1.1.49) in human epidermis. Values are expressed as moles of substrate consumed per kg dry weight and hour (MKH)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Subcorneal</th>
<th>Basal</th>
<th>Subcorneal</th>
<th>Basal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HOADH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>8</td>
<td>1.43±0.12</td>
<td>2.11±0.14</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>11</td>
<td>1.99±0.18</td>
<td>2.94±0.17</td>
<td>2.19±0.12</td>
<td>4.32±0.33</td>
</tr>
<tr>
<td>Neurodermatitis</td>
<td>7</td>
<td>2.05±0.18</td>
<td>3.48±0.20</td>
<td>1.34±0.17</td>
<td>3.09±0.48</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>8</td>
<td>1.82±0.13</td>
<td>2.24±0.22</td>
<td>0.52±0.10</td>
<td>1.16±0.13</td>
</tr>
<tr>
<td>Pityriasis rosea</td>
<td>8</td>
<td>1.76±0.20</td>
<td>2.45±0.15</td>
<td>1.99±0.23</td>
<td>2.22±0.29</td>
</tr>
<tr>
<td><strong>G6PDH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>6</td>
<td>0.65±0.07</td>
<td>0.73±0.03</td>
<td>2.33±0.18</td>
<td>1.75±0.14</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>18</td>
<td>0.75±0.12</td>
<td>0.63±0.12</td>
<td>1.85±0.21</td>
<td>1.44±0.31</td>
</tr>
<tr>
<td>Neurodermatitis</td>
<td>6</td>
<td>0.76±0.05</td>
<td>0.67±0.04</td>
<td>1.05±0.07</td>
<td>1.32±0.10</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>8</td>
<td>0.83±0.03</td>
<td>0.68±0.06</td>
<td>1.33±0.21</td>
<td>1.12±0.21</td>
</tr>
<tr>
<td>Pityriasis rosea</td>
<td>5</td>
<td>0.78±0.07</td>
<td>0.65±0.07</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Specimens taken from the trunk.
# 12 patients.

In the normal skin the activity of HOADH is higher in the basal part of the epidermis than in the subcorneal part. This is also true in varying degrees for all diseases examined. The results are in accord with the electron microscopic findings of a decreasing number of mitochondria in keratinocytes as they move from the basal layer towards the subcorneal parts of the epidermis (4, 23). In controls and non-involved psoriatic skin, the activity of HOADH decreased about 30%
when the cells leave the basal part and reach the subcorneal layer. In the psoriatic lesion this reduction was 50%. In the subcorneal parts of the parakeratotic psoriatic epithelium, Brody (4) noted a changed mitochondrial morphology which might indicate that their function is altered. It is not possible at this point, however, to link the enzymatic data to a specific histopathological picture such as parakeratosis or absence of the keratozylin layer. One reason is that the lesions of neurodermatitis and lichen planus, which have different histological characteristics (Fig. 1), display a similar decrease of HOADH as was shown in psoriasis.

The normal-looking skin in the psoriatic patient has been examined for chemical or histological signs for indications of a "latent psoriasis". These studies have been summarized by Wohlrab & Grünberg (21). The finding of an increased enzymatic activity of HOADH in the unaffected skin in psoriasis and in neurodermatitis may support the concept that a chemical alteration precedes clinical signs of the diseases. The process which leads to the increased activity of HOADH and the nature thereof needs further investigations.

The decrease in the enzymatic activity of HOADH in lichen planus is in agreement with the view that the basal degeneration also limits the functional capacity of the mitochondria. The damaged cells seem to utilize other metabolic pathways, as indicated by the higher activities of G6PDH in the basal epidermis.

From the present data it seems valuable to study individual enzymes not only with regard to the site from which a specimen is taken, but also with regard to similar clinical conditions. The object of such comparisons is to obtain a better understanding of the relationship between biochemical alteration and a specific histopathological pattern.

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REFERENCES

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