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β-HYDROXYACYL-CoA DEHYDROGENASE AND GLUCOSE-6-PHOSPHATE DEHYDROGENASE IN NORMAL HUMAN SKIN AND IN SOME PAPULOSQUAMOUS DISEASES OF THE SKIN[1]

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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.

[1] β-hydroxyacyl-CoA dehydrogenase, EC 1.1.1.35 (HOADH), glucose-6-phosphate dehydrogenase, EC 1.1.1.49 (G6PDH).

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 I.

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

Table 1. *Composition of the patient material*

Group	No. of patients	Ages of patients Range (Mean)	Duration of illness Range (Mean)
Controls	14	23–51 (33)	—
Psoriasis	24	17–69 (31)	0.1–33 (8) years
Neuro-dermatitis	7	25–70 (55)	2–7 (4) years
Lichen planus	8	19–70 (46)	1–16 (6) months
Pityriasis rosea	8	17–42 (28)	4–21 (11) days

frozen in cold isopentane (−86°) 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 germinal 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 *t*-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 summarized in Table II. HOADH was higher in the basal part of the epithelium (Fig. 2). The percental decrease of the enzymatic activity of HOADH in subcorneal epithelium as compared with the basal epidermis was calculated. In the controls the decrease was $32 \pm 4\%$ (mean and its standard error). In the non-involved and the affected psoriatic epidermis these figures were 32 ± 5 and $48 \pm 3\%$ respectively. The difference was statistically probable ($P < 0.02$). In neurodermatitis the corresponding values were 40 ± 7 and $51 \pm 8\%$.

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 epithelium 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 neurodermatite lesion no further increase occurred. In the lesion of lichen planus, HOADH was depressed ($P < 0.001$), 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-involved sites and the lesion.

The enzymatic activities of G6PDH are summarized 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

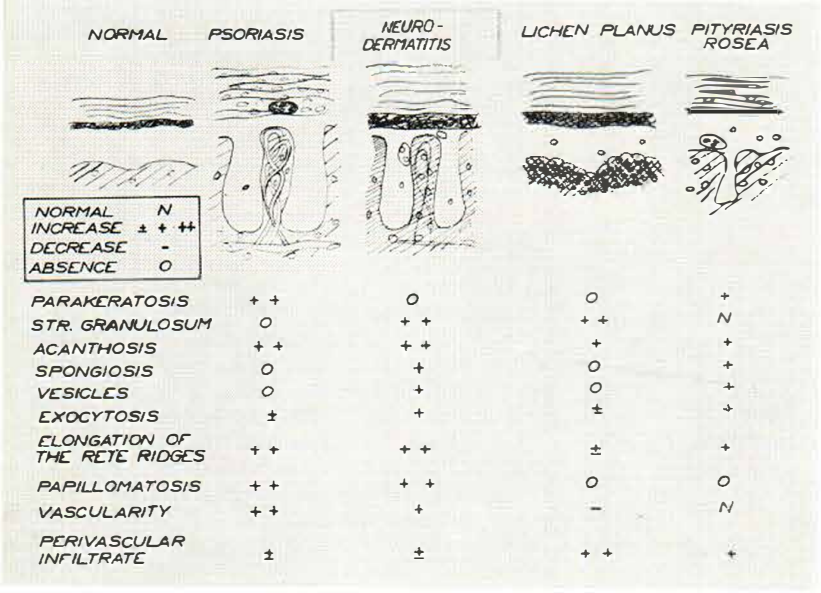

Fig. 1. Summary of the pathological findings in psoriasis, neurodermatitis, lichen planus and pityriasis rosea.

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)*

Group	Number	Non-involved epidermis		Involved epidermis	
		Subcorneal	Basal	Subcorneal	Basal
HOADH					
Controls	8	1.43±0.12	2.11±0.14	—	—
Psoriasis	11	1.99±0.18	2.94±0.17	2.19±0.12	4.32±0.33
Neurodermatitis	7	2.05±0.18	3.48±0.20	1.34±0.17	3.09±0.48
Lichen planus	8	1.82±0.13	2.24±0.22	0.52±0.10	1.16±0.13
Pityriasis rosea	8	1.76±0.20	2.45±0.15	1.99±0.23[a]	2.22±0.29[a]
	8	2.11±0.21[a]	2.21±0.13[a]		
G6PDH					
Controls	6	—	0.73±0.03	—	—
Psoriasis	18	0.65±0.07[b]	0.63±0.12	2.33±0.18[b]	1.75±0.14
Neurodermatitis	6	0.75±0.12	0.70±0.11	1.85±0.21	1.44±0.31
Lichen planus	8	0.76±0.05	0.67±0.04	1.05±0.07	1.32±0.10
Pityriasis rosea	5	0.83±0.03	0.68±0.06	1.33±0.21[a]	1.12±0.21[a]
	5	0.78±0.07[a]	0.65±0.07[a]		

[a] Specimens taken from the trunk.
[b] 12 patients.

the corresponding basal epithelium. Only in the lesions of lichen planus was this difference reversed ($P < 0.05$).

DISCUSSION

The assays of HOADH show that in the epidermis one prerequisite exists for enzymatic oxidation of fatty acids which could ultimately furnish substrates for mitochondrial energy production. 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%

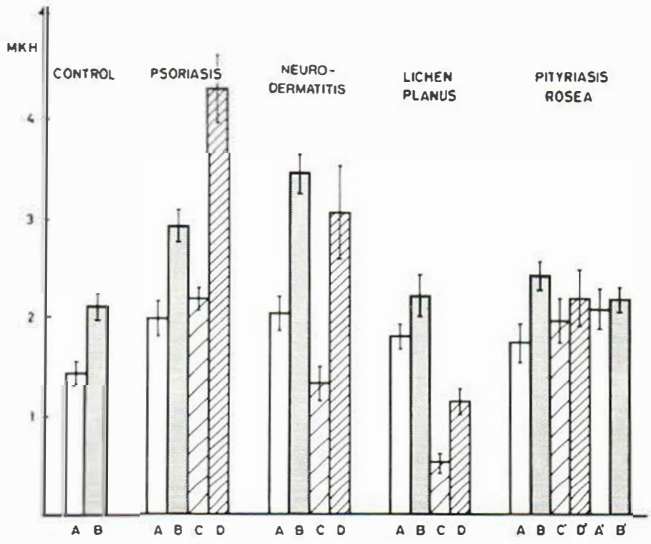

Fig. 2. Means of the activity of β-hydroxy acyl-CoA dehydrogenase (moles/kg dry weight/hour, MKH). The standard error is indicated on each bar. The letters at the bottom of the bars indicate subcorneal (*A,A'*) and basal (*B,B'*) epidermis taken from non-involved skin and subcorneal (*C,C'*) and basal (*D,D'*) epidermis taken from lesions. Primed letters refer to a biopsy site on the trunk, otherwise biopsies were collected from the forearm.

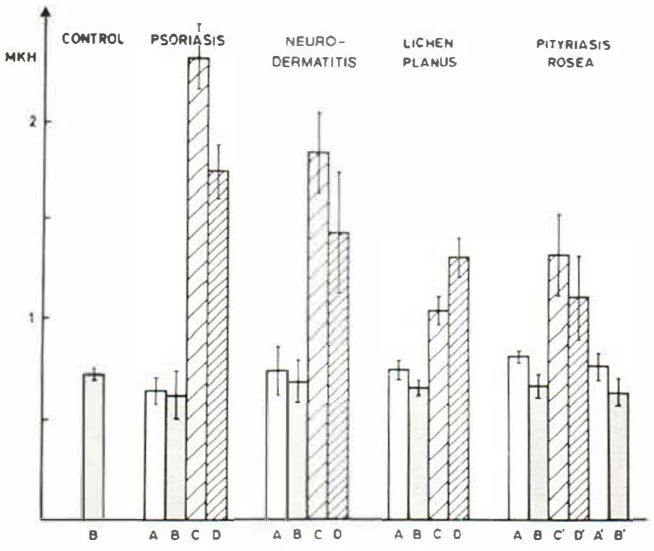

Fig. 3. Means of the activity of glucose-6-phosphate dehydrogenase. The convention is the same as in Fig. 2. In the control group the activity in subcorneal epidermis was not measured.

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 keratohyalin 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 & Grüneberg (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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