Acta Dermatovener (Stockholm) 53: 251–258, 1973

ATP AND ADP LEVELS AND EPIDERMAL REPLACEMENT RATE IN THE NORMAL HUMAN SKIN AND IN SOME PAPULOSQUAMOUS DISEASES OF THE SKIN

Hans Hammar

From the Departments of Dermatology and Histology, University of Uppsala, Uppsala, and the Department of Dermatology, Karolinska sjukhuset, Stockholm, Sweden

Abstract. Adenosine tri- and diphosphate (ATP, ADP) were measured in the subcorneal and basal layers of epidermis from patients with psoriasis, neurodermatitis and lichen planus and from healthy controls. In the controls the ATP content in the basal layers was 11.3 mmoles/kg dry weight and decreased to 9.8 mmoles/kg in the subcorneal layers. The ADP content varied between 1 and 2 mmoles/kg. The ATP levels in the controls decreased 38% after a 30-min period of anoxia with nitrogen as gas phase. In non-involved skin in patients with the various diseases, the adenylate levels were similar to those of the controls. In the psoriatic lesion the ATP content was increased 33% in subcorneal and 17% in basal epidermis. In neurodermatitis and lichen planus there was no difference in the ATP content between affected and non-involved skin. The effect of anoxia on epidermal adenylates in psoriasis and neurodermatitis was similar to that found in the controls but in lichen planus it was scarcely discernible. Using tetrachlorsalicylanilide as a marker, the epidermal replacement rate was found to be increased about 2-fold in the non-involved and 7-fold in the involved psoriatic skin as compared with the control rate. In 2 patients with lichen planus the rate was about 4 times the control rate when measured in lesions but was not increased in non-involved skin. Neither this rate nor the relative epidermal height showed any correlation with ATP and ADP levels, irrespective of the lesion studied.

Reports on energy metabolism in the epidermis have mostly referred to the enzymatic prerequisites for glycolysis and the citric acid cycle or studies on respiration (5, 7, 11, 12, 13, 20, 25). In the psoriatic lesion these investigations indicate a high energy production in epidermal cells as evidenced by enhanced activities of many enzymes and by increased respiration. The contents of some high-energy compounds have also been measured in skin sections by Halprin & Ohkawara, who found a 26% increase of ATP[1] in the psoriatic lesion (7). In order to determine whether the ATP content varied with respect to the different layers of the epidermis, microdissection of defined cellular layers was undertaken as described previously (8). By this procedure ATP and ADP were measured in psoriasis, neurodermatitis and lichen planus. The effect of prolonged anoxia on the content of adenine nucleotides was also studied as a measure of the metabolic requirements for high-energy compounds in the epidermis. In a group of patients with psoriasis and lichen planus, the rate of epidermal replacement was studied and compared with control skin and related to the content of adenine nucleotides.

MATERIAL AND METHODS

Punch biopsies were collected without anaesthesia from patients with psoriasis, neurodermatitis, lichen planus and from healthy controls. The number of patients in the different groups and the length of illness are summarized in Table I. The lesions were guttate or papular and the criteria for their diagnosis were the same as described earlier (9). The biopsies were taken from the extensor region of the forearm, one from the centre of a lesion and another from unaffected skin 40 mm away from the lesion. None of the patients had been treated during the month previous to the biopsy and, except for the present disease, they considered themselves healthy.

The biopsy material was immediately frozen in cold isopentane (−86°C) and kept dry at this temperature in a Dewar vessel until sectioned. In those patients whose material was used for the anoxia study, two biopsies were taken for the assays of ATP; one was frozen within 10 sec after the biopsy and the other after 2, 4, 15 or

[1] For abbreviations, see legend to Table II.

Table I. *Composition of the material of patients*

Relative epidermal height was measured as the ratio of the height of the subcorneal epithelium in an epidermal papilla to that over the adjacent corial papilla. Means and S.E.M. are given

Group	No.	Age of patients Range	Age of patients Mean	Duration of illness Range	Duration of illness Mean	Epidermal height Non-involved	Epidermal height Involved
Controls	17	18–33	24	—		2.17±0.15	—
Psoriasis	12	16–50	31	0.5–35	14 years	1.93±0.16	4.20±0.59
Neurodermatitis	4	54–71	63	3–12	7 years	1.67±0.03	3.10±0.30
Lichen planus	7	18–51	36	0.5–12	5 months	1.80±0.08	2.13±0.15

30 min. During this interval the biopsies were kept in 0.9% saline at 22°C and gassed with pure nitrogen in a Warburg vessel. Most of the material was incubated for 2 to 4 min or for 30 min. The sectioning was performed within 2 days and the further treatment of the material such as dissection and weighing was done as described earlier (8, 12). The dissected material consisted of tissue from the basal part of the rete ridges and from the adjacent subcorneal epithelium.

Assay conditions. ATP was extracted in 0.02 M NaOH and measured by the luciferase method modified according to Wettermark et al. (19, 24, 26). The details of the procedure are given in Table II. ADP was measured after conversion of ADP to ATP by phosphoenolpyruvate and pyruvate kinase (see Table II). In the instrument used, a 10 μl sample of 80 nM ATP gave a signal-to-noise ratio of 20 : 1. Extracts of epidermal material weighing about 200 ng gave this concentration of ATP. The sensitivity of the system permitted assays of samples weighing as little as 20 ng, but ordinarily about 7 to 15 times as much was used. Both ATP and ADP were run as standards together with appropriate blanks. The ATP standards were found to decrease 8% per hour during an assay, and its standard deviation was 8%. ATP standards were therefore interposed before, between and after measurements of the triplicates of epidermal materials in order to counteract this error. The coefficient of variation obtained from measurements on such triplicates was 18%.

Table II. *Conditions for the assays*

Substance measured	Pretreatment: Buffer	Substrate	Other additives	Volume (μl)	Temperature (°C)	Time of incubation (min)
ATP	—	—	0.02 M NaOH	7.61	60	15
ADP	37 mM Tris-(hydroxymethyl)-aminomethane[a] pH 7.2	2.1 mM Phosphoenolpyruvate[b]	14 mM KCl 19 mM $MgCl_2$ 1.1 U/ml PK[b]	26.4	22	90–120

Substance measured	Assay system: Buffer	Additives for measurement of product	Aliquot volume (μl)	Final volume (ml)	ATP measured by
ATP	3.7 mM EDTA[a] pH 9.8	10 mg/ml firefly extract, FLE 50[a] 5.4 mg/ml Apyrase[a] 0.02 M $MgSO_4$ 0.05 M K_2HAsO_4–KH_2AsO_4 pH 7.4	10	0.5	Luciferase induced flash
ADP	37 mM Tris-(hydroxymethyl)-aminomethane pH 7.2	as given for ATP	10	0.5	Luciferase induced flash

ADP = Adenosine 5′-diphosphate, AK = Adenylate kinase, EC 2.7.4.3, ATP = Adenosine 5′-triphosphate, EDTA = Ethylenediamine tetraacetic acid, PK = Pyruvate kinase, EC 2.7.1.40
[a] Sigma Chemical Co, St. Louis, USA.
[b] Boehringer Mannheim GmbH, Germany.

Table III. *ATP content in human epidermis*

Values are expressed as mmoles per kg dry weight. Means and S.E.M. are given

		Non-involved epidermis		Involved epidermis	
Group	No.	Subcorneal	Basal	Subcorneal	Basal
Controls	17	9.8±0.5	11.3±0.4	—	—
Psoriasis	12	9.1±0.8	11.2±0.6	12.1±0.6	13.1±0.4
Neurodermatitis	4	10.9±1.7	10.7±2.0	11.6±2.1	12.3±1.4
Lichen planus	7	9.7±0.7	10.9±1.3	10.2±1.0	10.4±1.4
Anoxia maintained at 22° in 0.9% saline and nitrogen atmosphere for periods indicated					
Controls, 2–15 min	8	9.3±0.6	11.1±0.6	—	—
30 min	3	6.5±1.7	6.1±2.3	—	—
Psoriasis, 2–15 min	6	10.2±0.6	12.1±1.4	12.1±0.6	13.6±0.9
30 min	3	6.3±2.0	5.8±2.2	7.7±0.2	8.5±1.8
Neurodermatitis, 30 min	3	7.0±2.0	7.5±2.1	9.2±3.5	9.2±3.0
Lichen planus, 30 min	4	7.6±1.3	6.9±0.9	7.6±2.0	8.7±2.3

The adenylate content was expressed as mmoles per kg dry weight (mMK).

Except for the first few measurements, specimens of human skeletal muscle were included as a biological standard at each assay, mostly in triplicate. The ATP content of these specimens was 18.2±1.1 mMK. ADP accounted for 3.4±0.6 mMK and the sum of ATP and ADP was 21.7±1.2 mMK (mean±S.E.M.).

The statistical treatment was carried out according to Snedecor (23) and Seeger (22).

The energy charge (EC) of the adenylate system according to Atkinson's definition (1) is

$$EC = \frac{C_{ATP} + 1/2\, C_{ADP}}{C_{ATP} + C_{ADP} + C_{AMP}}$$

The adenylate kinase reaction: $AMP + ATP \rightleftharpoons 2$ ATP, was assumed to be at equilibrium in the epidermal materials used. The equilibrium constant was set at 0.8 (4). An approximate value was then obtained for EC after the AMP content had been estimated from the condition set by the adenylate kinase reaction.

Relative epidermal height. For each biopsy obtained, several of the lyophilized sections were fixed and stained with haematoxylin and eosin. The height of the subcorneal epithelium of the sections was measured perpendicularly to the surface with the aid of an ocular micrometer. The maximal and the adjacent minimal height of the epithelium was recorded for each epidermal rete peg on the section. Ratios between such pairs were calculated. An analysis of the errors obtained for increasing numbers of the ratios indicated that an acceptable number must exceed 30. Usually, 50 ratios were counted. The standard error of the means was recorded for each biopsy. The geometric mean of these standard errors lay in the range between 0.06 and 0.15 in the various groups of patients or, in per cent of the means, in the range between 6 and 12%. The ratios are presented to further characterize the biopsy material in Table I.

Epidermal replacement rate. Tetrachlorsalicylanilide was used as a corneal marker according to Baker & Kligman (2). Corneal layers were counted on sodium hydroxide-treated sections in a phase contrast microscope. The material used in this part of the study differed to a certain extent from that in the main part and is therefore summarized in Table V.

RESULTS

The results of ATP and ADP measurements in the epidermis are summarized in Tables III and IV and in Fig. 1.

Controls

The ATP content was 11.3 mMK in the basal epidermis and it decreased to 9.8 mMK in the subcorneal layers. This difference was significant ($P < 0.01$). During anoxia no effect on ATP was evident in the first 2 to 15 min and only after 30 min was a drop in the ATP content of 38% found. This decrease was significant ($P < 0.01$). The subcorneal and basal epithelium were similarly affected.

The ADP contents in the two layers of epidermis studied did not differ significantly and no effects on the ADP level were found during anoxia. It varied between 1 and 2 mMK.

The energy charge of the adenylate system was calculated with regard to the assumptions indicated above. The result is summarized in Fig. 2. The values for epidermis were found to be about 0.9. They did not differ with respect to the two layers investigated. During anoxia some alteration towards lower values was noted, but no significant differences were found on comparison with initial values.

Table IV. *ADP content in human epidermis*

Values are expressed as mmoles per kg dry weight. Means and S.E.M. are given

Group	No.	Non-involved epidermis		Involved epidermis	
		Subcorneal	Basal	Subcorneal	Basal
Controls	17	1.3±0.5	2.4±0.6	—	—
Psoriasis	12	1.9±0.5	2.1±0.5	1.6±0.3	2.0±0.3
Neurodermatitis	4	1.7±0.8	1.7±0.9	1.1±0.5	1.2±0.7
Lichen planus	7	0.6±0.1	1.2±0.4	1.7±0.4	2.2±0.6
Anoxia maintained at 22° in 0.9% saline and nitrogen atmosphere for periods indicated					
Controls, 2–15 min	8	1.0±0.3	1.0±0.4	—	—
30 min	3	3.2±1.6	3.1±1.9	—	—
Psoriasis, 2–15 min	6	2.7±1.1	1.3±0.5	1.7±0.9	1.3±0.5
30 min	3	1.5±0.6	2.4±1.5	1.5±0.8	2.1±0.7
Neurodermatitis, 30 min	3	1.2±0.3	1.3±0.8	2.2±0.7	4.0±2.0
Lichen planus, 30 min	4	1.8±0.5	1.3±0.2	1.1±0.5	1.5±0.6

The relative epidermal height is presented in Table I. The controls displayed a slightly higher value than that found in the non-involved skin of the patient groups (Table I). This was due to a correlation with the age of the patients. The decrease in ratio was 0.12 per decade.

The epidermal replacement rate together with corresponding values for the relative epidermal height are given in Table V. These two factors showed no correlation with the adenylates measured.

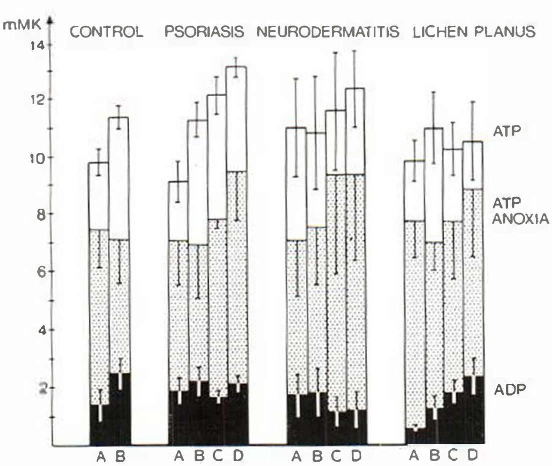

Fig. 1. ATP and ADP contents in epidermis. Each column represents the means and their standard errors, mmoles/kg dry weight (mMK). The top level indicates initial ATP content, the next level ATP after anoxia for 30 min and the bottom level the initial ADP content. Specimens were obtained from subcorneal (*A*, *C*) and basal (*B*, *D*) parts of epidermis in uninvolved (*A*, *B*) and involved (*C*, *D*) biopsy sites.

Psoriasis

In non-involved epidermis of the psoriatic patients, the ATP and ADP levels were unchanged when compared with those of the controls. In the lesion, however, the ATP content was increased 17% in the basal and 33% in the subcorneal epithelium ($P < 0.01$). Both in the non-involved skin and in the psoriatic lesion, the basal layers displayed the highest ATP levels as compared with subcorneal epithelium ($P < 0.01$). During anoxia a 30% decrease in ATP content was obtained after 30 min. During the first 2 to 15 min no

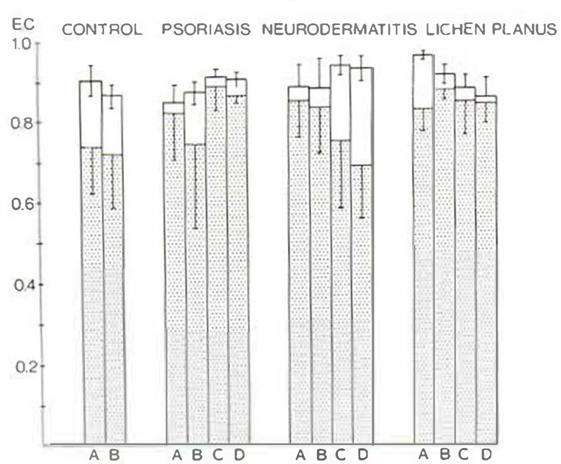

Fig. 2. Energy charge (EC) of the adenylate system. The assumption was made that the adenylate kinase reaction: ATP + AMP ⇌ 2 ADP was at equilibrium, and that the equilibrium constant was 0.8 (1). The top level indicates the energy charge before and the lower level after anoxia. The notation is the same as in Fig. 1.

Table V. *Epidermal replacement rate, number of corneal layers and relative epidermal height*

Tetrachlorsalicylanilide was used as a marker. Means and S.E.M. are given

Group	No.	Age of patients Range	Age of patients Mean	Epidermal height	Corneal layers	Epidermal layers replaced per day
Controls	10	24–81	37	1.75 ± 0.08	19.5 ± 1.6	0.89 ± 0.11
Psoriasis						
Non-involved	5	34–54	44	1.50 ± 0.09	23.7 ± 1.5	1.83 ± 0.25
Involved	6	34–54	44	2.89 ± 0.37	24.0 ± 0.9	6.36 ± 1.14
Lichen planus						
Non-involved	2	18–43	31	1.51, 1.69	21, 22	1.36, 1.40
Involved	2	18–43	31	2.57, 2.11	62, 40	5.20, 3.06

significant changes were observed. In the psoriatic patients the ADP levels were similar in both layers and in the biopsy sites analysed and were not obviously changed after anoxia (Table IV).

The energy charge was not altered when compared with controls. The epidermal replacement rate was increased both in non-involved and involved psoriatic skin as compared with controls (Table V): $P < 0.001$. In psoriasis, the lesion displayed the highest levels when compared with non-involved skin ($P < 0.01$). The relative epidermal height was increased in the lesions, as shown in Tables I and V. Neither of these two factors could be correlated to the adenylate contents in non-involved or diseased skin.

Neurodermatitis and lichen planus

The ATP levels in these two conditions were not changed significantly when compared with the non-involved skin and neither was any difference found between the two layers of epidermis studied. The ATP content was similar to the control level. This lack of difference was most obvious in lichen planus (Fig. 1). The ATP content was decreased 27% in neurodermatitis ($P < 0.01$) and 14% in lichen planus ($P > 0.05$) after 30 min of anoxia. The ADP levels and energy charge lay within the range of controls, regardless of layer or biopsy site.

The epidermal replacement rate was recorded in 2 patients with lichen planus (Table V). It was increased in the lesions, but the values in non-involved skin lay within 2 S.D. of the control mean. In both lesions the relative epidermal height was increased when compared with non-involved skin, as shown in Tables I and V. It showed no correlation, however, to the adenylate content.

DISCUSSION

Controls

Adenylate levels. The ATP values found in the epidermis are high when compared with other tissues. In the liver, kidney, pancreas, brain and blood, ATP has been found to range between 1 and 12 mmoles/kg dry weight, and only muscle and the adrenal marrow displayed higher levels, 15 to 140 mmoles/kg dry weight, when various animals were analysed (18, 21). The values given in Table III are about 5 to 8 times as high as those reported in skin sections by Halprin & Ohkawara (7) and twice that recently reported by Härkönen & Hopsu-Havu in blistering epidermis (14). ADP was also measured by Halprin & Ohkawara (7), who found the level twice as high as that given in Table IV. The reason for these discrepancies probably lies in the different assay systems and techniques for treatment of the tissues used by those authors.

The energy charge of the adenylate system as outlined by Atkinson (1) gives a relative measure of the energy level within the cells. A decrease means facilitation of ATP synthesis, while high values are indicative of various anabolic processes. The energy charge differs in various tissues and the calculation made here indicates a value near 0.9 in epidermal layers. If the data of Halprin & Ohkawara (7) were used in the same way as presented above, the energy charge would be 0.27 in control skin and 0.37 in psoriatic lesion. As pointed out by Atkinson (1) the energy charge of the adenylate system will vary with the relative concentrations of the three adenylates on the assumption that adenylate kinase (EC 2.7.4.3) is present and in excess. The adenylate kinase reaction should then be at equilibrium at all times. As will be reported in a subsequent paper (10), this enzyme displayed activities between 3 and 8 moles of substrate converted per kg dry weight and hour of incubation at 38°C in the epidermal material under discussion. These findings are in agreement with the view that the enzymatic activity should be sufficient to maintain the reaction of adenylate kinase at equilibrium.

Adenylate levels during anoxia. The experiments with anoxia ought to throw light on the turnover of adenylates in the skin. A decrease of ATP, together with an accumulation of ADP, was to be expected from the findings of Gatfield et al. for brain tissue (6). These authors noted a 20 to 30% reduction of ATP during 30 sec of ischaemia. A similar value was noted in the islets of Langerhans and in the kidney (16, 17). In the skin, however, the turnover of adenylates was conspicuously slower and 30 min was required to obtain similar changes (Table III). During anaerobic incubation of epidermal material, Härkönen & Hopsu-Havu (14) also observed rather slow ATP degradation. An analysis of the turnover of the adenylates in the epidermis by other techniques is needed to elucidate this discrepancy between the skin and other tissues.

The ATP decrease during anoxia found in controls (38%) was equivalent to 2 to 4.5 mMK ATP. This reduction of ATP within the cells is in keeping with the concept that the allosteric inhibition of ATP in the phosphofructokinase step (EC 2.7.1.11) is diminished in order to increase glycolysis. The low disappearance rate of ATP in epidermis as compared with other tissues indicates also that the epidermal cells can restrict their consumption of high-energy adenylates to the range of their glycolytic capacity. This must be of great importance for the viability of a tissue exposed to very variable ambient conditions, as is the case for skin.

Epidermal replacement rate. The rate obtained by Baker & Kligman for the forearm was 1.20 (2) and in a recent report on older patients by Baker & Blair it was 1.08 in women and 0.72 in men (3). The present result of 0.89 is in agreement with these findings. When the material was divided according to sex, no difference was evident.

Psoriasis

The increase of the ATP content in psoriasis was similar to that found by Halprin & Ohkawara (7), although their ATP levels were found to be much lower. The increase was greatest in the subcorneal epithelium. In spite of the higher ATP content available for anabolic reactions, the subcorneal cells cannot complete the keratinization, which indicates other defects in this mechanism than those dependent in high-energy adenylates.

The energy charge in psoriasis was probably the same as in controls as far as the present data revealed. This means that more ATP was made available by expanding the adenylate pool in the epidermal cells of a psoriatic patch rather than by changing their energy charge.

The ATP content in psoriasis decreased during anoxia to an extent similar to that found in controls. Respirometric measurements displayed almost the same oxygen consumption in basal epidermis of controls and psoriatic patients during initial incubation without additives to the medium (11). No discrepancies were encountered until succinate was added to the medium. The findings indicate that the epidermal cells in psoriasis behave like normal cells when the resources are restricted. On the other hand, under optimal conditions they show quite a different picture (11). Cell kinetic data also reveal an increased turnover both in the non-involved and the involved psoriatic epidermis, and, as recently found, also in epithelium of the oral mucosa (for ref. see 15). The replacement rate indicated in Table V is in agreement with such results.

Neurodermatitis and lichen planus

The paucity of the material analysed in these two diseases might be a reason why the ATP levels did not vary between the layers studied. During anoxia, however, ATP was decreased in neurodermatitis but not descernibly in lichen planus. In the lichen planus lesion the activities of glyceraldehydephosphate (10) and glucose 6-phosphate dehydrogenases (9) were increased almost as much as in psoriatic epidermis. This could mean that glycolysis is already rapid in epidermis of the lichen planus lesion and that the anaerobic conditions imposed during anoxia cannot greatly increase this capacity. Further data on the metabolism in this disease other than that of the decreased activity of an intramitochondrial enzyme (9) must be awaited in order to determine whether this hypothesis is relevant.

CONCLUSIONS

The results presented show that healthy epidermis is rich in ATP and ADP as compared with several other tissues. Under anaerobic conditions it can restrict its demands for high-energy adenylates and is able to metabolize endogenous substrates over prolonged periods of time. High ATP levels were still found in subcorneal epithelium, indicating a need for high-energy compounds for the purpose of synthesis or keratinization. The psoriatic lesion shows increased ATP levels in both basal and subcorneal layers. The expanded adenylate pool displayed in this disease was not found in neurodermatitis and lichen planus. If the high epidermal replacement rate found in lichen planus can be supported by kinetic studies as shown in psoriasis (15), further studies related to the different types of keratinization in psoriasis and lichen planus might be fruitful.

ACKNOWLEDGEMENTS

This study was supported by the Swedish Medical Research Council (19X-2593), the Astrid Karlson Foundation, Uppsala University, the Edvard Welander and Karolinska Institutet Foundations, Stockholm, and the Swedish Psoriasis Association, through both its Uppsala Regional and its National Board, Stockholm.

REFERENCES

1. Atkinson, D. E.: Citrate and the citrate cycle in the regulation of energy metabolism, pp. 30. *In* The Metabolic Roles of Citrates (ed. T. W. Goodwin). Academic Press, London, 1968.
2. Baker, H. & Kligman, A. M.: Technique for estimating turnover time of stratum corneum. Arch Derm (Chicago) *95:* 408, 1967.
3. Baker, H. & Blair, C. P.: Cell replacement in the human stratum corneum in old age. Brit J Derm *80:* 367, 1968.
4. Barman, T. E.: Enzyme Handbook Springer-Verlag, Berlin, 1969.
5. Braun-Falco, O. & Petzoldt, D.: Zur Histotopie von Enzymen des energieliefernden Stoffwechsels in der Epidermis bei Psoriasis vulgaris. Arch Klin Exp Derm *230:* 223, 1967.
6. Gatfield, P. D., Lowry, O. H., Schultz, D. W. & Passonneau, J. V.: Regional energy reserves in mouse brain and changes with ischaemia and anaesthesia. J Neurochem *13:* 185, 1966.
7. Halprin, K. M. & Ohkawara, A.: Carbohydrate metabolism in psoriasis. J Invest Derm *46:* 51, 1966.
8. Hammar, H.: Glyceraldehydephosphate dehydrogenase and glucose-6-phosphate dehydrogenase activities in psoriasis and neurodermatitis and the effect of dithranol. J Invest Derm *54:* 121, 1970.
9. — β-hydroxyacyl-CoA dehydrogenase and glucose-6-phosphate dehydrogenase in the normal human skin and in some papulosquamous diseases of the skin. Acta Dermatovener (Stockholm) *51:* 93, 1971.
10. — Adenylate kinase, ATP phosphohydrolase and glyceraldehyde phosphate dehydrogenase activities in the normal human skin and in some papulosquamous diseases of the skin. Acta Dermatovener (Stockholm) *53:* 259, 1973.
11. Hammar, H. & Hellerström, C.: The oxygen consumption of the germinal epithelium in normal and psoriatic skin. Brit J Derm *83:* 371, 1970.
12. Hammar, H., Thyresson, N. & Brolin, S. E.: Enzyme activities in the germinal layer of normal and psoriatic skin. Acta Dermatovener (Stockholm) *48:* 175, 1968.
13. Herdenstam, C.-G.: On the in vitro metabolism of labeled glucose in normal and psoriatic skin slices. Acta Dermatovener (Stockholm) *42:* Suppl. 47, 1962.
14. Härkönen, M. H. A. & Hopsu-Havu, V. K.: Energy metabolism of human epidermis during prolonged suction leading to blister formation. Acta Dermatovener (Stockholm) *51:* 340, 1971.
15. Kaidbey, K. H. & Kurban, A. K.: Mitotic behaviour of the buccal mucosal epithelium in psoriasis. Brit J Derm *85:* 162, 1971.
16. Kessler, R. H.: Effects of ischemia on the concentration of adenine nucleotides in the kidney of anesthetized dogs. Proc Soc Exp Biol Med *134:* 1091, 1970.
17. Krzanowski, J. J. Jr, Fertel, R. & Matschinsky, F. M.: Energy metabolism in pancreatic islets of rats. Diabetes *20:* 598, 1971.
18. Long, C. (ed.): Biochemist's Handbook, pp. 427, 507. Spon, London, 1961.
19. Rasmussen, H. & Nielsen, R.: An improved analysis of adenosine triphosphate by the luciferase method. Acta Chem Scand *22:* 1745, 1968.
20. Rassner, G.: Aktivitätsmuster von Enzymen des energieliefernden Stoffwechsels in normaler menschlicher Epidermis und bei Psoriasis vulgaris. Arch Klin Exp Derm *226:* 111, 1966.
21. Rauen, H. (ed.): Biochemisches Taschenbuch, 2nd ed., vol. 2, pp. 338, 361. Springer-Verlag, Berlin, 1964.
22. Seeger, P.: Variance Analysis of Complete Designs, pp. 67, 80. Almqvist & Wiksell, Stockholm, 1966.
23. Snedecor, G. W.: Statistical Methods, 5th ed., pp. 291, 394. The Iowa State College Press, Ames, 1956.
24. Strehler, B. L. & Totter, J. R.: Firefly luminescense in the study of energy transfer mechanisms. I. Substrate and enzyme determination. Arch Biochem Biophys *40:* 28, 1952.
25. Stüttgen, G.: Zur Atmung und Glykolyse der normalen und krankhaft veränderten Haut. Arch Klin Exp Derm *201:* 507, 1955.

26. Wettermark, G., Tegnér, L., Brolin, S. E. & Borglund, E.: Photokinetic measurements of the ATP and ADP levels in isolated islets of Langerhans. *In* The Structure and Metabolism of the Pancreatic Islets (ed. S. Falkmer, B. Hellman & I. B. Täljedahl). Pergamon, London, *2:* 275, 1970.

Received December 11, 1972

H. Hammar, M.D.
Department of Dermatology
Karolinska sjukhuset
S-104 01 Stockholm 60
Sweden