

use this dose 2 to 4 times weekly and not increase the dose during the treatment.

In this way the time it takes to heal patients gets longer and a larger percentage of the patients do not heal completely. Another possibility is to use this scheme for seven weeks and subsequently start increasing the light dose. In this way a large proportion of the patients do not unnecessarily receive a high PUVA-dose daily. Our present impression is that it is not the accumulated dose but the accumulated overdose that is important with regard to possible carcinogenicity.

We feel therefore that PUVA-treatment of psoriatic patients should definitely continue but that unnecessarily high PUVA-doses should not be given. With regard to the risks with PUVA-treatment one must keep in mind that other types of treatment for psoriasis do not seem completely innocent. Coal tar, so frequently used in USA, contains several carcinogens, and coal tar is a potent carcinogen on laboratory animals. UVB or sun therapy for psoriasis may be more or may be less dangerous than PUVA-treatment. We do not know today. More work on cellular genetic effects of different antipsoriatic agents made in as relevant a way as possible, is needed.

References

1. Baden, H. P., Parrington, J. M., Delhanty, J. D. A. & Pathak, M. A.: DNA synthesis in normal and xeroderma pigmentosum fibroblasts following treatment with 8-methoxypsoralen and long wave ultraviolet light. *Biochim Biophys Acta* 262: 247, 1972.
2. Parrish, J. A., Fitzpatrick, T. B., Tannenbaum, L. & Pathak, M. A.: Photochemotherapy of psoriasis with oral methoxsalen and longwave ultraviolet light. *N Engl J Med* 291: 1207, 1974.
3. Swanbeck, G. & Thyresson, M.: Induction of respiration-deficient mutants in yeast by psoralen and light. *J Invest Dermatol* 63: 242, 1974.
4. Swanbeck, G., Thyresson-Hök, M., Bredberg, A. & Lambert, B.: Treatment of psoriasis with oral psoralen and longwave ultraviolet light. Therapeutic results and cytogenetic hazards. *Acta Dermatovener (Stockholm)* 55: 367, 1975.
5. — Unpublished data.
6. Wolff, K.: Photochemotherapie der Psoriasis. *Deutsch-Schwedisches Symposium Photomedizin*, Oberursel, 1975.

Gunnar Swanbeck, M.D.
Monika Thyresson-Hök, M.D.
Department of Dermatology
Karolinska sjukhuset
S-10401 Stockholm 60
Sweden

Received March 18, 1976

Anders Bredberg, M.D.
Bo Lambert, M.D.
Department of Clinical
Genetics
Karolinska sjukhuset
S-10401 Stockholm 60
Sweden

An Immunohistochemical Study of the Skin of Healthy Individuals

In a Letter to the Editor (*Acta Dermatovener (Stockholm)* 55: 398, 1975) E. H. Beutner et al. criticized our article: "An immunohistochemical study of the skin of healthy individuals" (*Acta Dermatovener (Stockholm)* 54: 271, 1974) on several points. We should like to deal with each of these points in the following remarks.

On no occasion did we state that the fluorescence of the epidermal basement zone and blood vessel walls was *invariably* "conspicuous". Our micrographs naturally represent sections in which the staining patterns were most clearly observable. Although in the other biopsies the phenomena described were sometimes less distinct, they were always easily detectable to the experienced eye. Our experience in this field also covers a period of 12 years; at present two thousand biopsy specimens per annum are being processed in our laboratory.

The following considerations may help to explain the discrepancies between our observation and those made by Beutner et al.

1. Beutner et al. based their criticism partly on the assumption that the extensor surface of the forearm is not light-exposed, a view with which we do not agree. (Moreover our examination was carried out in the summer months of 1973.) One reason for choosing this particular part of the skin is the fact that this area of the (clinically uninvolved) skin is usually biopsied for diagnostic purposes in systemic lupus erythematosus. In biopsies of the skin of the back, a region generally less exposed to light, the IF staining patterns which are characteristic of this disease are less frequently demonstrable (Baart de la Faille-Kuyper, E. H., *Lupus Erythematosus*. An Immunohistochemical and Clinical Study of 485 Patients. Schotanus & Jens, Utrecht, 1969, pages 40 and 70). In biopsies of the skin of the back of healthy individuals we did not come across a single instance of the patterns mentioned for the skin of the arm with anti-IgG and anti-albumen reagents. The frequency of granular staining for IgM and of vessel wall staining with the anti-complement reagents was considerably lower. The use of anti-C3d and anti-C4,3 (=C4+C3c+C3d), however, revealed staining of the epidermal basement zone in all cases (unpublished observations). The foregoing seems to provide evidence that besides the choice of a particular part of the body

(rheological differences?). seasonal differences may play a role in the demonstrability of various IF patterns.

2. Differences in age also influence the appearance of certain IF patterns. In children under the age of 14 years we never observed the homogeneous patterns caused by deposition of IgG and albumen in the skin of the arm. However, in this age group, deposits of IgM are relatively more frequent at this site (unpublished observations).

3. The immunological specificity of the antisera is indeed one of the most serious pitfalls of immunohistochemistry. The statement of Beutner et al., that we did not mention the immunological characteristics of our reagents, is incorrect. It is hard to believe that none of the ten writers of the letter noticed that, when mentioning the subject of specificity of the antisera, we were referring to other articles.

4. Discrepancies between the results of experiments in which different anti-C3 reagents are used may be explained as follows: Most of the commercially available anti-C3 reagents are directed against C3c (see C. D. West et al., *J Immunol* 96:650, 1966). These investigators have "shown that titers of antibody to weaker determinants of β_1 C globulin (B and D) reach a peak within 6 to 10 days after booster immunisation with protein in adjuvant and then fall rapidly" . . . "antibody to the strong antigenic site (A) remains in high titer over long periods". Anti-C3c (=anti-A) fails to demonstrate very characteristic IF patterns in the skin of healthy individuals.

We wonder how R. H. Cormane, who subscribes to the views mentioned in the letter, can have missed the IF patterns described by us, since he

used the same anti-C reagents (Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam) as we did (see *Br J Dermatol* 87:466, 1972). The anti-C3d and the anti-C4.3 produced the patterns, described by us, up to dilutions of 1:180!

It is unlikely that 5 of our 23 healthy skin donors will be "prone to develop some sort of immune complex disease". We excluded the existence of autoallergic- or any other diseases in these persons. They are still in perfect health. On the other hand, we wish to stress that not all patients suffering from immune complex diseases have Ig-C complexes in their skin (Baart de la Faille-Kuyper et al., "Occurrence of vascular IgA deposits in clinically normal skin of patients with renal disease", *Kidney Int.*, in press).

We have no reason to fear that our observations will in any way impair the significance of IF examination of the skin for diagnostic purposes: on the contrary, an experienced observer will be able to distinguish between "physiological" and the well known pathological IF patterns.

Far from detracting from the value of our observations on normal skin, the criticism of Beutner and colleagues seems to emphasize their significance.

E. H. Baart de la Faille-Kuyper, M.D.

H. Baart de la Faille, M.D.

J. B. van der Meer, M.D.

Department of Dermatology

University Hospital

Catharijnesingel 101

Utrecht

The Netherlands

Received March 19, 1976