With intact skin, the flux calculated from the steady-state rate measurements and the total diffusion of hydrocortisone in 24 h were 50-fold larger. Furthermore, tenfold higher concentrations were encountered in untreated skin samples after 24 h (Table III).

DISCUSSION

From these data, we conclude that in hairless rats, follicles do not contribute significantly to the TEWL. According to TEWL data, the barrier function of the horny layer of the regrown skin should be normal. Furthermore, under our experimental in vitro conditions, hydrocortisone at 1% in an hydroalcoholic vehicle migrated mainly via the shunt pathway, as determined by its concentrations in the skin as well as by the flux through the skin. This indicates that in percutaneous absorption the shunt pathway may have, at least in the first 24 h, a far greater importance than generally assumed in the literature (1, 6).

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A Prospective Study of the Koebner Reaction and T Lymphocytes in Uninvolved Psoriatic Skin

BARBARA S. BAKER,[1] A. V. POWLES,[2] S. LAMBERT,[1] H. VALDIMARSSON[3] and L. FRY[2]

[1]*Department of Immunology, St. Mary's Hospital Medical School, and* [2]*Department of Dermatology, St. Mary's Hospital, London W2, England, and* [3]*Department of Immunology, Landspitalinn, Reykjavik, Iceland*

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T lymphocyte and dendritic cell subpopulations were counted in untraumatized, uninvolved skin of 27 patients with psoriasis. Eight of the patients proved to be Koebner-positive, as determined by tape stripping and punch biopsy, and 19 Koebner-negative. In the epidermis the CD4/CD8 T cell ratio was significantly higher in the Koebner-positive vis-à-vis Koebner-negative patients (median CD4/CD8=1.68 and 0.75, respectively: $p<0.05$). This resulted from a small increase in CD4 and a larger decrease in CD8 epidermal T cells in the Koebner-positive group. However, numbers of epidermal dendritic cells did not differ significantly between the two groups. In the dermis the CD4/CD8 T cell

ratio was also higher in the Koebner-positive than in Koebner-negative patients (median of 3.56 and 2.57, respectively). These findings demonstrate that the tendency of uninvolved skin of psoriatic individuals to become lesional after trauma is associated with a predominance of CD4 over CD8 T cells in the epidermis. (Received February 12, 1988.)

B. Baker, Dermatology Research, St. Mary's Hospital, Praed St., Paddington, W2 1NY, England.

Although poorly understood, it is well documented that localized psoriasis can develop after injury to uninvolved skin of psoriasis patients (Koebner reaction). Furthermore, all injured areas on a given individual, at a given point in time, react in a similar manner, suggesting that the Koebner reaction is regulated, at least in part, by systemic factors (1). We have recently postulated that the abnormal epidermal cell growth in psoriasis is induced by factor(s) released by activated CD4 T cells, subsequent to interaction with antigen-presenting Langerhans' cells in the epidermis (2). During growth, keratinocytes produce an Interleukin-1-like factor, ETAF (Epidermal Thymocyte-Activating Factor) which is a potent chemoattractant of T cells (3). In vitro production of this factor is low when keratinocytes are confluent, but can be greatly increased by disrupting the monolayer. In this way, injury to the skin could stimulate keratinocyte ETAF production, leading to an enhanced influx of T cells into the epidermis and initiation of a psoriatic lesion.

However, Eyre & Krueger showed that only 25% of unselected psoriasis patients which were injured and followed prospectively were Koebner positive (1). We were therefore interested to study the uninvolved skin of Koebner-positive and Koebner-negative psoriasis patients, prior to trauma, and determine whether Koebner reactivity might be correlated with numbers, distribution and activity of dendritic cell and T lymphocyte subpopulations.

MATERIALS AND METHODS

Patients

Thirty-seven patients with chronic plaque psoriasis of varying extent, who had received no systemic treatment previously and no topical treatment for at least 2 weeks, were tested for Koebner reactivity. The uninvolved skin on the back of each individual was tape stripped until erythema and glistening were observed; a 3-mm punch biopsy was removed from the uninvolved skin of the posterior upper arm at least 3 cm from a psoriatic lesion. The appearance of a psoriatic lesion at the site of injury was assessed clinically at 2-week intervals up to 6 weeks post-trauma; 8 out of 37 individuals (21,6%) proved Koebner-positive by this method. Furthermore, the results obtained by tape stripping and punch biopsy showed 100% correlation. The first 27 biopsies obtained were studied blind before the clinical results were known. In addition, biopsies of normal skin from 6 individuals undergoing minor surgery were also studied.

Counting of T lymphocyte and dendritic cell subpopulations

The punch biopsies were immediately frozen in liquid nitrogen and embedded in Tissue Tek II OCT compound (Lamb, London) and stored at −80°C. Sections were cut on a cryostat, air-dried for at least 30 min, and either stained immediately or stored at −80°C. T and dendritic cell populations were identified by a double-staining flourescence technique as previously described (4). In brief, chloroform/acetone-fixed sections were given 20-min incubations with biotin-conjugated Leu 2a (suppressor/cytotoxic T cells), Leu 3a (helper/inducer T cells) or OKT 6 (Langerhans' cells) monoclonal antibodies, followed by biotin-conjugated sheep anti-mouse antibody (Amersham, Bucks, England), and, finally, rhodamine-labelled avidin (Vector Labs, Burlingame, Calif., USA). The sections were then immediately stained for HLA-DR antigens by incubation for 30 min with monoclonal anti-HLA-DR (YE2/36 HLK) antibody (5), followed by flourescein-labelled rabbit anti-rat antibody. All sections were mounted in 10% phosphate-buffered saline in glycerol and examined under the fluorescence microscope. Total T cell and DR+ T cell numbers were counted in 50 high-power fields (using a ×50 objective) of the epidermis, and in the papillary and reticular dermis of a

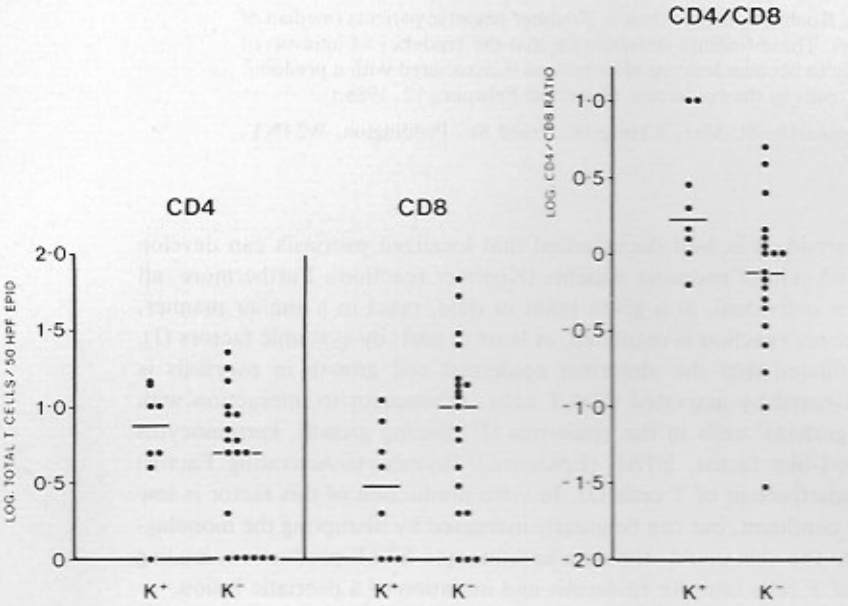

Fig. 1. Total CD4 and CD8 T cell numbers and CD4/CD8 ratios in the epidermis of uninvolved skin of Koebner-positive and Koebner-negative psoriasis patients prior to injury. Data are presented as $\log_{10}$ of values.

single 3-mm section. As the samples of normal skin were not 3-mm punch biopsies, but variable in size, it was not possible to compare their dermal T cell counts with those of uninvolved psoriatic skin. Epidermal dendritic cells expressing OKT 6 determinants, which were DR+ (DR+ T6+) or DR− (DR− T6+), were also counted in 50 high-power fields of epidermis.

Expression of results and statistical analysis

Each group of results was expressed as the median. The difference between groups of data was analysed using the Wilcoxon two-sample test.

RESULTS

T Lymphocytes

Epidermis. In the epidermis of 6 normal individuals, numbers of total CD8 exceeded those of total CD4 T cells (medians of 7 and 3 per 50 high-power fields, respectively) giving a median CD4/CD8 ratio of 0.45. Very few DR+ T cells were present in these biopsies.

The numbers of both total and activated (DR+) CD4 T cells in the epidermis of uninvolved skin from Koebner-positive (K+) psoriasis patients were moderately increased compared with those in Koebner-negative (K−) and normal epidermis. For total CD4 T cells the median values were 7.5 and 5.0, and for DR+ CD4 T cells, 2.5 and 2.0 per 50 high-power fields of K+ and K− epidermis, respectively (Fig. 1). The difference between the patient groups was not significant.

In contrast, total numbers of CD8 T cells were markedly lower in the epidermis of the K+ compared with the K− and normal groups; median CD8 T cell numbers were 3 and 10 per 50 high-power fields of K+ and K− epidermis, respectively (Fig. 1). Activated (DR+) CD8 T cells, however, were few in all biopsy specimens. Thus the ratio of CD4/CD8 T cells in the epidermis of the K+ patients was significantly increased compared with that of the K− patients (median CD/CD8) ratios were 1.68 and 0.75, respectively; $p<0.05$) (Fig. 1).

Dermis. In the dermis of uninvolved skin of psoriatic patients, similar numbers (per 3-mm section) of CD4 (median values of 31.5 and 36.0) and CD8 (median values of 10.5 and 14.0) T cells were present in the K+ and K− groups, respectively. As in the epidermis, there was a higher ratio of CD4 to CD8 T cells in the K+ patients (median CD4/CD8 T cell ratios were 3.56 and 2.57, respectively), but this difference was not statistically significant. In addition, a higher proportion of both CD4 (84% vs. 64%) and CD8 (47% vs. 20%) T cells were activated in the K+ than in the K− patients.

Dendritic cells. Numbers of dendritic cell subpopulations (DR+T6+ and DR−T6+) did not differ between Koebner-positive and -negative individuals (data not shown). Total dendritic cell numbers of both groups were within the normal range reported previously (4).

DISCUSSION

In agreement with a previous study (1), only 21.6% of psoriasis patients proved to be Koebner-positive by tape stripping and punch biopsy. Thus trauma alone is not sufficient to induce a psoriatic lesion. This study suggests that the balance between numbers of CD4 and CD8 T cells in the epidermis may be a contributory factor in determining whether an individual can mount a psoriatic responce to injury. In particular, a high concentration of CD8 T cells within this compartment appears to be associated with resistance to the development of a lesion. On the other hand a decrease in CD8 T cell numbers leading to a predominance of CD4 over CD8 T cells may lower the threshold required for the pathogenic process to proceed after injury.

The ratio of CD4 to CD8 T cells in the epidermis at any given time may be influenced by local factors such as the persistence of foreign antigen (eg. bacterial or viral) in the skin and/or by systemic factors. Systemic factors have been implicated in the Koebner reaction on the basis that all injured areas react in a similar manner on a given subject (1). Indeed, in this study there was 100% correlation between the results obtained with tape stripping and punch biopsy in an individual patient. Furthermore, Stankler reported that serum from patients recovering from psoriasis inhibits the Koebner reaction, whereas that from patients with active disease does not (6).

Thus it is conceivable that, under the influence of local and/or circulating humoral factors, the epidermal influx, distribution and activation of T cell subpopulations in the uninvolved skin of psoriatic individuals may contribute to their reactivity to injury.

It should be noted that, in contrast to an earlier study (4), CD4 T cells were observed in the epidermis of normal skin, although numbers were very small. This discrepancy is probably due to the fact that only five high-power fields rather than 50 were counted in the previous study.

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The Pharmacokinetics of Selenium in Psoriasis and Atopic Dermatitis

G. M. FAIRRIS,[1] PAULINE J. PERKINS,[1] ANDREA D. LAWSON[2] and G. M. BLAKE[2]

[1]*Department of Dermatology, Royal South Hants Hospital, Southampton, and*
[2]*Department of Nuclear Medicine, Southampton General Hospital, Southampton, Hampshire, England*

Fairris GM, Perkins PJ, Lawson AD, Blake GM. The pharmacokinetics of selenium in psoriasis and atopic dermatitis. Acta Derm Venereol (Stockh) 1988: 434–436.

The pharmacokinetics of [^{75}Se-L]-selenomethionine was studied in 10 patients with psoriasis, 10 with atopic dermatitis and 10 healthy subjects. Values for the gut absorption and the rate of endogenous excretion of [^{75}Se-L]-selenomethionine, the exchangeable total-body selenium and plasma selenium concentration showed no significant differences between either patient group and the controls. The results suggest that there is no gross abnormality of selenium pharmacokinetics in either disease, and fail to explain why previous studies have found reduced selenium concentrations and selenium-dependent glutathione peroxidase activity in psoriasis and atopic dermatitis. (Received April 5, 1988.)

G. M. Fairris, Department of Dermatology, Royal South Hants Hospital, Graham Road, Southampton, SO9 4PE, Hampshire, England.

A reduction in the activity of red cell selenium-dependent glutathione peroxidase (1) and the concentration of selenium in whole blood, plasma and leukocytes (2, 3) has been reported in patients with psoriasis or atopic dermatitis. We have investigated whether these changes might be associated with reduced gut absorption of selenium, increased endogenous excretion or reduced values of exchangeable total-body selenium.

PATIENTS AND METHODS

Ten subjects with psoriasis and 10 with atopic dermatitis who had been referred to the Department of Dermatology in Southampton were recruited to the study. Ten healthy controls, with no history of skin disease, were recruited from amongst hospital personnel. Each control was matched with one patient with psoriasis and one with atopic dermatitis as regards age and smoking habits. The study was approved by the Hospital's Ethical Committee. Only people between the ages of 25 and 65 years, who could not conceive, and who were not taking diuretics or any selenium-containing supplements were enrolled.

[^{75}Se-L]selenomethionine (Amersham International PLC) was chosen as a tracer of whole-body selenium kinetics as organic selenium is known to be the principal component of dietary selenium (4). Each subject received 20 kBq (0.5 μCi) of [^{75}Se-L]selenomethionine intravenously and a shadow shield whole-body counter (WBC) was used to measure total body retention 7 days later. The WBC measurements were used to determine the rate of endogenous [^{75}Se-L]selenomethionine excretion over this period. On the seventh day, each subject received an oral dose of 100 kBq (2.5 μCi) of [^{75}Se-