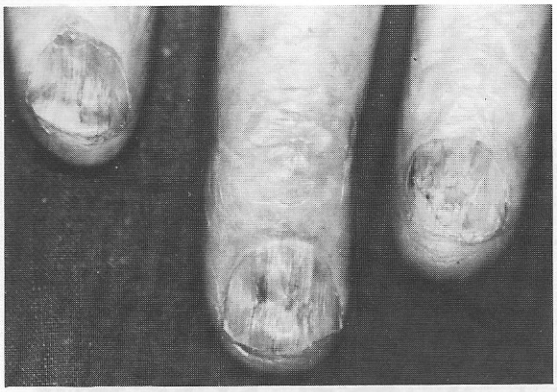

Fig. 3. Nail-changes of the same type as in Fig. 1 appearing 1.5 years after reinstitution of penicillamine.

14-year-old girl with Wilson's disease who, after 1 year of penicillamine treatment, developed lichenoid skin changes on her hands, legs and feet, nail-changes and stomatitis (3). The lesions disappeared when penicillamines was withdrawn. Because of a deterioration of the underlying disease, penicillamine had to be reinstituted whereupon the oral lesions as well as nail-changes recurred. The nails showed ridging, white streaks, fragmentation of the free end and pseudoseparation of the nailplate. Another type of nail-changes, "Yellow nail syndrome", has been reported with penicillamine by Lubach & Marghescu (4). Their patient had been treated with penicillamine for 2 years because of chronic polyarthritis when she developed a Yellow nail syndrome. Penicillamine was withdrawn and the nails were normalized about 6 months later. The causal relationship between the medication and the nail-changes was not tested with provocation.

The nail-changes in the present case thus show some resemblance to the changes described by Thivolet et al. (3) with longitudinal ridging, fragmentation and separation of the nailplate. In the present case a causal relationship has been proved since the same changes reappeared when penicillamine was reinstituted.

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Localized Bullous Pemphigoid, a T Cell-mediated Disease? Electron Microscopic and Immunologic Studies

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Two new cases of the rare, nonmucosal and nonscarring localized variety of pemphigoid are described. With reference to the data in the recent literature, the disease was classified as Localized Bullous Pemphigoid (LBP). The ultrastructural and immunologic findings are described and are briefly discussed in the context of the possible mechanisms leading to local subepidermal tissue injury in LBP. Although classical features of humoral responsiveness (in vivo bound IgG and complement at the epidermal basal membrane-zone (BM-zone)) were observed, a possible additional role of T cell mediated immunity in generating this local disease is considered.

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It is established that the nonmucosal forms of the localized varieties of pemphigoid can occur in two

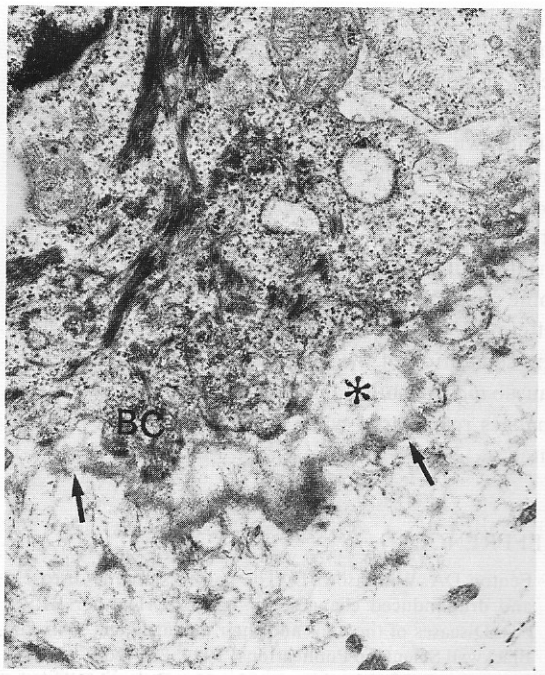

Fig. 1. Electronmicrograph (patient 2, ×8 760). * = Cleft formation. The floor of the blister is formed by the basal lamina (arrow). Half desmosomes are reduced. BC = basal cell.

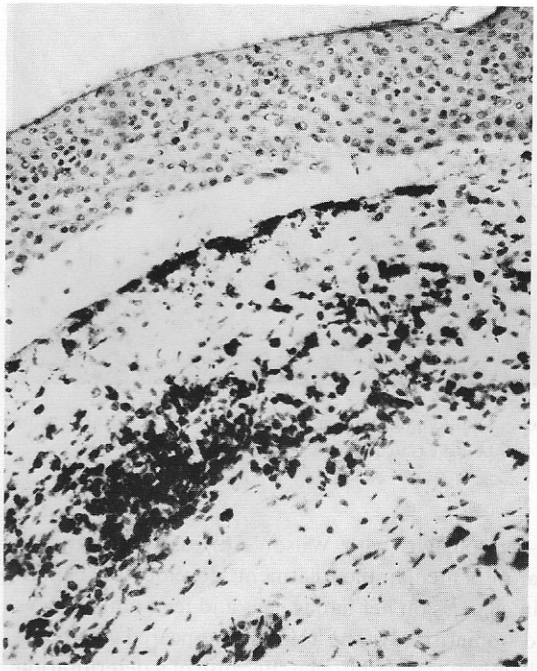

Fig. 2. PAP-method, Leu-3a staining (patient 2, ×192). Note the large number of Helper T (Leu-3a$^+$) cells in the upper dermis and also in connection to the basal membrane.

forms: one with blistering resulting in atrophy and scarring (Brunsting & Perry type) (1), and the other with nonscarring bullous lesions (2). In both varieties the direct immunofluorescence (DIF-method) is positive for IgG and/or complement, while the test for circulating basal membrane (BM)-antibodies is rarely positive (3). Salomon et al. (2) have recently summarized 31 cases of the latter nonscarring variety previously reported in the literature and have introduced the term localized bullous pemphigoid (LBP) for this disease. Here we discuss the clinical, histomorphological and immunological findings in two new cases that were classified as LBP.

CASE REPORTS

For three years, case 1 (male, 52 years) had suffered from localized, recurring, sharply defined erythematous, vesiculobullous and partly erosive eruptions accompanied by a burning sensation in the neck. The lesions resembled subacute eczema. Focally, hypopigmentation without atrophy or scarring was observed. The light-microscopy and DIF-examination of the area at the border of blistering skin was compatible with bullous pemphigoid. The histology revealed a predominantly lymphocytic infiltrate and some eosinophils were concomitantly present in the subepidermal areas of blister formation. Histologically, no atrophy or fibrosis was seen. In addition to IgG a linear BM-deposition of complement (C1Q and C3) was seen, but IgA, IgE and fibrinogen were absent. Circulating BM-zone antibodies could not be detected.

For about one year, patient 2 (male, 70 years) had suffered from a chronic eruption on the upper part of the back. There was one single circumscript bullous and erosive lesion (2 à 2 cm). Initially, a fixed drug reaction was considered. He had also had atopic dermatitis for years. The histology and DIF-findings of the area at the border of blistering skin were compatible with pemphigoid. In and around the subepidermal blister formation a predominantly lymphocytic infiltrate with a few eosinophils were observed. No signs of atrophy or fibrosis were seen. Linear IgG (IgG1 and IgG4) and C3 were seen in the BM-zone. IgG2, IgG3, C1Q, IgM, IgA, IgE and fibrinogen were absent. BM-zone circulating antibodies were absent.

Electron microscopy

The observations in both cases were comparable. In both cases the blister was formed by a focal separation of the basal cells from the basal lamina. The floor of the initial blister was formed by the basal lamina which showed irregularities and disruptions (Fig. 1). Half-desmosomes were totally lacking in the basal cells of the skin surrounding the blister in case 1 (Fig. 1). The half-desmosomes were reduced in number in case 2. The intercellular spaces between the basal cells and keratinocytes were widened in both cases.

In patient 2, additional immunological phenotyping of the

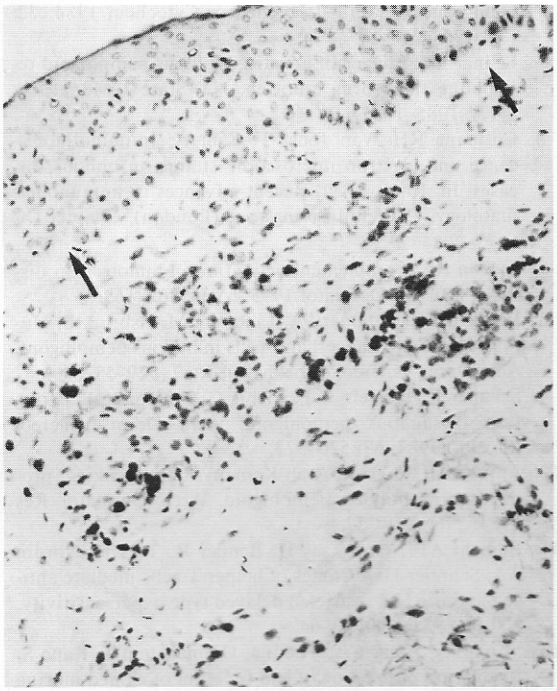

Fig. 3. PAP-method, Leu-2a staining (patient 2, ×187). A restricted number of Leu-2a$^+$ cells are present in the dermis. In areas of blister formation (arrows) no Leu-2a$^+$ cells are seen.

cellular infiltrate was performed (PAP-method) (4). Frozen sections were cut and immunostained by the indirect peroxidase method using monoclonal antibodies anti-leu 4, anti-leu 2a, anti-leu 3a, anti-leu 6, anti-HLA-DR, anti-HLA-DP, anti-HLA-DQ and anti-Interleukin-2 receptor (IL-2R) (Becton and Dickinson Monoclonal Center Inc, Mountain View, CA).

A large number of Leu-3a$^+$ cells (Helper T cells) were seen in the upper dermis at the site of blister formation in connection with the BM-zone (Fig. 2). Significantly lower numbers of Leu-2a$^+$ cells (Cytotoxic/Suppressor T cells) were seen scattered in the dermis. No Leu-2a$^+$ cells were seen at the BM-zone in the regions of blister formation (Fig. 3). Leu 6$^+$ cells (dendritic Langerhans' cells) were seen in the epidermis and also at the dermal site of the basal membrane. The majority of lymphocytic cells in the dermis were positive for HLA-DR, HLA-DP and HLA-DQ. Interleukin-2 receptor (IL-2R) positive lymphocytic cells and IL-2R bearing eosinophils, were also observed in the upper dermis. The lesions in both patients (cases 1 and 2) could be resolved within 1 week with topical corticosteroids (clobetasol propionate 0.05%) (Dermovate®-cream).

DISCUSSION

The location of the lesions in case 1 was similar to those in the cases described by Brunsting & Perry (1), but no scarring had developed during the course (four years!) of the disease. As far as we know, localized bullous pemphigoid (LBP) located on the back (case 2) has not been reported (2). LBP, clinically resembling a fixed drug eruption as was seen in case 2, has been observed by Fellner & Engber (5). The electron microscopic observations in LBP have not yet been described in detail. We observed a considerable disruption of the basal lamina (Fig. 1) in both cases at the sites of blister formation. These alterations of the basal lamina were similar to those observed in disseminated forms of bullous pemphigoid (6). In both cases a predominantly lymphocytic infiltration was seen.

In contrast to the most commonly disseminated variety of bullous pemphigoid (DBP), eosinophils in LBP occurred in significantly lower amounts. In DBP the formation of "antigen (BM-zone)-antibody-complement" complexes is thought to play a key role in the chemotaxis of eosinophilic granulocytes and the blister formation (7). Humoral immune responsiveness might be better understood in cases of DBP rather than in the cases of LBP. The predominance of mononuclear cells (T-lymphocytes) in the lesions of LBP and our observations in case 2, might evoke speculations on possible antigen presentation in situ to T cells and subsequently, as the consequence, the perpetuation of this local disease. However, also in DBP interesting observations have been described in favour of antigen presentation in situ. Emtestam et al. (8), reported a redistribution of Langerhans' cells towards the BM-zone and an increase of the total number of Langerhans' cells in the lesional skin. Other authors reported a significantly increased Helper T cell population and HLA-DR positive T cells in the peripheral blood and have suggested that Helper T cell activation might be involved in the acute phase of DBP (9). In addition, in DBP a decreased interleukin-2 (IL-2) considered to be due to IL-2 consumption has been reported (10). In DLT-hypersensitivity it is presumed that in the inductive phase the Helper T cells, upon presentation of antigen in the conjunction with HLA molecules (MHC system) by an antigen presenting cell, can develop into Inducer T cells (11). IL-2R can be expressed by T cells, but apparently also by nonlymphoid cells (12). Subsets of activated T cells may possibly produce eosinophilic differentiation factors responsible for the release of eosinophil precursors. In case 2, IL-2R was apparently also expressed on eosinophils. The observations in case 2 might favour antigen processing at the local level leading to T cell mediated recruitment of eosinophils.

The lack of leu-2a$^+$ cells in the region of active blister formation is against a role of Cytotoxic T cells in the injury of the BM-zone. The prompt response to topical steroids in the present cases of LBP has previously been described by others (3) and resembles the response to steroids in allergic eczema. This might possibly represent another argument in favour of an important role in localized bullous pemphigoid (LBP) of T cell mediated immunity in terms of antigen processing and tissue injury.

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Acitretin Monotherapy in Acrodermatitis Continua Hallopeau

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In a patient affected with acrodermatitis continua Hallopeau, acitretin (Ro 10-1670) monotherapy resulted in a complete clearance of pustulation at a dosage of 45 mg per day. At this dosage the leukotriene B_4-induced intraepidermal accumulation of polymorphonuclear leukocytes was markedly inhibited. ***Key words: Polymorphonuclear leukocytes; Chemotactic response.***

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Successful treatment with the aromatic retinoid etretinate in Acrodermatitis continua Hallopeau (ACH) has been reported in a few cases (1, 2). In this communication we describe the clinical results of acitretin (Ro 10-1670) in a case of ACH. In this patient the influence of acitretin therapy on the chemotactic response of polymorphonuclear leukocytes (PMN's) was assessed in an in vivo assay.

CASE REPORT

A 69-year-old white man presented with a 2-year history of progressing redness, scaling, and pustulation of his fingertips. The second and third finger of the right hand as well as the second finger of the left hand were involved. At first he had noticed a roughening of the nail plates and subsequently complete onycholysis occurred. Due to extreme tenderness and itching of the skin lesions the patient was severely handi-