

THE NATURE AND ROLE OF EPIDERMAL REGRESSIVE CHANGES IN THE DEVELOPMENT OF THE PSORIATIC LESION

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Abstract. Damaged epidermal cells present in psoriatic lesions were investigated using histochemical and histomorphological methods including ultrathick sections. In early lesions these cells were found throughout the epidermis, being particularly numerous in the upper part of the latter and around the adnexa. In a later developmental stage the damage to the keratinocytes in the suprapapillary region was found to precede the damage to the basement membrane. These findings, together with the difference between the damaged keratinocytes lining the ascending side and the venous limb of the papilla respectively with regard to degree of severity of the damage, suggest that blood stasis is the cause of the regressive changes in the suprapapillary epidermis. The enzymatic activity of non-specific esterases and acid phosphatases was increased and that of succindehydrogenases and DPN-diaphorase was decreased in damage keratinocytes. The significance of these findings in relation to the genesis and development of psoriasis is discussed. The view is expressed that there is a causal relationship between damage to the epidermal cells and proliferation of epidermis.

Damaged epidermal cells (DEC) found in psoriatic lesions (PL) have been assumed to be the sequel of exudation and leukocytic immigration, leading to parakeratosis and Monroe-abscesses (10, 11, 15). It has been shown that parakeratosis is not due to accelerated epidermopoiesis and shortened cell transit time (2). It has also been demonstrated that parakeratosis incorporates damaged keratinocytes (10, 11). The view has been expressed that the alternation of orthokeratosis with parakeratosis is caused by a rhythmic suprapapillary exudation (10). The question as to why only some isolated capillaries exudate has not yet been answered. This paper discusses an alternative pathomechanism assumed to be involved in the genesis of damaged epidermal cells and sequels of the latter.

MATERIAL AND METHODS

Samples from lesions were taken by punch biopsy. The specimens were carefully selected so as to ensure that the lesions satisfied the criteria of psoriasis vulgaris.

Histochemical studies

Ten specimens of both early and developed psoriatic lesions were histochemically studied with special reference to the presence of damaged keratinocytes. Immediately after removal they were frozen by immersion in dichlorodifluoromethan cooled by liquid nitrogen, kept in a refrigerator at 90°C, sectioned on a Harris cryostat and stained for the following enzymic activities:

Non-specific esterases
Acid phosphatases (Gömöri)
Succinic dehydrogenase (SDH)
DPN diaphorase.

Marks et al. (8) investigated keratinocytes on the basis of the observation that the activity of non-specific esterases and acid phosphatases was increased whereas that of SDH and DPN diaphorases was decreased in damaged keratinocytes. In the present investigation special attention has also been paid to the activity of these enzymes in damaged keratinocytes.

Histomorphological studies

48 specimens of papules 1-3 mm in size were stained with hematoxylin eosin, van Gieson, and PAS for light microscopy. Three specimens were fixed in 3% glutaraldehyde buffered to pH 7.4 with 0.1 cacodylate buffer and post-fixed in 1% OsO₄. Thereafter they were dehydrated by washings in graded ethanol solutions and embedded in epoxy resin. Ultrathick sections were made on the LKB ultratome and stained with 1% toluidine blue.

RESULTS AND COMMENTS

Defective basement membranes associated with suprapapillary DEC have been considered to be evidence that exudation and leukocytic immigration causes damage to these cells (10, 11). However, in this investigation it was found that the papillary basement membrane may remain intact and does not show any signs of thickening in the presence of DEC (Fig. 1). The behaviour of the papillae may differ inasmuch as one papilla may cause DEC of varying degrees of severity, while the adjacent one remains inactive. This difference in the behaviour of papillae has so far not been observed in dermatological disease of a clear-cut inflammatory-exuda-

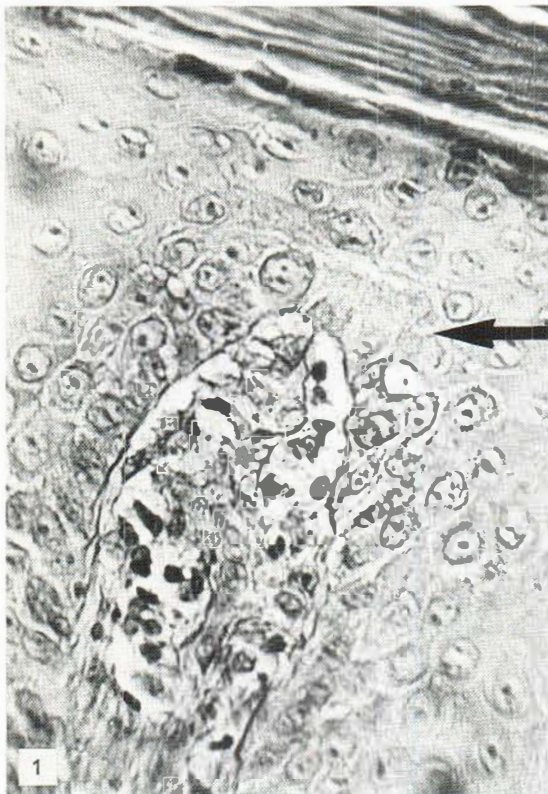


Fig. 1. Beneath the parakeratotic layer downwards to the tip of the papilla and the right side of the latter, damaged keratinocytes showing widened intercellular spaces and a thin uninterrupted basement membrane are shown.

tive nature. The selectivity of the papillary behaviour indicates different stages in the development of the pathological process, depending on the length and thickness of the rete ridges enveloping the papillae and the elongation, tortuosity and dilatation of the papillary capillaries. The latter state causes intravascular stasis. The stasis again causes deficient nutrition of the overlying epidermal plate and leads to damage to adjacent keratinocytes. In the next evolutionary stage destruction of the basement membrane and a necrotactic invasion of leukocytes may occur. The epidermis adjacent to the straight part of the papillary basement membrane showed no signs of spongiosis, whereas in the epidermis at the tip of the papilla and in the bulging part effaced cell structures and spongiosis are seen (Fig. 2). This indicates that the site of DEC is on the venous limb of the papillary capillary resulting from intravascular stasis. A further finding was papillae with double-arched tips, the left arch being short

and the right one wide, the latter showing signs of impaired cell quality and oedema in the adjacent epidermis (Fig. 3). The formation of parakeratosis over this tiny zone occurs in the next stage in the development of the disease. The epidermal area above the rete ridges often shows orthokeratosis. This, together with the above discussed observation of parakeratosis at the tips of the papillae, clearly explains the alternation of orthokeratosis and parakeratosis.

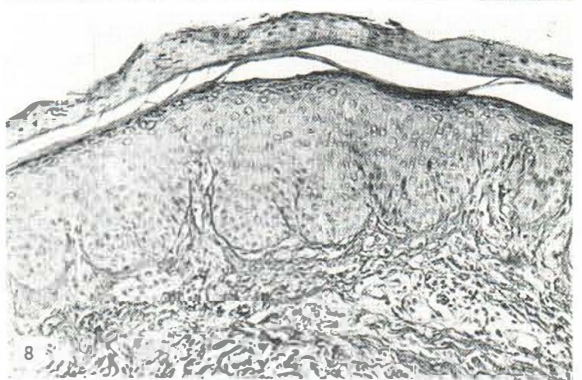
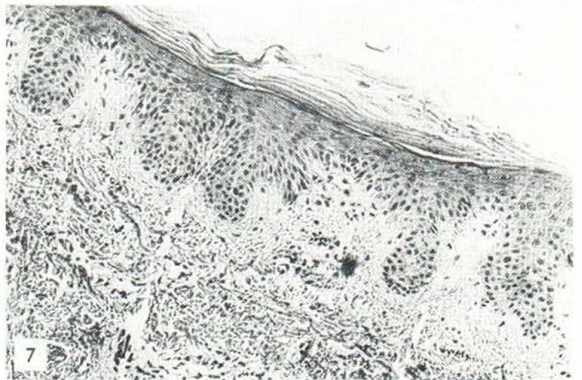
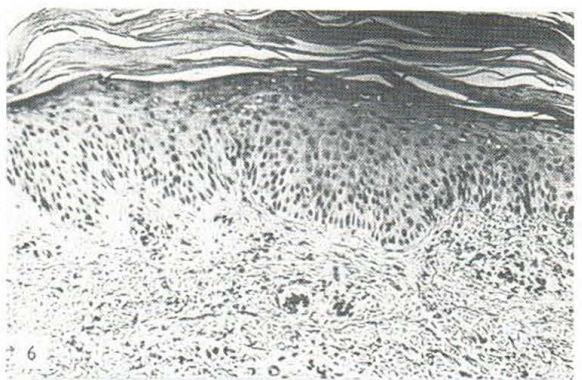
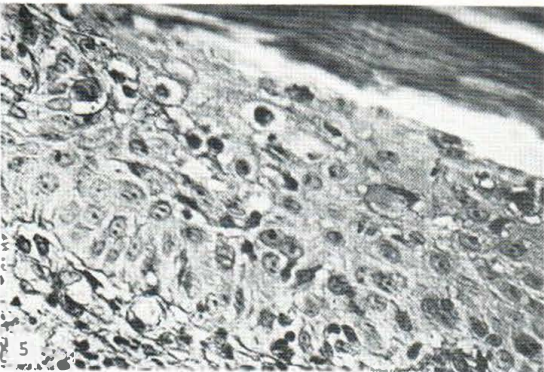
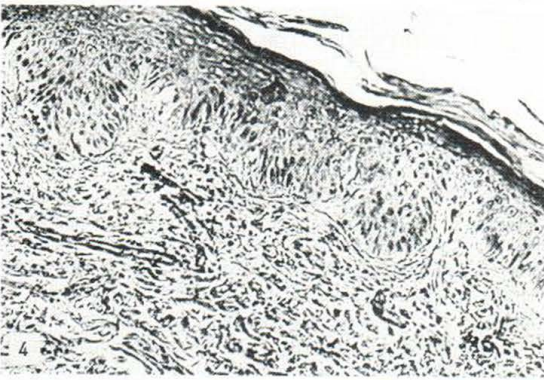
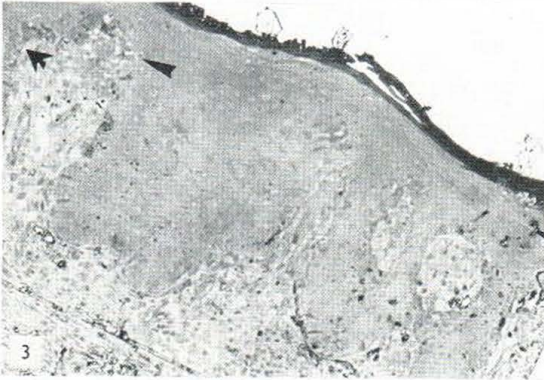
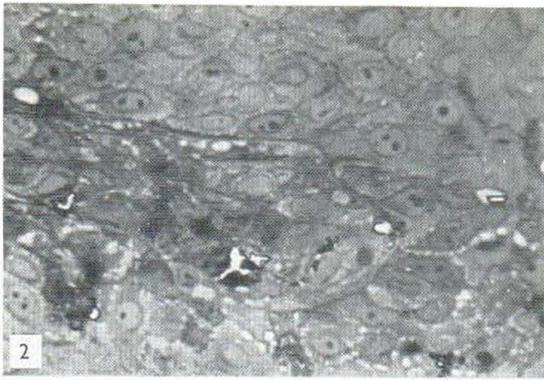
The sections of initial and early lesions showed a variety of changes which essentially reflect three evolutionary stages in the development of the disease. In the first stage a zone of damaged keratinocytes in the upper epidermis is visible; these are associated with no or only minute changes in the basement membrane (Figs. 4, 5), thus suggesting that the damage to the cells is toxic in character.

In the second stage proliferative changes are seen. The rete ridges beneath the damaged zone show a tendency to lengthen (Figs. 6, 7). An inflammatory reaction in the upper part of the corium may coexist with these changes.

In the third stage the detached parakeratotic zone is shown which represents the original necrobiotic zone. Beneath the latter an acanthotic epidermis is seen (Fig. 8).

Pinkus et al. (11) found in early psoriatic lesions a mound of parakeratotic cells which usually contained masses of leukocytic nuclei. This observation was confirmed in all my sections of early lesions, the mound invariably being situated at the orifices of the adnexa (Figs. 9, 10, 11, 12). Histochemical studies on damaged epidermal cells present in mature PL demonstrated that the activity of SDH and DPN diaphorases in the epidermis at the tips of the papillae (Figs. 13, 14) and throughout the middle and upper part of the epidermis was weaker in early lesions than in normal epidermis (Fig. 15).

A double-arched papilla and a decreased SDH and DPN activity were observed in a lighter zone of keratinocytes, extending towards a focal parakeratotic disc (Fig. 16). There was evidence of non-specific esterase and acid phosphatase activity in a zone of keratinocytes extending along the acrosyringium as far as the lower part of the acanthotic rete ridge (Figs. 17, 18). A marked enzymatic activity in some detached keratinocytes in the periadnexal zone indicated dissolution of damaged cells and suggested that the keratinocytes



above the bulging, right side of the papilla. (Ultrathick section.) Fig. 3. Normal palissading of basal cells to the left of the widened, double-arched papilla (arrow) and basal colligation on the part corresponding to the bulging side (arrow head). (Ultrathick section.) Fig. 4. Early psoriatic lesion showing a continuous zone of damaged keratinocytes with picnotic excentric nuclei, effaced cell contours in the upper part of the epidermis and signs of a mild inflammatory reaction in the upper corium. Fig. 5. Early psoriatic lesion showing severe necrobiotic changes in the upper part of the epidermis and a thin uninterrupted basement membrane. Fig. 6-7. Early psoriatic lesion in the second developmental stage showing irregular acanthosis, hypogranulosis, orthokeratosis and parakeratosis, and signs of a mild inflammatory reaction in the upper corium. Fig. 8. Elimination of the parakeratotic layer en bloc, regular acanthosis and signs of a mild inflammatory reaction in the upper corium.

Fig. 2. A thin uninterrupted basement membrane, widened intercellular spaces and damaged cells in the area

adjacent to the acrosyringium are particularly exposed to toxic influences. It has previously been reported that microabscesses showing mild spongiosis have a predilection for the acrosyringium (9). The view has been expressed that there is a quantitative relationship between microabscesses and pustular psoriasis (3, 4, 6, 7) and that the acrosyringium is involved in the formation of the pustules (9, 14). The migration of leukocytes to the spongiform pustules has been considered to be a necrotactic reaction to epidermal cytolysis (9, 12).

DISCUSSION

Damaged keratinocytes at the tips of the papillae and in the area surrounding them were found to be asymmetrically distributed. The epidermal cells above the straight part of the basement membrane lining the rete ridges, showed no changes at all (or only minute ones) in some sections, whereas those in the bulging part, which probably corresponds to the descending venous limb of the capillary, showed signs of a necrobiotic process. Double-arched papillae represent an extreme deformity of the bulging part of the papillae. Due to the tortuosity of the papillary capillaries the papilla may bulge on either side. This suggests the presence of blood stasis resulting in decreasing the oxygen tension (13) in the elongated, dilated and distorted venous limb of the papillary loop. Insufficient energy supply, therefore, gives rise to a lytic process in the keratinocytes, the nutrition of which depends on the particular capillary providing it. The alternation of regressive epidermal changes at the tips of the papillae and reactive regeneration of the adjacent rete ridges, reflect a vicious circle which results in the maintenance of the lesion. This vicious circle brings about a long-lasting Koebner system incorporated in the psoriatic lesion. The decrease in SDH and DPN activity in the area over the tips of the papillae was found to be correlated to the elongation and/or width of the papillae. In early lesions the activity of SDH and DPN diaphorase was found to be decreased throughout the upper part of the epidermis with that in the adjacent, normal epidermis. There was an increased non-specific esterase and acid phosphatase activity in a broad zone along the epidermal part of the adnexa and at the tips of the papillae. Some detached keratinocytes in the periadnexal zone also showed increased enzymatic activity. This indicates a tendency to



Fig. 9. Early psoriatic lesion showing a mound of parakeratosis and leukocytic nuclei in its centre. A hair follicle is seen, extending to the centre of the mound.

Fig. 10. Early psoriatic lesion showing a mound of parakeratosis and a microabscess in its centre. A dilated adnexum in the upper part of the corium is seen, filled with parakeratotic cells in a zone corresponding to the centre of the mound (arrow). Fig. 11. Detail of Fig. 10. A mound of parakeratosis and leukocytic nuclei, a necrobiotic zone in the upper part of the epidermis and rete ridges showing signs of lengthening, a dilated and hypertrophied adnexum filled with a compact parakeratotic cell mass, cell disarrangement and necrobiosis in the hypertrophied wall are all visible. Fig. 12. A parakeratotic mound in the adnexal orifice, surrounded by a zone of vacuolized cells with pycnotic nuclei in the upper part of the epidermis. Fig. 13. Decreased SDH activity above the tips of the papillae (arrows). Fig. 14. Decreased DPN-diaphorase activity above the tips of the papillae. Fig. 15. Early psoriatic lesion showing decreased DPN-diaphorase activity in the upper part of the slightly acanthotic epidermis and increased enzymatic activity in the normal epidermis. Fig. 16. Double-arched tip of papilla. A lighter zone is visible above the bulging side of the papilla. It is seen to extend upwards to the parakeratotic zone and represents decreased DPN-diaphorase activity. Fig. 17. Increased non-specific esterase activity in a broad zone around the epidermal part of the adnexum and in some detached cells in the adjacent epidermis (arrows).

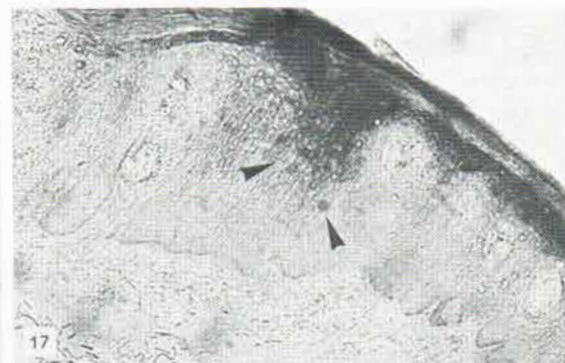
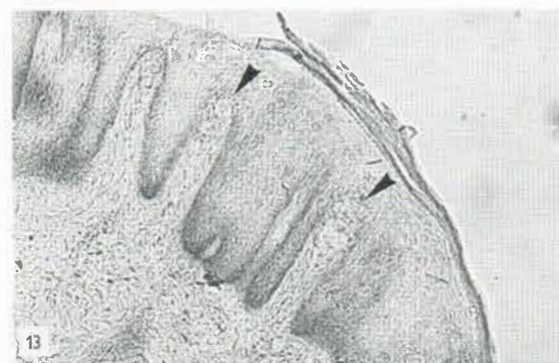
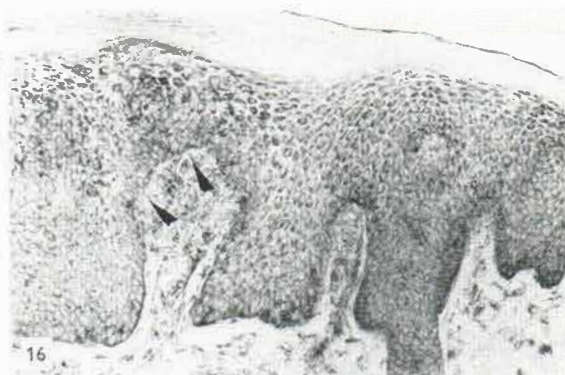
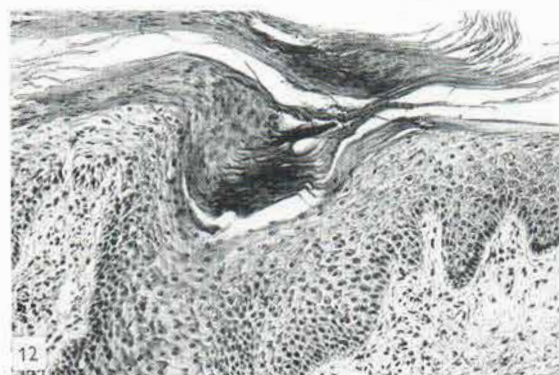
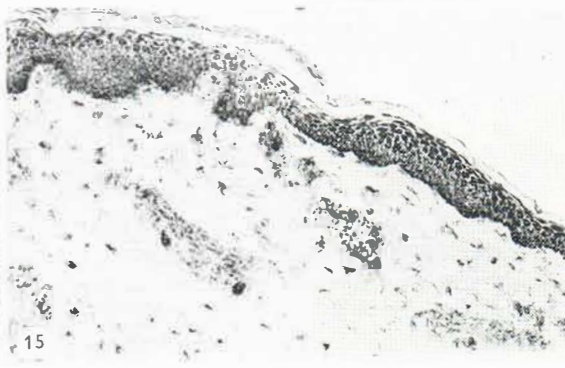
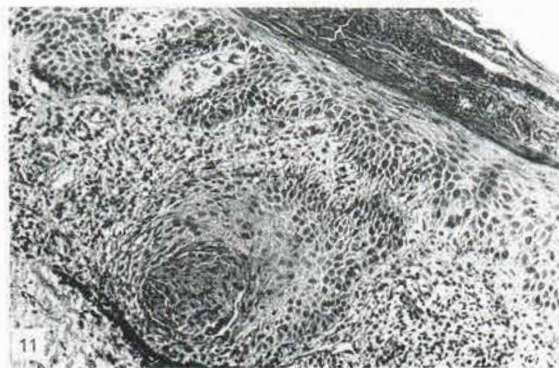
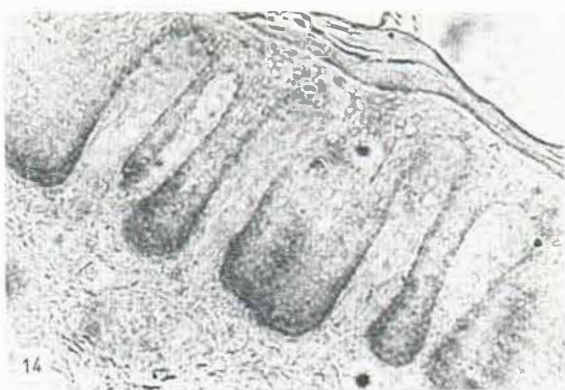
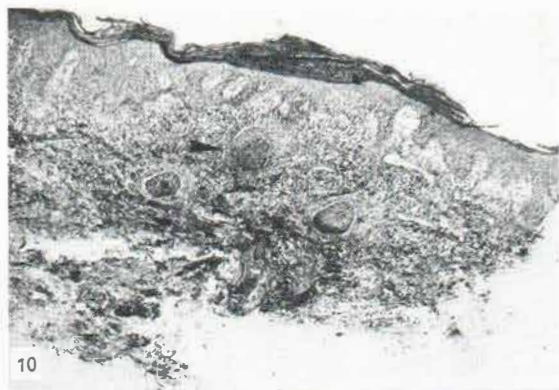




Fig. 18. Positive acid phosphatase activity is shown in some cells adjacent to a hair follicle (arrow).

wards necrobiotic cell detachment in this area. The elimination of the necrobiotic upper stratum of the epidermis en bloc and replacement of the latter by a detached parakeratotic plate, which was observed in early lesions, together with the rapid onset of a reparative regeneration of the epidermis brings to mind the events involved in a mild Lyell's necrolysis. It has previously been reported that the susceptibility of the upper epidermal layer to histiotoxic influences is greater than that of the lower part (1). A mound of parakeratotic cells intermingled with masses of leukocytic nuclei was often found in early lesions and was invariably situated at the orifices of the adnexa. The abundant blood supply of the area around the adnexa appears to act as a channel, enhancing the transport to the epidermis and the concentration of histiotoxic agents in the latter. The findings in this investigation suggest that two necrobiotic mechanisms are involved in the origin of the damage to the epidermal cells in PL, viz. a toxic mechanism in early lesions and a hypoxibiotic one due to papillary stasis in the mature PL. In the early stage the damage may be caused by the action of infectious or other endogenous histiotoxic agents on the epidermis. It is well known that microabscesses may be absent in mature psoriatic lesions. If they are present in the latter it may be assumed that a histiotoxic agent keeps on damaging the epidermis. On the basis of this hypothesis the transformation of the microabscess into pustular psoriasis by an excessive inflow of toxic agents into the epidermis would be expected in these cases. The findings throughout the developmental stages of the psoriatic lesion suggest

that proliferation of epidermal cells in PL is invariably linked to DEC and is not autochthonous in character.

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