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STUDIES ON THE ULTRASTRUCTURE OF PSORIASIS AND OF THE "NORMAL" SKIN OF PSORIATICS

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Abstract. Biopsy specimens from the psoriatic plaques and from the normal skin of the same 12 patients were studied by means of electron microscopy. Beside the well known characteristics of psoriasis, the morphological signs of cytolysis have been found. The electron microscopic changes of the symptom-free regions might be explained partly by the elevated mitotic rate and partly by a slight lysis. The possible role of cytolysis and of lysosomes, respectively, is discussed, although further investigations are considered necessary to prove it.

The ultrastructure of psoriasis does not seem to be cleared up in every respect although the main characteristics have been described by several authors (6, 9, 10, 14, 16, 25, 29). Furthermore, some data indicate that the clinically symptom-free skin sites of psoriatics show certain alterations which can be summarized in the term 'latent' or 'subclinical psoriasis' (3). Thus it is known that in the dermis the number of nerve fibres and Schwann cells is increased (27, 28), and the capillary network is changed both morphologically (23) and functionally (12). As regards the epidermis, differences have been found in the uptake of tritiated thymidine (1, 11), in the DNA content (30), in regeneration capacity (4), and in the reactions following the local application of vitamin A (21) as compared with normal skin.

No data are available, however, about the ultrastructural differences between the normal and the psoriatic's symptom-free skin. Therefore the aim of our present work was to analyse the electron microscopic structure of the psoriatic lesion as well as the lesion-free areas of the same patients. Some preliminary results of our investigations have been demonstrated at the Fourth Symposium on Dermatology, Brno (18).

MATERIALS AND METHODS

Our material was obtained from 12 patients suffering from psoriasis. Ten of them had not received any therapy at the time of, or prior to, the excision, while the remaining 2 were in the fourth and sixth week of treatment and showed considerable improvement as regards the symptoms. In 3 cases we repeated the excision in a completely symptom-free period of 8 months.

The biopsy specimens were taken from the lesions of the forearm and at the same time from the normal skin at a distance of at last 5 cm from the plaque.

The material was fixed in 3% glutaraldehyde in 0.1 M phosphate buffer at pH 7.2 for 4 hours at 4°C, washed in the same buffer solution overnight, postfixed in 1.5% OsO_4 buffered with 0.2 M *s*-collidine at pH 7.2 for 2 hours at 4°C. Dehydration was carried out with ethanol and propylene-oxide, embedding in Durcupan AMC. Sections were cut on an LKB Ultrotome III, contrasted with uranylacetate and lead citrate according to Reynolds (22). Micrographs were taken with a TESLA BS 413 A electron microscope.

RESULTS

1. *Psoriatic plaques*

Alterations can be found in every layer of the psoriatic epidermis.

The lamina basalis showed a considerable loosening manifested in the presence of a much wider space between the cell membrane and the former. The multilayering of the basal lamina is conspicuous, too.

In the layers of the living epidermis a well defined widening of the intercellular space was found (Fig. 1). This causes a bridge-like occurrence of the desmosomes between the adjacent cells. In the intercellular space a fine granular substance of varying electron density is to be seen. There are many desmosomes which have lost their contact with the opposite cells and with the

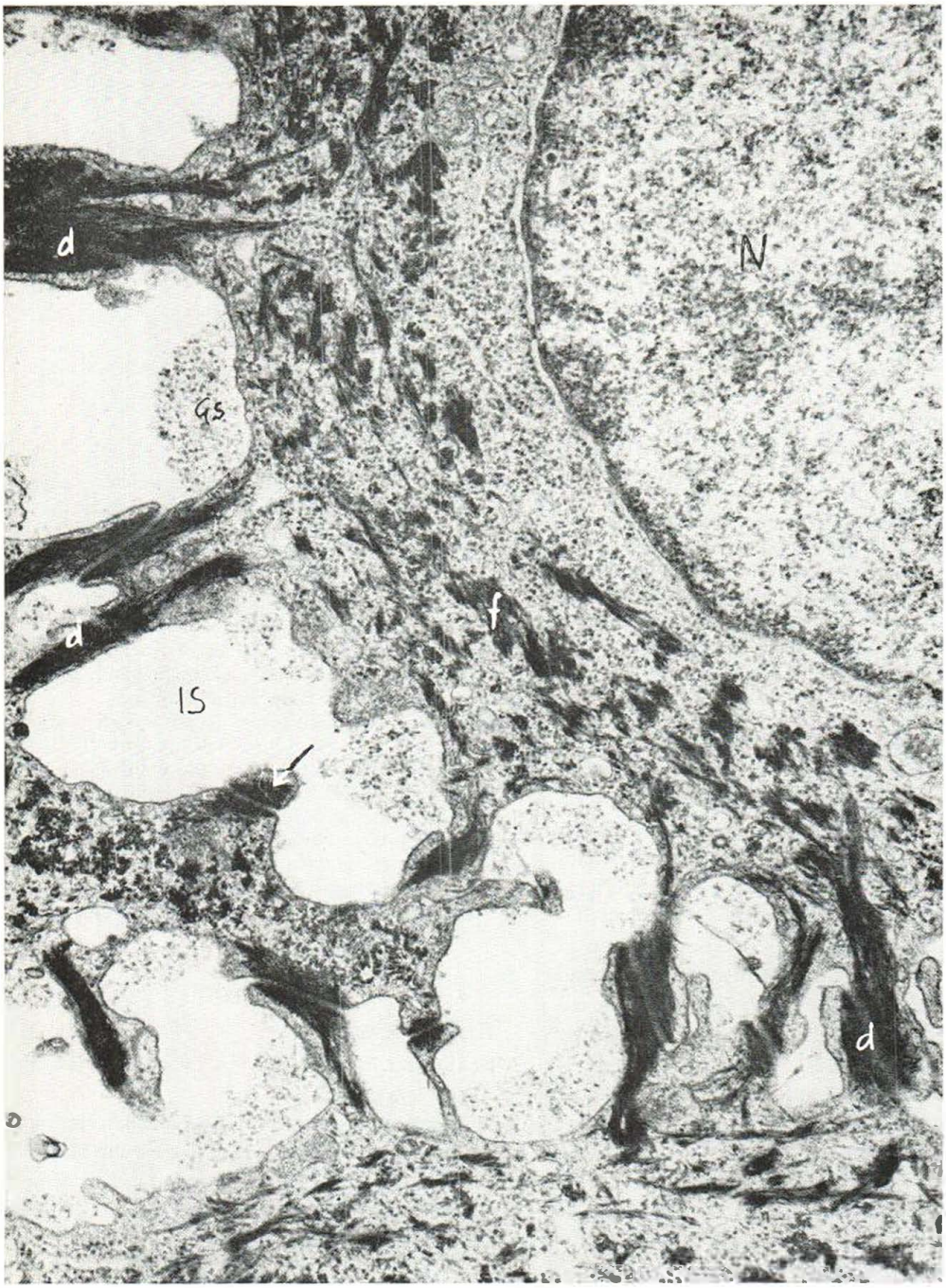

Fig. 1. Widened intercellular spaces (*IS*) in the spinous layer. The stretched desmosomes (*d*) have a bridge-like appearance and some of them have lost contact with the adjacent cells as well as with the tonofibrils (*arrow*). *f*, tonofibrils; *Gs*, granular substance; *N*, nucleus. × 27 000.

tonofilaments too. In general, the numbers of desmosomes and tonofilaments have decreased.

In the epidermal cells the cytoplasm shows a considerable vacuolization. The vacuoles are sometimes small and without any content, in other cases they are much larger and contain a fine

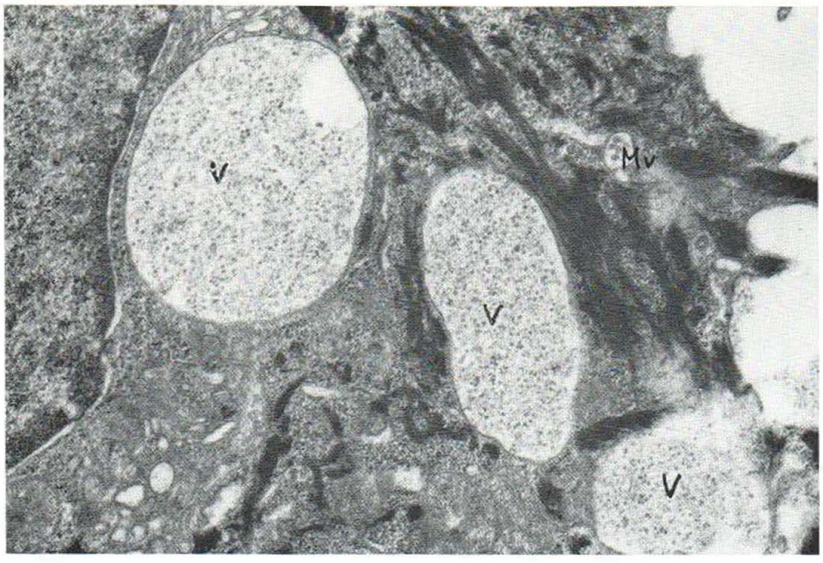

Fig. 2. Membrane-limited large vacuoles (*V*) in the cytoplasm of a spinous cell containing granular material. *M*, multivesicular body. × 18 000.

granular substance resembling the content of the intercellular space (Fig. 2). In properly orientated sections one can observe the communication of the intracellular vacuoles with the cell surface forming an exocytosis-like morphological phenomenon (Fig. 3).

Beside the lytic vacuoles, different degrees of cell alterations were found in every specimen of our material. The mildest was a discrete perinuclear lysis (Fig. 4), and in several cases it extended onto the whole cytoplasm. In such cells the lysis of the nuclei was also apparent (Fig. 5). The place of the necrotic epithelial cells was occupied by immigrated inflammatory cells (Figs. 6, 7). The tonofilaments and keratohyalin granules are relatively resistant to these lytic processes, whereas the organelles of common cell functions—mitochondria, endoplasmic reticulum, ribosomes etc—are very soon involved.

The numbers of membrane-coating granules (Selby-Odland bodies) have increased in the upper spinous layer and the multivesicular bodies were also common here.

The number of keratohyalin granules is reduced

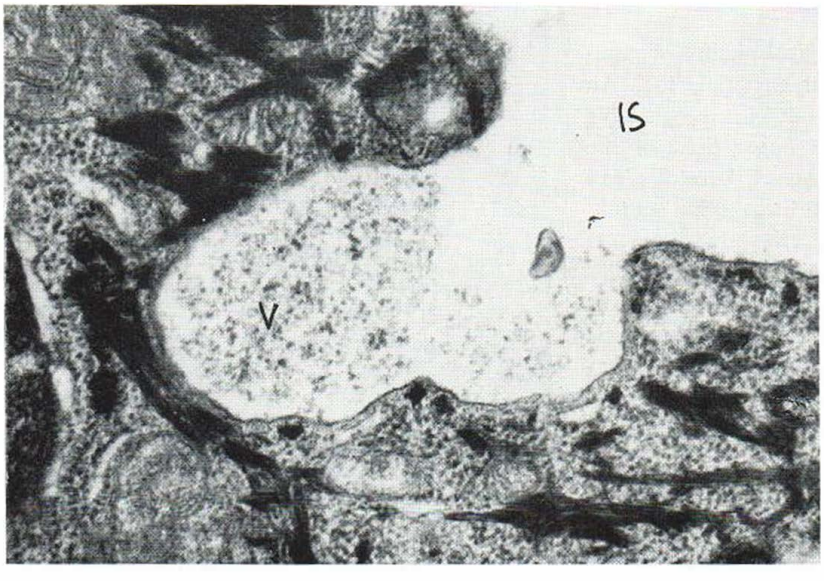

Fig. 3. The communication of an intracellular large vacuole (*V*) with the intercellular space (*IS*). × 39 200.

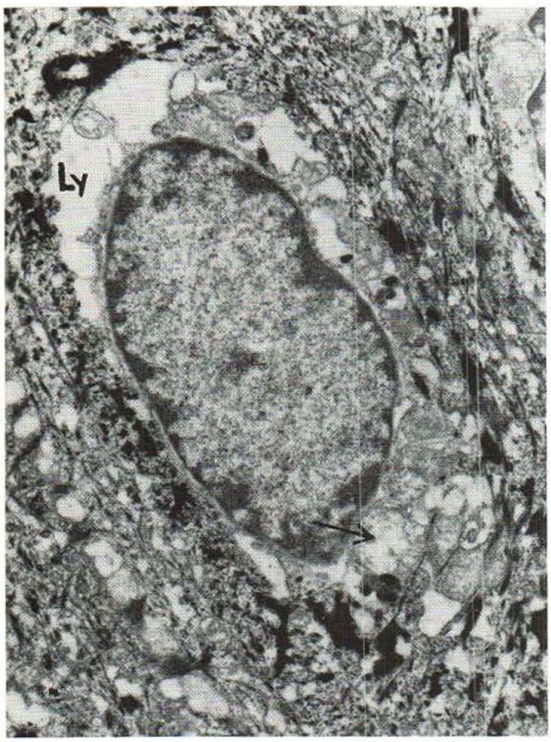

Fig. 4. Lysis (*Ly*) in the perinuclear region. Arrow indicates swollen mitochondria with crystolysis. × 8 800.

and their size is considerably smaller as compared with intact epidermis.

Another conspicous feature of the psoriatic lesion is the almost complete absence of melanin granules in all layers of the epidermis—a fact that might explain the leukoderma usually seen after the healing of the plaques.

The well known morphological picture of parakeratosis was present in our material, too. An incomplete keratinization results in recognizable cell components even in the upper parts of the horny layer. A peculiar form of keratotic cell was found in our material: these cells contain a great number of irregularly orientated filaments of high electron density in seemingly empty spaces or in osmiophobe material (Fig. 8). They are most probably the equivalents of the B type horny cells described by Orfanos (19) although their structure is more irregular and looser.

2. *Symptom free-areas*

Our investigations showed un-animously that these regions were also considerably involved from an ultrastructural point of view. Some of the above-related pathological changes were present in the "normal" skin of patients suffering from active psoriasis, and in the advanced stages of improvement as well as even in the totally symptom-free period of 8 months. The ultrastructural changes were more pronounced in the lower part of the epidermis while the upper spinous and granular layers and the stratum corneum in general appeared to be relatively intact.

The lamina basalis is similar to that of the psoriatic plaque, namely it is swollen and not so clearly outlined as in normal skin. At several places a multilayering of the lamina basalis can also be observed.

The most characteristic pathological phenomenon is the considerable widening of the intercellular spaces and the presence of fine granular substance in it (Fig. 9). Numerous microvilli-like protrusions are to be seen on the surface of the epithelial cells which as a rule do not have any contact with the adjacent cells.

A great number of desmosomes display con-

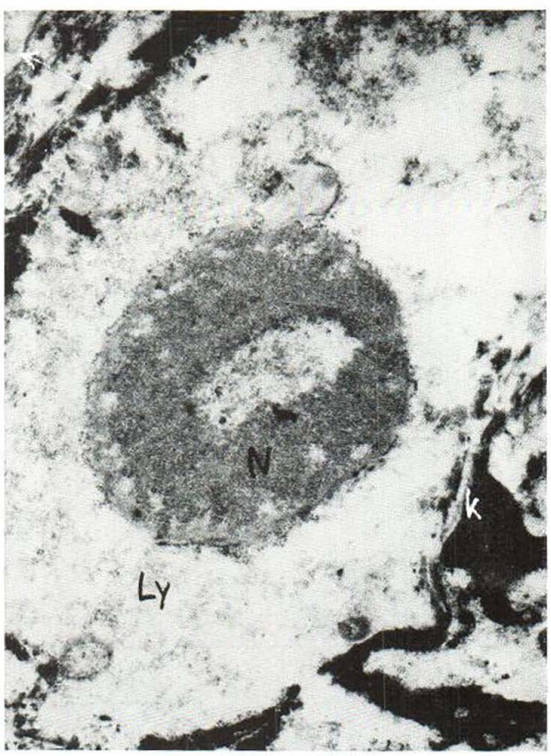

Fig. 5. Granular cell in the state of almost complete lysis (*Ly*). *N*, the remnant of the nucleus; *k*, keratohyalin; →, cell membrane. × 16 400.

spicuous disintegration, while others, appearing to be of intact structure, have lost their connection with the tonofilaments.

The vacuolisation of the cells is evident in different degrees. Single vacuoles, large confluent areas (Fig. 10), or even perinuclear lysis of the cytoplasm can be seen in a great number of the cells. The tonofilaments are not so well orientated as in the normal epidermis and the structure of keratohyalin suggests some alteration of its composition. The increased number of membrane-coating granules is apparent. A normal quantity of melanin granules is present.

The deepest parts of the horny layer are somewhat loosened as compared with normal stratum corneum. In other respects the horny layer seems to be normal, apart from the presence of some horny cells with filamentary inner structure seen also in the psoriatic lesion.

DISCUSSION

Our results concerning the psoriatic lesion are in accordance with the data of other authors (6, 9, 10, 14, 16, 25, 29) apart from the morphological expression of lytic processes which has been accentuated in our material and had not been mentioned hitherto except in the paper of Tsvetkova et al. (26). In agreement with the latter we have found that in the psoriatic lesion proliferating and lytic areas alternate. The ratio between these two processes seems to be in relation to the type of the disease, i.e. while in the invasive forms the lytic process predominates, in lesions of static character proliferation proceeds according to the above authors.

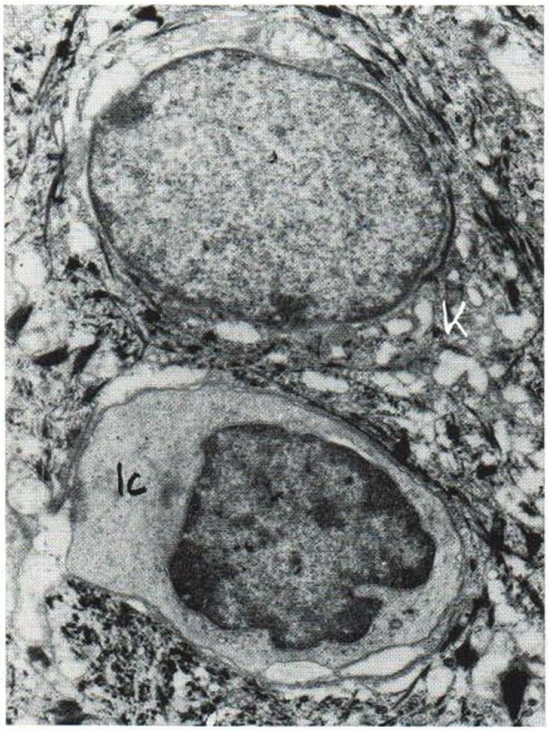

Fig. 6. Immigrated cell (*lc*) among the keratinocytes. *K*, keratinocyte with cytoplasmic vacuolisation. × 8 640.

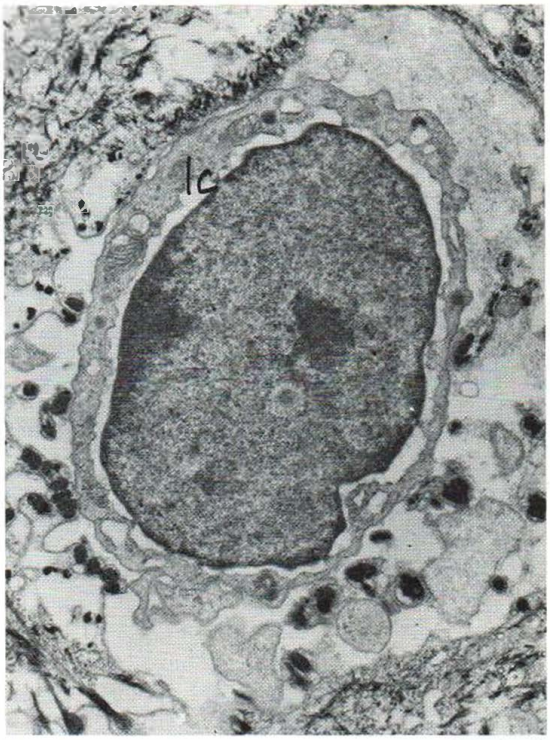

Fig. 7. An immigrated cell (*lc*) has replaced one of the necrotic epithelial cells. × 8 800.

Our further results obtained on the "normal" skin of psoriatics provide ultrastructural evidence for the existence of so-called subclinical psoriasis. These pathological changes—in accordance with the other morphological, functional and biokinetical alterations—allow us to draw the conclusion that in psoriasis not only the sites of the actual lesions but also the distant skin regions and probably the whole epidermis is involved in the disease. The alterations might be present independent of the symptoms or of the type of lesion.

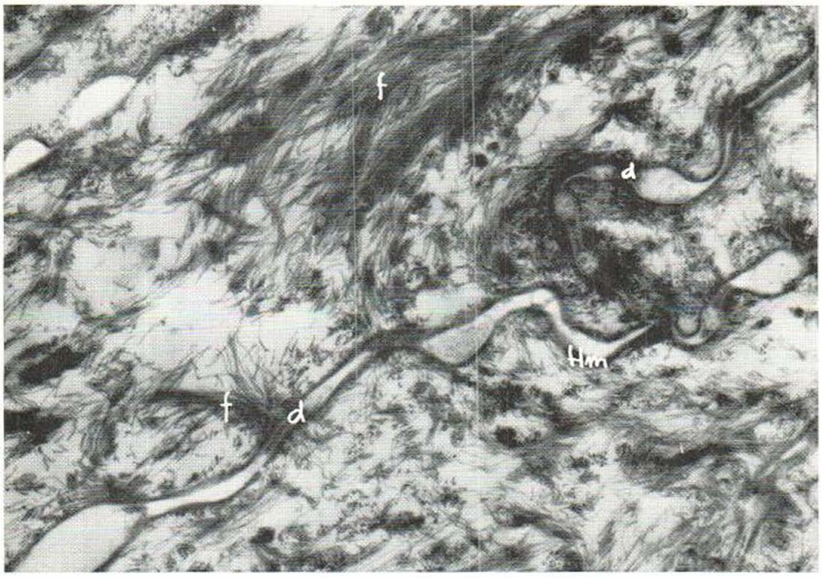

Fig. 8. The other type of horny cell which can be seen in psoriasis. *f*, electron-dense fibrils; *d*, the remnant of desmosomes; *Hm*, horny cell membrane. × 20 500.

Some of the ultrastructural changes seen in the psoriatic "normal" skin might be interpreted as the morphological expression of the increased epidermopoietic activity (1, 11) as they are in some respects similar to those found by Mishima & Pinkus (17), Karasek & Oehlert (13) after stripping. The other characteristic of the symptoms—namely the signs of cytolysis—might be typical of psoriasis, since they can also be seen though to a greater extent in the psoriatic lesion and dominate the feature of psoriasis pustulosa (24) which is regarded as the exudative form of psoriasis.

On the basis of our recent work it is difficult to determine the exact role of cytolysis in the pathogenesis of psoriasis. When the figures of Rupec (24) are compared with ours, the similarity is striking. Therefore we feel free to suppose that the lysis results in the formation of Munro-Sabouraud microabscess and this process differs only quantitatively from the development of the spongiform pustule.

On the other hand the lysis might be considered as the consequence of hypoxia caused by a maximal epidermal activity which according to Christophers & Braun-Falco (8) cannot be further increased by stimuli. Since this condition prevails only in the centre of the plaque (8) this is probably not the case.

The hereditary character of psoriasis (15) suggests a genetic defect, the nature of which is obscure. The histochemical work of Reid & Jarret (21) indicates that the lysosomes in the "normal" skin of psoriatics are unstable. Jarrett & Spearman (20) have found an early release of acid phosphatase and sulphatase in the actively spreading psoriatic lesions, which in their opinion may stimulate mitotic activity and lead to akanthosis. The morphogenetic investigations of psoriatic plaques (2) and the increased number of lysosomes (5) point also in this direction. Furthermore the symptoms of psoriasis cannot be explained as the consequence of a high epidermopoietic activity since, as the latter does not lead to parakeratosis, a disturbance of cellular differentiation must be simultaneously present (7). In psoriasis the cytolysis might interfere with the differentiation process and at the same time might induce hyperregeneration.

Apart from the evidence presented by Reid & Jarrett (21) there are no data concerning the instability of lysosomes in the symptom-free skin of psoriatics. At present, one can only surmise that the slightly increased mitotic rate of the "normal" areas (1, 11) might also be maintained by a discrete lytic process.

We think that the theory of the genetically unstable lysosomes can be used as a working hypothesis in connection with the pathogenesis of psoriasis. It certainly has the advantage that the signs

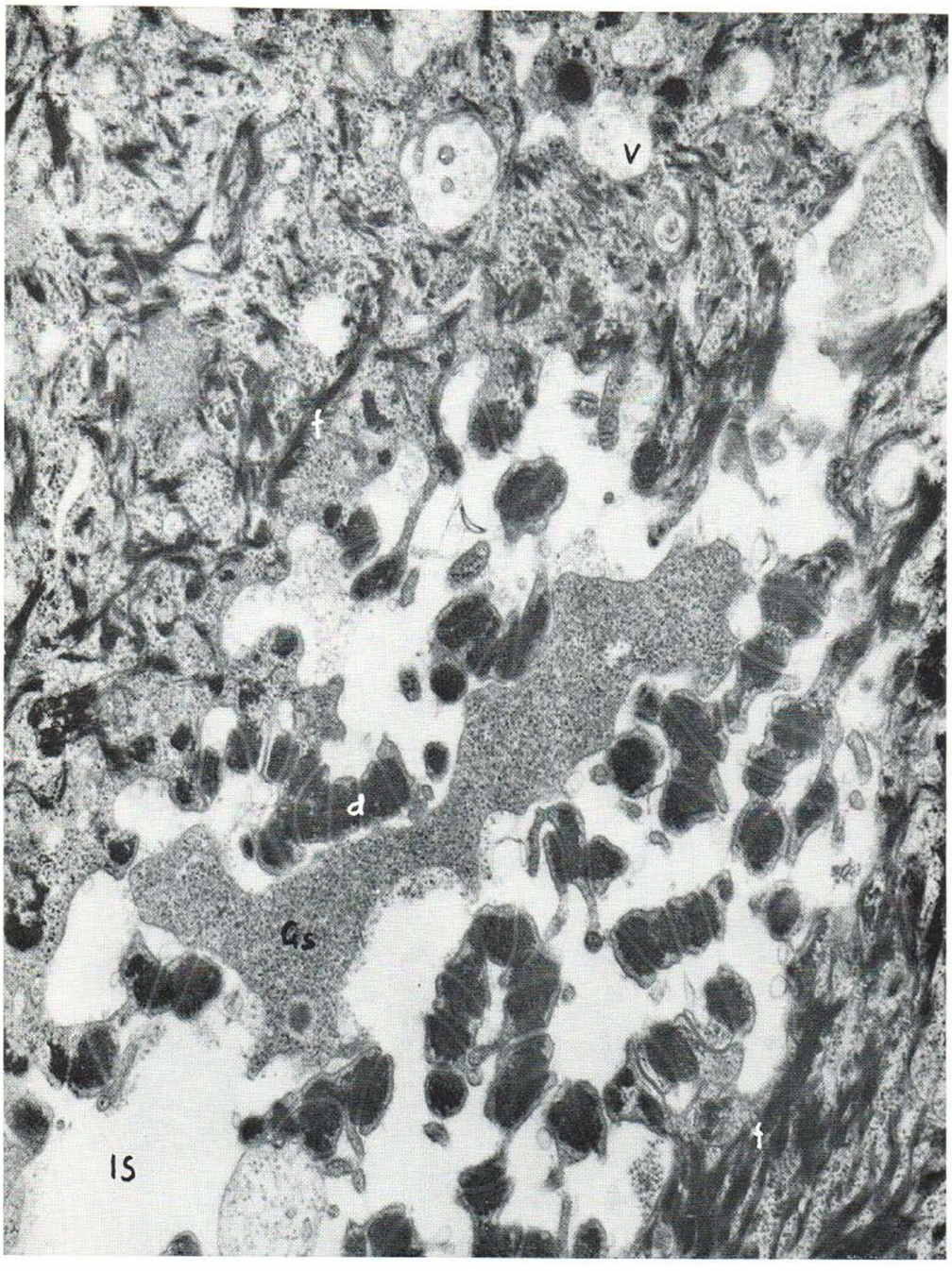

Fig. 9. Widened intercellular space (*IS*) in the "normal" psoriatic epidermis. *Gs*, granular substance; *f*, tonofibrils; *d*, desmosomes; *V*, cytoplasmic vacuole. × 25 000.

of subclinical psoriasis and the flare up of the symptoms—the latter being caused by the increased breakage of lysosomes as a response to the action of endogenic or exogenic factors—can be explained thereby. To prove beyond doubt the pathogenetic role of lysosomes, further investiga-

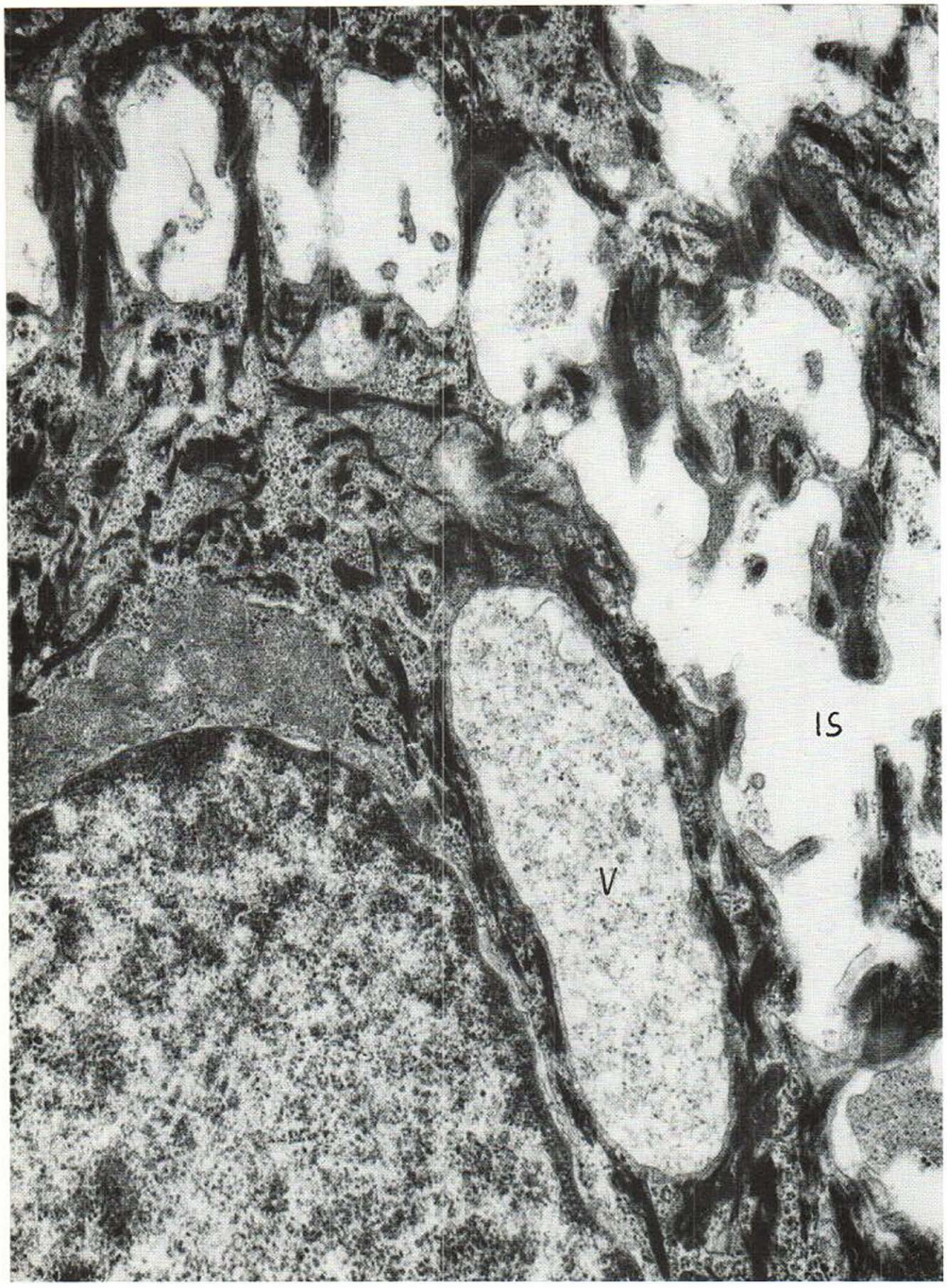

Fig. 10. Large vacuole (*V*) in the cytoplasm of a spinous cell in the "normal" psoriatic epidermis. *IS*, intercellular space. × 25 000.

tions are needed, first of all in connection with hydrolytic enzymes in symptom-free regions and periods, and in the different stages of psoriasis.

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