

CELLULAR CHANGES IN THE BASALOID CELL PAPILLOMA

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Abstract. Electron microscopic analyses of basaloid cell papillomas of the solid and papillomatous types are reported. The submicroscopic organization is described. Some of the ultrastructural findings, e.g. an increased number of mitochondria, a certain mitochondrial polymorphism, the occurrence of irregularly shaped intracytoplasmic vesicles, the abundance of endoplasmic reticulum hypertrophy and the remarkable presence of microtubule-like structures, an unusual finding in a material fixed at the temperature used, are indicating an altered metabolic activity. The alternating presence and absence of keratohyalin is found to be sub-micromorphologically related to the formation of A- respectively B-cells. This is compared with the formation of parakeratosis in psoriatic lesions without keratohyalin. A formation of orthokeratosis as seen by the light microscopical procedure seems possible without preceding occurrence of keratohyalin.

Key words: Basaloid cell papilloma; Seborrheic keratosis; Keratinization; Orthokeratosis; Parakeratosis; Microtubules

The cellular changes in the psoriatic epidermis indubitably culminate in the formation of the para-

Abbreviations

AF = anchoring filaments
D = desmosome
DF = anchoring fibrils
EM = nuclear envelope
ER = endoplasmic reticulum
ID = intercellular disc
IV = cytoplasmic invagination
JG = junction granules or half-desmosomes
KH = keratohyalin
KR = karyoplasmic remnant
KP = keratin pattern
LB = lamina basalis
M = mitochondria
N = nucleus
O = Odland bodies or keratinosomes
R = ribosome
T = tonofilament bundles
TF = tonofilaments
TM = tonofilamentous material or amorphous masses
TS = intracytoplasmic thread-like structure
V = membrane-bordered vesicle

keratotic horny layer. The omnifarious submicroscopic cellular alterations of psoriatic epidermal cells, particularly represented by a paucity of tonofilaments, a poor differentiation of the desmosomes, the abundance of cell organelles, the absence of or marked decrease in keratohyalin, present a most attractive morphological explanation of the surceasing keratinization in psoriasis (6, 9).

The most salient feature in the panorama of the lacking psoriatic epidermal cellular differentiation preceding the parakeratosis is the deficiency of keratohyalin. Briefly, this conjectures that, among other things, the synthesis of keratohyalin is actually of vital significance in orthokeratosis.

When studying keratinization, it is of interest to analyse another biological process characterized by the formation of orthokeratosis without keratohyalin, as visualized by the light microscopical procedure, e.g. the basaloid cell papilloma.

The basaloid cell papillomas present a multifaceted, often bewildering, clinical and histological appearance (1, 10, 11, 13). A thorough submicroscopic analysis of the basaloid cell papillomas is given by Braun-Falco et al. (2, 3). According to these authors the main cell in the basaloid cell papilloma or seborrheic keratosis is of basaloid type, which has an undeniable ability to differentiate. They emphasize a predominance of the nucleus in relation to the cytoplasm, the abundance of mitochondria, the perinuclearly arranged tonofilament bundles, the perikaryon and the presence of well differentiated desmosomes with a reduced occurrence in the basal layers of the tumour. They also mention the abundance of ribosomes with accentuation in the suprabasal layers. Keratohyalin often occurs but may show an ambiguous absence, especially as regards the orthokeratosis and hyperorthokeratosis characteristic of the tumour.

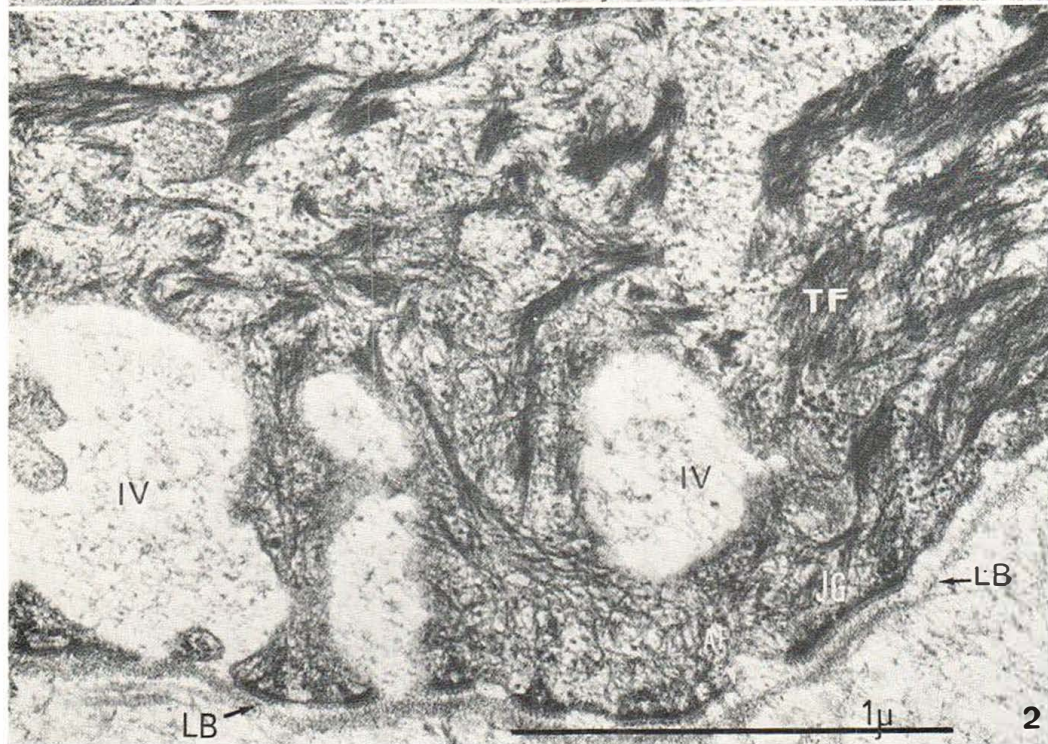
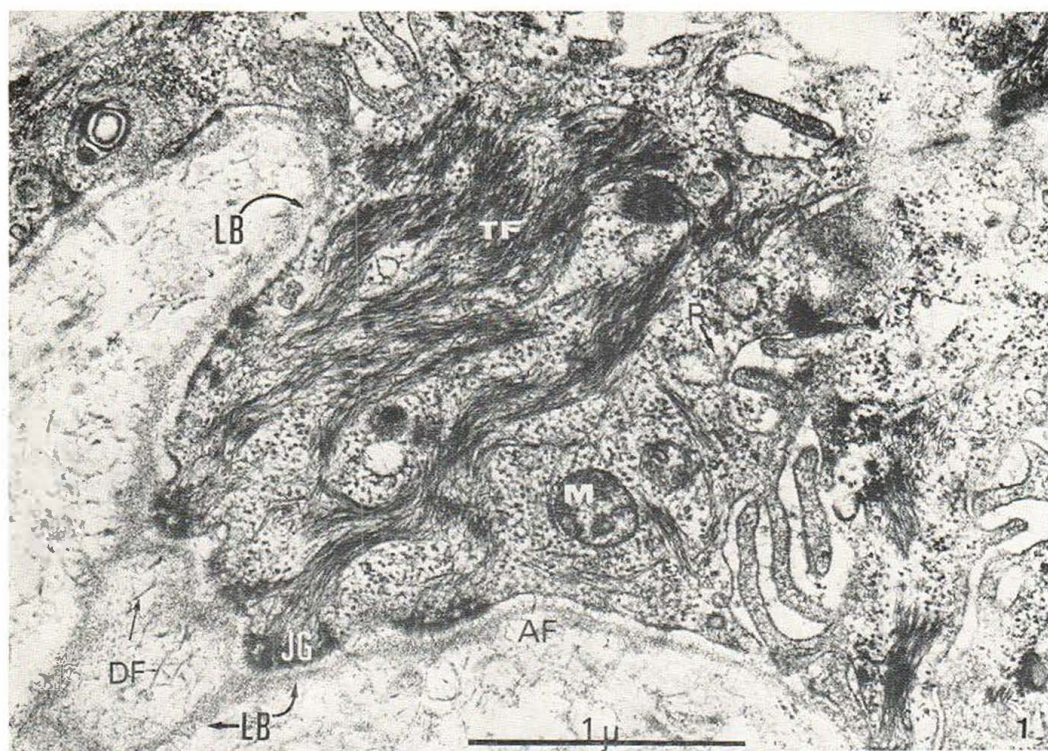


Fig. 1. Section of basal cell from basaloid cell papilloma and part of the dermo-epidermal junction. $\times 36\,000$.

Fig. 2. Part of basal cell with voluminous invaginations and lamina basalis. $\times 58\,000$.

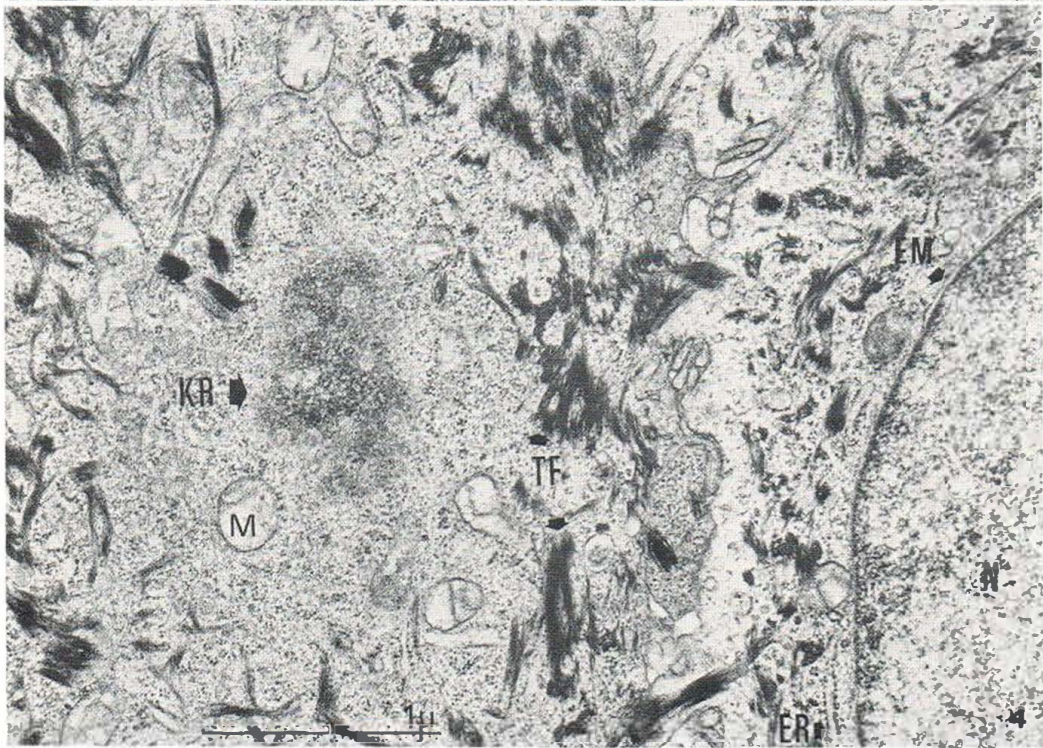
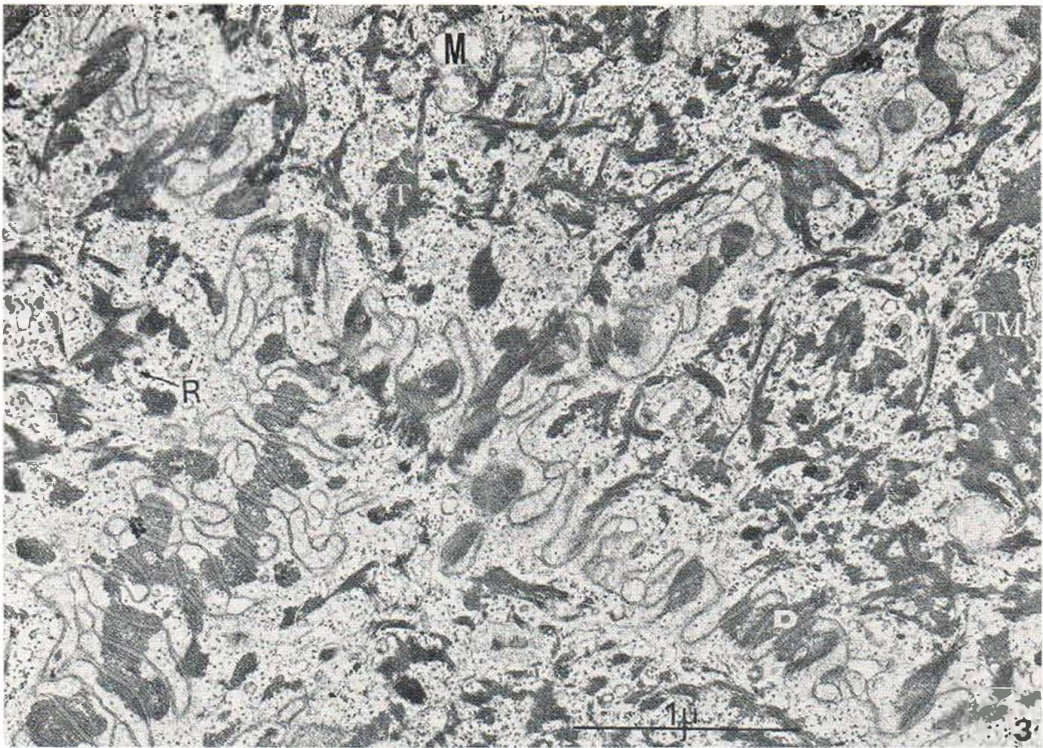


Fig. 3. Parts of epidermal cells of basaloid cell papilloma with cell borders. $\times 30\ 000$.

Fig. 4. Parts of epidermal cells presenting a portion of preserved nucleus and a deteriorated nucleus. $\times 31\ 000$.

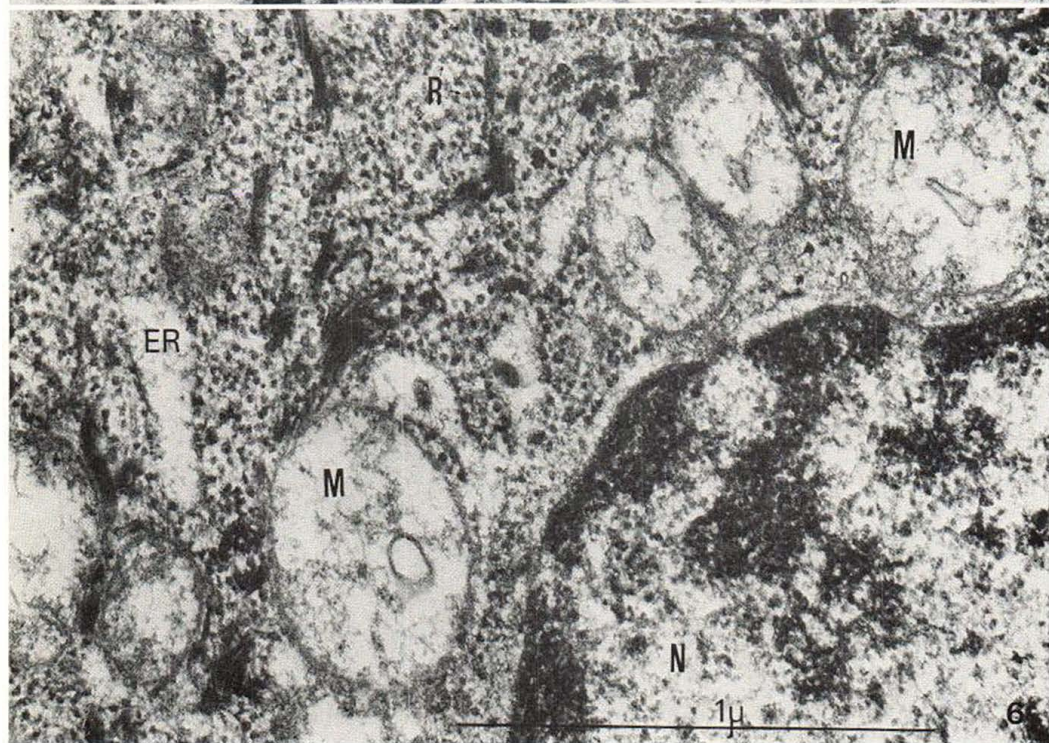
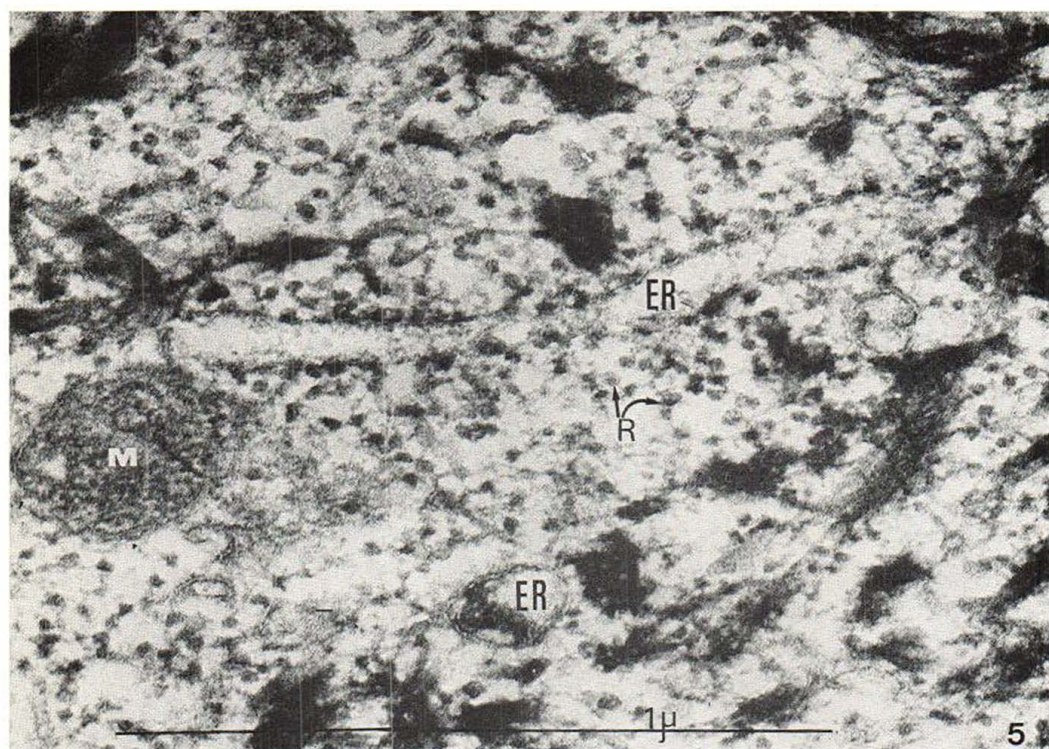


Fig. 5. Detail of cytoplasm of an epidermal cell showing well developed endoplasmic reticulum. $\times 95\ 000$.

Fig. 6. Portion of cytoplasm and nucleus of an epidermal cell. $\times 62\ 000$.

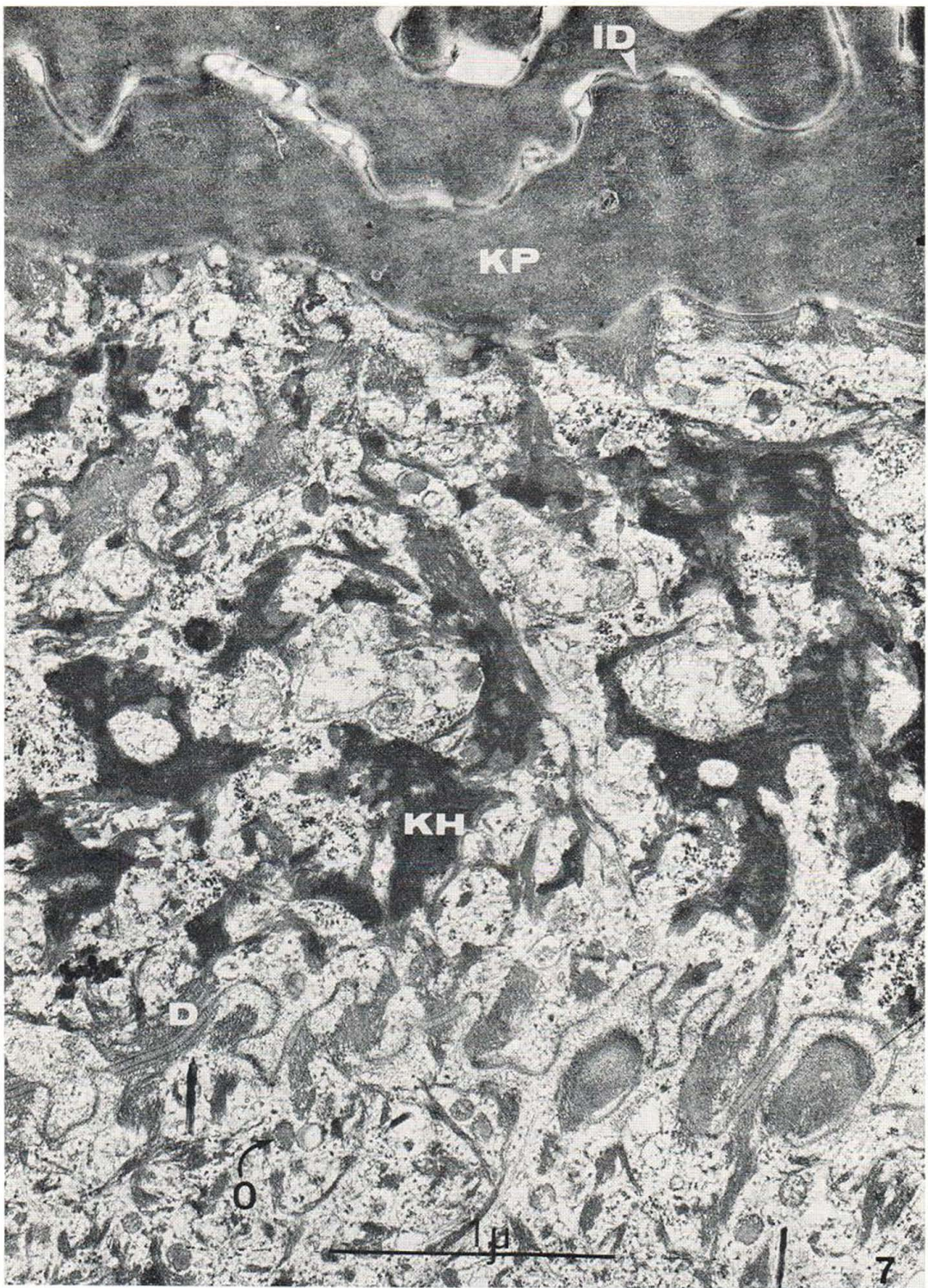


Fig. 7. Section through four successive cell layers showing Odland bodies, keratohyalin, and keratin pattern. $\times 44\,000$.



Fig. 8. Detail of epidermal cytoplasm containing a membrane-bounded vesicle. $\times 143\ 000$.

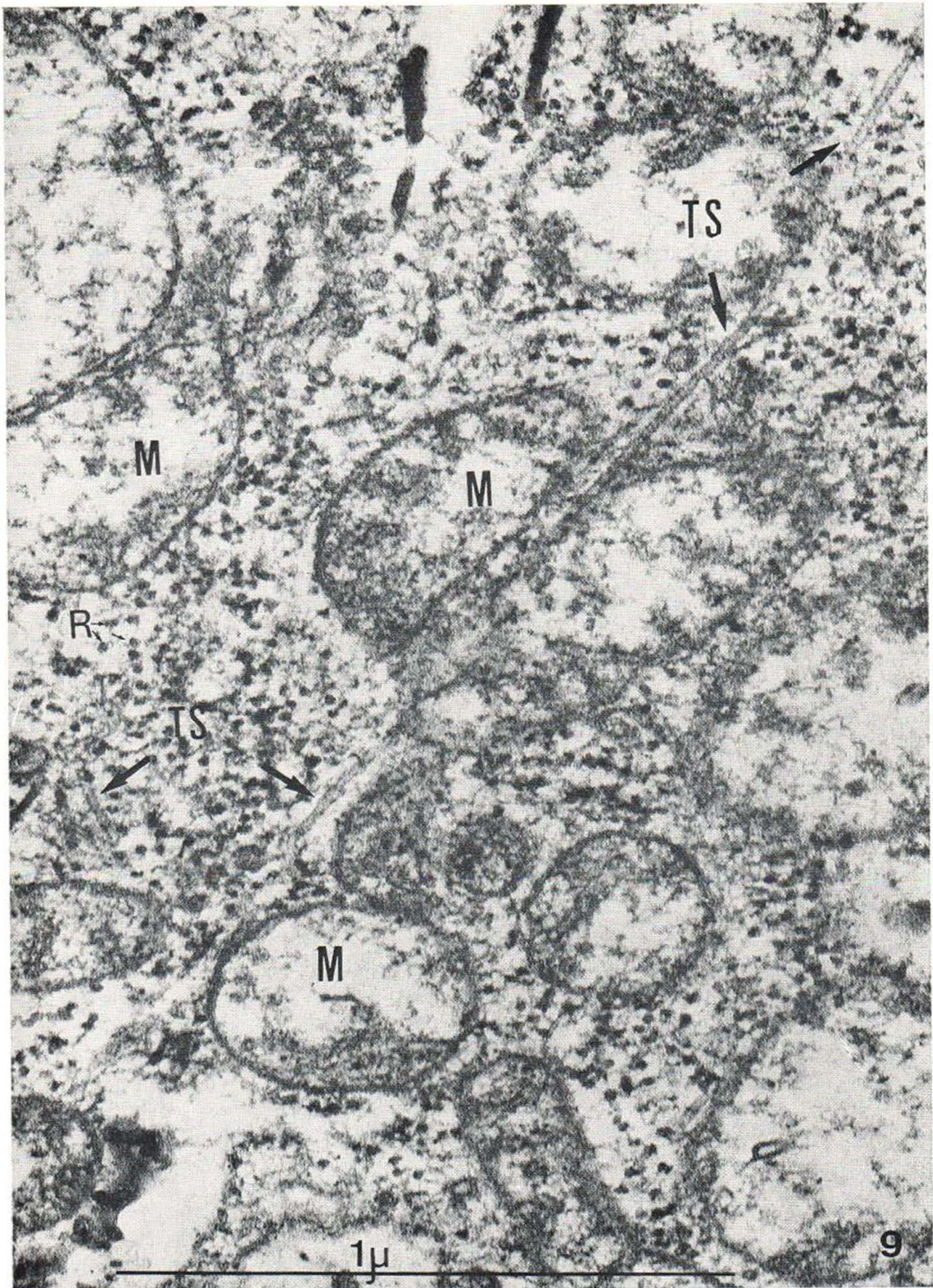


Fig. 9. Details of cytoplasm showing thread-like structures, mitochondria, and ribosomes. $\times 96\ 000$.

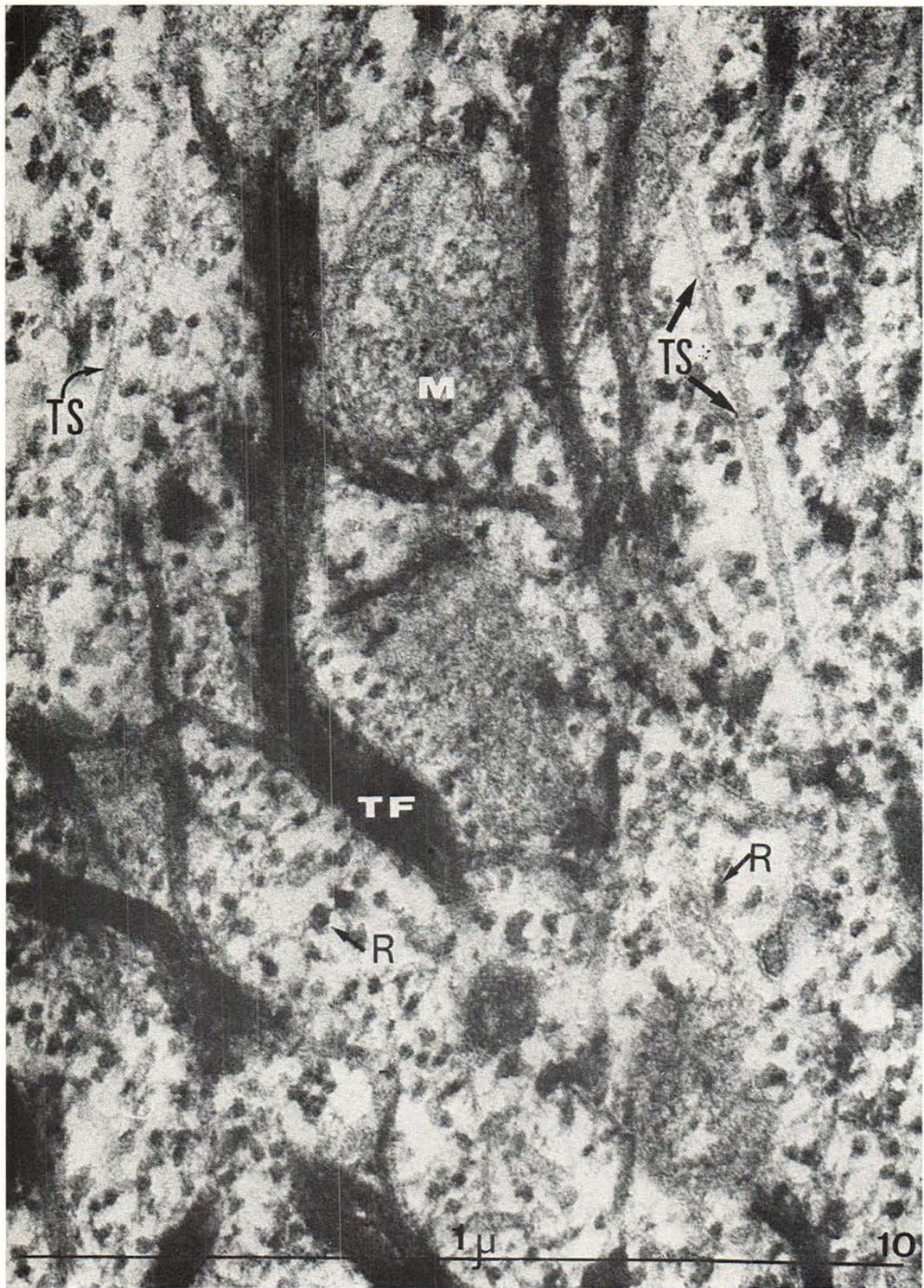


Fig. 10. Micrograph showing cytoplasmic details with thread-like structures. $\times 135\ 000$.

MATERIAL AND METHODS

The material consisted of 5 patients with clinically and histologically well defined basaloid cell papillomas of the solid and papillomatous type. Samples for examination were excised in toto under local anaesthesia and were taken from the trunk.

Specimens for electron microscopy were fixed in 4% glutaraldehyde buffered with a phosphate solution at pH 7 for 6 hours at 4°C. Postfixation was performed in 2% osmium tetroxide buffered with phosphate solutions for 2 hours at 18°C, and the specimen were rinsed in the phosphate buffer solution. After dehydration in increasing concentrations of acetone the specimen were embedded in Vestopal W. The sections were stained with uranyl acetate and lead citrate.

RESULTS

The basaloid cell papilloma or the seborrheic keratosis or the verruca senilis is a benign epidermal tumour submicroscopically delineated by a virtually normal lamina basalis separating the neoplasm from the dermis (Figs. 1, 2). The lamina basalis measures 300–400 Å in thickness and is separated from the epidermis by a space of lesser density, the lamina lucida, approximately 300 Å thick. This space is frequently seen bridged by material of the same density and similar structure as that of the lamina basalis, the anchoring filaments (7, 8). These bridges are found on the side of the basal cells connected with the junction granules or half-desmosomes (Figs. 1, 2). The lamina basalis locally appears amphibologically double-contoured but no invaginations of the continuous electron scattering membrane appear. Beneath the lamina basalis is a fairly broad, less dense area containing dispersed, small fibrillar structures—anchoring fibrils (7). Vesicles with a diameter of 300–800 Å presumably of micropinocytotic character are found locally as invaginations of the plasma membrane between the half-desmosomes or free in the vicinity of the lamina basalis. Numerous voluminous invaginations of the basal cells partly delineated by plasma membrane are found between this membrane and the outerface of the lamina basalis (Fig. 2).

The superabundant cell type in the solid and papillomatous basaloid cell papilloma is a small basaloid cell which is indicatively analogous to the cells of the epidermal basal cell layer than to the cells of the basal cell carcinoma (4). This cell type (Fig. 3) shows fairly well differentiated desmosomes, however, locally decreased in number, sometimes in agreement with, sometimes at variance with, the

observations of previous investigators. The existence of a tonofilament–desmosome relationship is unquestionable. The ubiquitous, uniform cells have normally differentiated unit membranes and are separated by intercellular spaces of ostensible variation in volume, caused in each case by multifolded invaginations.

The cytoplasm of many of the basaloid cells is characterized by an abundance of well differentiated tonofilament bundles (Fig. 3) mostly haphazardly arranged. Ubiquitously intermingled with such cells are cells predominantly containing amorphous masses, e.g. aggregations of a material resembling the tonofilamentous material in its contrast behaviour (Fig. 3). This indicative dimorphous state of tonofilamentous differentiation is also observed in one and the same cell (Fig. 3). With regard to the tonofilamentous differentiation, three types of cells are thus present. In particular, these amorphous masses are seen in the proximity of ribosomes or aggregations of ribosomes.

The association between the tonofilament bundles and the desmosomes is well developed in all layers of the tumour. The desmosomes appear well differentiated with a submicroscopic morphology in agreement with previous analyses as published by Orfanos (12) and Rupec (14), among others (Figs. 3, 7). The endoplasmic reticulum often appears hypertrophic, independent of cell level (Fig. 5), with numerous attached and randomly dispersed ribosomes in cytoplasm. There is a cytoplasmic abundance of ribosomes, randomly dispersed and ubiquitously seen singly and often pentagonally outlined when felicitously cross sectioned (Figs. 5, 6, 10).

The mitochondria occur in increased numbers throughout the lesions but present multitudinous configurations. They may show advanced cristolysis (Fig. 6). On the other hand they have fairly well differentiated cristae, often with the coexistence of a rather amorphous or grainy electron-scattering material (Figs. 4, 6, 9, 10). The mitochondria evince distinct variations in shape and volume (Figs. 4, 6, 9, 10). The polymorphism does not show any relationship to cell layer, i.e. juxtaposed cells may thus contain quite differently shaped mitochondria.

Irrespective of the level in the tumour, the nuclei appear oval or irregularly shaped with a differentiated nuclear envelope. The dispersion of chromatin is variable and may show differing localization. Nucleoli are often seen, having a porous character.

The stratum granulosum (Fig. 7) is mostly represented by a single layer of keratohyalin, though cells

without or with poorly differentiated keratohyalin do occur. Odland bodies or keratinosomes were found irregularly distributed in the basaloid cell papilloma. A stratification is seen, with the corneal layer in A-cells having a more homogeneous keratin pattern and B-cells having an irregular fibrous structure. When preceded by a keratohyalin-containing granular layer, corneal cells of the A-type are differentiated, succeeded by B-cells. Without the occurrence of keratohyalin there is an abrupt formation of B-cells. The corneal cells are bordered by a trimorphous membrane consisting of two strongly electron-scattering layers about 30–50 Å thick and a more weakly scattering interspace of about the same size (Fig. 7). The attachment plaques are no longer visible and the intercellular discs have become extremely dense and strongly electron-scattering. A peculiar vesiculating degeneration of the intercellular discs is often observed (Fig. 7).

Irrespective of the cellular level, amphibological irregularly shaped areas of strongly electron-scattering granular material are observed in cells virtually lacking preserved nuclei. These sometimes porous areas seem to represent different degrees of nuclear and nucleolar deterioration, as depicted in Fig. 4. Within such supposed disintegrated nuclear structures (and also in preserved nuclei) small, dense particles may be observed (Figs. 4, 6), having the same submicroscopical properties as ribosomes.

The cytoplasm of many basaloid cells in section contains vesicles of varying shape and size, delimited by a trimorphous membrane measuring about 80–100 Å, i.e. about the same size as the unit membrane (Fig. 8), and clearly ribosome-like particles are dispersed in a discrete, slightly reticulated amorphous material.

In the cytoplasm of the epidermal cells of the basaloid cell papilloma, a thread-like or tube-like amphibological structure, often of considerable indeterminate length and constant diameter (180–190 Å) is observed (Figs. 9, 10). There is a central longitudinal space of weaker electron scattering property, demarcated by two poorly distinguished longitudinal zones showing considerable enhancement of contrast, and indicating a separating structure between the cytoplasm and the thread-like or tube-like configuration. This thread-like structure is found haphazardly localized in the cytoplasm, often without any demonstrable connection with other known cell organelles.

DISCUSSION

The basaloid cell papilloma or seborrheic keratosis presents a particular submicroscopic organization, as reported by Braun-Falco *et al.* (2) and described in the present study. One apparent feature of the cellular differentiation is the final formation of orthokeratosis, either beginning with A-cells when preceded by a keratohyalin-containing granular layer or, without the occurrence of keratohyalin, an abrupt formation of B-cells. Despite the absence of nuclear structures and lipid droplets in those B-cells, their cytoplasm somehow resembles that of the parakeratotic cells of the psoriatic stratum corneum (9a). As orthokeratosis is the product of the normal epidermis, which substructure is well known, it is of interest to observe certain aberrant features of the tumour cells, despite which a morphologically normal terminal point is reached. In all levels of the basaloid cell papilloma, there is a paucity and irregular distribution of Odland bodies, in contrast to the abundance of those organelles in normal epidermis. The keratohyalin is either missing or occurs only in a single layer of the stratum granulosum, which seems poorly differentiated and often cannot be observed by light microscopical procedures. The complex of the tonofilament bundles and the desmosomes is well preserved throughout the tumour. These circumstances certainly play an important role in the preceding process of orthokeratosis. The lack of this differentiation of the tonofilament–desmosome complex in psoriasis predisposes to the formation of parakeratosis, and together with the paucity of Odland bodies, results in deficiency or absence of keratohyalin (9). The epidermal cells of the basaloid cell papilloma, however, have the ability to form orthokeratosis. The orthokeratosis of this tumour could depend on, or at least be heralded by, the well differentiated tonofilament–desmosome complex which is certainly lacking in psoriasis. As in the psoriatic epidermis, there is a paucity of Odland bodies and frequently also of keratohyalin. The poorly differentiated Odland bodies of psoriatic epidermis (9) do not occur in this material.

Multiple invaginations of the unit membrane facing the lamina basalis are repeatedly found, partly as micropinocytotic vesicles and partly as considerably more voluminous invaginations, presumably reflecting an enhancement of nutritional activity. As further signs of an acceleration of cellular metabolism could also be interpreted the abundance of ribosomes, the increased number of mitochondria and the hyper-

trophic endoplasmic reticulum. A derangement of the mitochondrial function is indicated by signs of deterioration of the organelles.

An altered cellular metabolism or an abnormal cytoplasmic differentiation is indicated, as reflected by the occurrence of cells containing tonofilament bundles in juxtaposition to cells containing amorphous masses of the same electron-scattering properties as tonofilamentous material. The occurrence of such masses as a sign of altered cellular metabolic activity has been observed in psoriatic lesions (7).

The lamina basalis appears as a continuous structure with no epidermal cytoplasmic protrusions and an intact configuration of the junctional structures. Localized thickenings of the lamina basalis are seen opposite the half-desmosomes. Increase in width of the basement membrane is also reported in normal skin and split-skin autografts (5). The occurrence of duplicated lamina basalis is comparatively rare. These observations may indicate some altered nutritional function of infraposed structures.

A vesicular degeneration of the intercellular discs occurs, similar to that in psoriasis (9) of the stratum corneum, although not accompanied with the same degree of desquamation.

The vesicles haphazardly occurring in the cytoplasm are observed in sections from many specimens. They are bordered by a unit membrane-like structure. Without disavowing other possibilities, they may represent invaginations of the intercellular space, also reflecting some kind of altered metabolic activity. The thread-like or tube-like structures repeatedly found in the cytoplasm of cells from different parts of the basaloid cell papilloma seem to be similar to the slender tubules described as cytoplasmic microtubules, as presented in some surveys of ultrastructural analyses (14, 15, 16). These tube-like cytoplasmic configurations have been ascribed several possible functions. These may be supportive or contractile or serve microcirculatory purposes or participate in deviant cellular growth.

The microtubules seem to have a certain orientation in, for instance, the axonemes, mitotic spindles and phagocytizing cultivated macrophages. The haphazard orientation of the thread-like or tube-like structures in the present material which, despite of a certain divergence in diameter, is similar to the microtubules, does not allow of any ascription. If one assumes that the microtubules may be multifunctional, they can somehow participate in deviant cellular growth, as in the present tumour.

It is well known that the microtubules are cold-sensitive but a simultaneous use of glutaraldehyde and osmium tetroxide is reported to preserve those configurations though, however, such preservation has also been described when using ice-cold glutaraldehyde and osmium tetroxide postfixation. Thus the fixation used in the present material does not contradict the possibility of the tube-like structures being microtubules. However, the exact function of the tube-like configurations observed in the cytoplasm of the epidermal cells of the basaloid cell papilloma remains a mystery.

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