STRUCTURAL ORGANIZATION OF THE STRATUM CORNEUM IN CERTAIN SCALING DISORDERS OF THE SKIN*

DAVID N. MENTON, PH.D.† AND ARTHUR Z. EISEN, M.D.‡

ABSTRACT

The structural organization of the stratum corneum in several scaling disorders of the skin has been studied in alkali swollen frozen sections with the light microscope, and in tape striped specimens with the scanning electron microscope. In psoriasis, lichenification, and lamellar ichthyosis, which are characterized by high epidermal mitotic activity, the stratum corneum lacks the neatly stacked cellular arrangement typical of normal stratum corneum. In direct contrast the stratum corneum of patients with ichthyosis vulgaris appears nearly normal in this respect. Of the scaling disorders studied, ichthyosis vulgaris is also unique in having normal, or even subnormal epidermal mitotic activity. This suggests that the columned stacking pattern of the normal stratum corneum is incompatible with a high mitotic activity.

Under normal condition the stratum corneum of the mammalian integument is a highly organized structure with its constituent horny cells arranged in vertical columns of neatly stacked cells, each of which interdigitates with the cells in the adjacent columns (1–3). Evidence has been presented (1–3) that this organizational pattern begins at a deeper level within the epidermis, and it has been suggested that it is due to a sequential pattern of mitosis in a specific population of basal cells. This provides for a continuous procession of cells which become flattened as they ascend and are added to the overlying column.

Although the significance of this morphological organization of the horny cell remains to be determined, its widespread occurrence in the skin of all mammals so far examined indicates that it is basic to some fundamental aspect of cutaneous function. Menton and Eisen (3) have postulated that there may be a close relationship between the degree of stacking of the cells in the stratum corneum and the ability of this layer to serve as an effective water barrier. Indirect evidence in support of this hypothesis was seen in the fact that stratum corneum from the palmar and plantar surfaces, which is known to be a much less effective barrier to transepidermal water loss (4–8), lacks this characteristic columnar organization (3). On the other hand, the absence of a well organized arrangement of the horny cells on the palms and soles could simply reflect the higher mitotic rate which occurs in normal palmar and plantar epithelium (9, 10). It is also possible that the two phenomenon (i.e., the rate of mitotic activity and the barrier function) could both be related to the stacking pattern of the cells in the horny layer.

To explore these possibilities further it seemed reasonable to examine the organization of the stratum corneum in a number of pathological conditions in which there is known to be an increase in transepidermal water loss and also an acceleration in epidermal cell turnover, and to compare the morphology of the stratum corneum in these conditions with that in a cutaneous disorder characterized by a disturbance in barrier function without a significant alteration in mitotic activity. This report deals with the cellular morphology and organization of the stratum corneum in psoriasis, lichenified skin, and lamellar ichthyosis. These diseases are characterized by a hyperproliferation of epidermal cells (11–13) and, with the possible exception of lichenification (for which information is at present unavailable), in which there is also a significant increase in transepidermal water loss (14). These disorders are compared to ichthyosis vulgaris, where hyperkeratosis is not associated with an increase in cell turnover, but in which
there is some increase in transepidermal water loss (11, 12, 14).

MATERIALS AND METHODS

Specimens of human skin were obtained from patients by punch biopsy following local anesthesia. Samples of skin were taken from the lateral aspect of the upper arm and/or from the trunk in three patients with psoriasis, two patients with lichenified skin, one patient with lamellar ichthyosis and three patients with ichthyosis vulgaris.

The spatial arrangement of the cells in the stratum corneum was studied at the light microscope level in frozen sections of unfixed blocks of tissue that were cut perpendicular to the stratum corneum in an American Optical cryostat at 6 μ and swollen in 0.1 M sodium hydroxide (15). These preparations were quickly examined under a Zeiss Nomarski differential interference-contrast microscope or a Nikon phase contrast microscope, and photographed on Kodak Ektrapan film using a Wratten No. 58 (green) filter. Additional samples of stratum corneum from areas adjacent to those biopsied were removed by repeated applications of Scotch Double Stick Tape (Minnesota Mining and Manufacturing) for study with the scanning electron microscope. The tape to which the horny cells were firmly attached was then made to adhere to the metal specimen holders, with the “tissue side” up, dried in a desiccator, and coated with chrome in a vacuum evaporator to enhance contrast and minimizing charging. This material was subsequently examined with a Cambridge Stereoscan scanning electron microscope.

RESULTS

Psoriasis

Histologically, psoriasis is characterized by a greatly folded dermo-epidermal junction, thinning of the suprapapillary level of the epidermis, parakeratosis and hyperkeratinization (16). Weak alkali treatment of cryostat sections of psoriatic stratum corneum results in marked swelling of the individual horny cells without apparent disruption of the cell membranes even after quite brief exposure (2–3 min) of the frozen sections to 0.1 M sodium hydroxide solution (Fig. 1). A clear oval nuclear zone is visible in most psoriatic horny cells during the first minute of alkali treatment but subsequently disappears (Fig. 1). In addition, the psoriatic cornified cells swell to an even greater degree than normal horny cells from the volar surfaces. This change is particularly striking because ordinarily the horny cells from the volar surfaces are much more affected than those from the rest of the skin (3). The first two or three layers of psoriatic horny cells above the stratum granulosum swell earlier and more extensively than the more superficial cells.

The most striking observation we have found in our light microscope preparations of alkali-treated specimens of psoriatic stratum corneum from the trunk and limbs is the very obvious absence of a columnar organization in the horny cells (Fig. 1). This finding is consistent with the scanning electron microscope studies where, under low magnifications, the horny cells appear to overlap each other in a more-or-less random manner with no evidence of a columnar organization (Fig. 2). In addition, when observed under phase contrast or Nomarski optics, the plasma membrane of psoriatic horny cells appears to bristle with small “nipple-like” projections that are easily observed both in cross sections and in intact cells (Figs. 1, 6). These structures can be seen in normal stratum corneum, but except in skin from the palms and soles, they are never as well developed as in the psoriatic specimens. With the scanning electron microscope these nipple-like projections appear

Figs. 1, 7, 10 and 14 are cross-sections of unfixed skin sectioned in a cryostat and treated with 0.1 M sodium hydroxide. Alkali treatment swells the horny cells to several times their normal thickness and in so doing reveals their spatial organization in the stratum corneum. These photomicrographs were taken with either a Nikon phase contrast microscope or a Zeiss Nomarski interference contrast microscope, as indicated.

Figs. 2–5, 8, 9 and 11–13 are scanning electron micrographs of tape stripped specimens. All micrographs are views of the deep surface of the horny cells. The angle at which the specimen is photographed affects magnification and shape of the cells largely in the Y axis. For this reason the degrees of decalusion from a perpendicular point of view are given for each photograph.

Fig. 1. Cross section of psoriatic stratum corneum. Horny cells are disorganized and clearly lack the stacked pattern typical of normal stratum corneum. A nuclear zone is often visible within the cells (arrows). Phase contrast optics. × 931.

Fig. 2. Scanning electron micrograph of psoriatic horny cells. The cells are characterized by a plaque-like appearance with irregularly serrated edges and scattered small villus structures on the cell surface. These horny cells lack the grooves and depressions found on cells from all other normal and pathologic stratum corneum studied. The lack of an organized spatial arrangement of the cells is evident. × 985.
as irregularly scattered, short, villous-like protuberances, and are very common on the surface of the cells from psoriatic stratum corneum (Figs. 2–4). Although similar structures may be seen in scanning electron micrographs of normal stratum corneum, they are usually much shorter and much less obvious than in the psoriatic skin. On normal volar surfaces the corresponding “villi” are generally more abundant than on the trunk and limbs and tend to have a broad foliate appearance (3). The villous projections on the horny cell surfaces of psoriatic as well as normal skin (3) are thought to be desmosomal in nature. Not only are they consistent in shape, and distribution, with desmosomes but they are also of the same size (approximately 0.3–0.4 μ in diameter) as the cross sections of desmosomes seen in the normal stratum corneum transmission electron micrographs. The irregularly serrated borders typical of the psoriatic horny cell are due, in part at least, to these abundant villus processes (Figs. 2–4) which occasionally appear to be attached to the underlying cells (Fig. 4).

The most striking morphological features of the psoriatic horny cells, as compared to normal cells from the stratum corneum of the trunk or limbs, are their plaque-like appearance, their almost complete lack of surface folds and depressions, their irregular, rather than typical hexagonal shape (Figs. 2, 3) and their increased thickness. A “stiffness” of the cells is suggested by the finding that they do not conform to the grooves in the underlying adhesive (Fig. 2) as do normal cells. Although in the scanning microscope it is impossible to measure accurately the thickness of cells, the surface diameters of the psoriatic cells measure from 35–45 μ as compared to normal horny cells which range in diameter from 40–50 μ. It is uncommon in our scanning electron micrographs of psoriatic horny cells to see evidence of the cell nuclei. Occasionally, however, a distinct circular depression, suggestive of the presence of a nuclear zone, is seen (Fig. 5). The orifices of the hair follicles that were observed in the horny layer appear to be unobstructed passages. No sweat ducts were observed in our samples.

Lichenification

Lichenification involves a change in the epidermis, characterized by hyperkeratosis, acanthosis and scattered parakeratosis (16). In view of this it is perhaps not surprising that sodium hydroxide swollen frozen sections of lichenified skin are similar in many respects to psoriatic specimens. In particular, the lichenified horny cells lack the normal columnar organization, show evidence of a clear nuclear zone, and while they swell more than cells from normal stratum corneum, they never swell as much as psoriatic horny cells (Fig. 7). The lack of a columnar organization is also evident in scanning electron micrographs of lichenified horny cells (Figs. 8, 9) which reveal shallow grooves extending randomly across the surfaces of the cells, delineating the margins of horny cells with which they were originally overlapped.

The horny cells of lichenified skin appear to be thicker than those in psoriatic skin. In addition, they seem to be more flexible than psoriatic cells as evidenced by their ability to conform more closely to the contours of both the underlying adhesive and the adjoining cells (cf. Fig. 2 with Figs. 8 and 9). The surface diameter of horny cells from lichenified skin is significantly smaller than normal, (about 20μ) and like psoriatic horny cells, they generally lack a distinct hexagonal shape.

The surface of lichenified horny cells is also covered with a population of villous-like structures, but these are generally more foliate in appearance than those seen in the psoriatic cells (cf. Figs. 3 and 9) and they occasionally form a whorl-like pattern on the surface of each cell (Fig. 9). An interesting finding is the presence of scattered, slit-like, holes in the surface membrane of the horny cells (Fig. 8). Although these slits may be an artifact of preparation, they

Fig. 3. Higher magnification of the villus-like structures on the surface of the horny cells which are consistent in size, shape and frequency with desmosomes. X 2,713. 0°

Fig. 4. Villus processes at the edge of a horny cell which appear to be in contact with an adjacent cell (arrows). X 9,296. 35°

Fig. 5. Circular depressions (arrows) are occasionally observed in the centers of psoriatic cells with the scanning electron microscope. They presumably reflect a nuclear zone in the parakeratotic cells. X 1,575. 25°

Fig. 6. The villus-like processes on the horny cells are clearly visible in these surface views of intact psoriatic cells floating in 0.1M sodium hydroxide solution. Nomarski interference-contrast optics. X 723.
have only been observed in lichenified stratum corneum.

**Lamellar Ichthyosis**

This condition is characterized by marked hyperkeratosis, a normal or slightly thickened granular layer and occasionally an excessively folded dermo-epidermal junction (17). The most striking morphological alteration in the stratum corneum in lamellar ichthyosis is the complete lack of organization of the spatial arrangement of horny cells, and the uncommon resistance of these cornified cells to treatment with sodium hydroxide as evidenced by their inability to swell to the same degree as normal horny cells (Fig. 10).

With the scanning electron microscope (Figs. 11-13) one can see grooves that run randomly
across the surfaces of these cells, much like those observed in lichenified skin; again these grooves appear to be depressions left on the surfaces of the cells by the edges of randomly overlapped cells that have been removed during the tape stripping process. Apart from this the surfaces of the lichenified horny cells are covered with low, irregularly anastomosing, ridges similar to those seen in normal horny cells, but they are usually more marked. Well-developed villus structures are lacking on the cell surfaces. The individual horny cells are polygonal rather than hexagonal in shape (Fig. 12) and their smooth borders tend to be slightly elevated as if the cells were poorly attached to their neighbors (Figs. 11–13). Many examples of plugged hair follicles were observed in strippings from the deeper levels of the stratum corneum (Fig. 11), but the coiled sweat ducts which were observed appear to be patent.

Although it is difficult to calculate the average diameter of the horny cells from lamellar ichthyosis because of their highly irregular shape, they appear to range from approximately 30 μ in the narrowest dimension to 45 μ in their longer dimension. The horny cells are slightly thicker than normal, but not as thick as those from psoriatic or lichenified skin.

**Ichthyosis Vulgaris**

This condition is characterized by moderate hyperkeratosis and absence of the granular layer (16, 17). The horny cells in ichthyosis vulgaris resemble those of the normal stratum corneum in that they are neatly organized into columned stacks (Fig. 14) and have very small scattered villi. When viewed with the scanning electron microscope, however, the cell borders appear to be more sharply delineated than those of normal horny cells, but they have the same smooth and generally hexagonal shape (Fig. 15). The area of overlap of the cells in adjacent stacks is much broader than normal (Fig. 15). The small villus-like processes on the cell surface are less obvious than those of either psoriatic or lichenified stratum corneum, and closely resemble those of normal stratum corneum. The cells are thicker but smaller in diameter than normal horny cells, being approximately 40 μ in diameter.

**DISCUSSION**

The most significant finding in this study is that the horny cells of the stratum corneum in psoriasis, lamellar ichthyosis and lichenification lack the columnar arrangement which characterizes these layers in normal skin, and that each condition is distinguished by the altered appearance of the horny cells.

In scanning electron micrographs it can be readily observed that the margins of horny cells from both normal and abnormal stratum corneum leave groove-like depressions on the surface of those horny cells with which they overlap. In the normal stratum corneum this results in a uniform depression around the lateral margin of each horny cell due to the even imbrication of adjacent stacks (3), while in the disorganized stratum corneum of lichenified skin and lamellar ichthyosis, the groove-like depressions run randomly across the surface of the horny cell. Psoriatic stratum corneum, though obviously disorganized, lacks these depressions or grooves on the cell surfaces, perhaps due to the rigidity of the cells. The rather tough, inflexible aspect of these cells is also suggested by the lack of folded or fragmented psoriatic horny cells. The surfaces of the horny cells in all of the scaling disorders studied have, to a greater or lesser extent, an interesting population of villus-like structures. These villus structures are generally not well developed in horny cells from normal skin, except on the palms and soles where they are very highly developed but tend to be more foliate in appearance (3). In psoriatic stratum corneum the villi are particularly striking and numerous and are similar to those described by Orfanos et al. (18). They have also been observed on psoriatic horny cells in the hydrated state under phase contrast and Nomarski optics and have been seen in normal stratum corneum with the light microscope (19–21).

It has previously been proposed that the vil-

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**Fig. 10.** Cross-section of stratum corneum from lamellar ichthyosis demonstrating the absence of a columned stacked organization typical of normal stratum corneum. Nomarski interference contrast optics. × 752.

**Fig. 11.** Low power scanning electron micrograph of stratum corneum from lamellar ichthyosis. Keratin-filled follicular orifices (FO) and the spiral path of sweat ducts (arrows) are frequently seen. The cells appear to be centrally attached and frequently have elevated smooth edges. × 193. 45°
lus processes correspond to the sites of desmosomal attachment (3, 21). This view is supported not only by their size and location, which are consistent with their being desmosomes but, in addition, when psoriatic horny cells were forcibly separated by the electron beam of the scanning electron microscope at high magnification, we have noted a tendency for these villus processes to remain attached to adjacent horny cells.

The organization of the stratum corneum in ichthyosis vulgaris is of particular interest in that the horny cells are arranged in normal appearing columns, a finding which clearly distinguishes this condition from the other scaling disorders examined. However, this is not to say that the cornified cells in ichthyosis vulgaris are normal; but they only appear to differ from normal cells in that they adjoin and tend to overlap each other more broadly than in normal stratum corneum. Nevertheless, they retain the essentially hexagonal shape of normal horny cells, which is believed to be a minimum perimeter phenomenon resulting from the perimeter of the cells in each stack being encroached upon by the cells in approximately six adjacent stacks (13). The disorganized horny cells of psoriasis, lichenified skin and lamellar ichthyosis, by comparison, are very irregular in shape and only rarely appear hexagonal in surface view.

It may be of considerable significance that the loss of the normal stacking pattern in psoriasis and lamellar ichthyosis is associated with a markedly increased epidermal mitotic activity and cell turnover (11, 13, 17, 22). The psoriasis-form changes seen in lichenified skin might also be expected to include high mitotic activity and increased epidermal cell turnover which would be consistent with the observed loss of the normal stacking pattern. In contrast, mitotic activity is normal or actually lower than normal in ichthyosis vulgaris (11, 14, 17), and in this case the stacking pattern of the horny cells within the stratum corneum is essentially normal. The data presented indicate that disorders associated with increased epidermal cell turnover result in an abnormal stacking arrangement within the stratum corneum. The high mitotic rate in normal palmar and plantar skin (9, 10) and its lack of the stacking pattern (3) are also consistent with this proposal.

Although factors controlling the normal columned arrangement of cells in the stratum corneum are unknown, they must reside in the "living" portion of the epidermis. Sequential mitotic activity in a proliferative pool of basal cells under each column of cells in the stratum corneum may be partly responsible for the stacked arrangement (3), and indeed, there is evidence that the pattern of mitotic activity is non-random in mammalian epidermis (23, 25, 26). Mackenzie (26) has presented evidence that the basal cells underlying each column of horny cells act as a functional unit. Those cells with a mitotic potential are reported to reside in a ring at the periphery of each unit and produce differentiating cells which move centrally and subsequently migrate through the stratum spinosum to the stratum corneum. If mitosis plays an organizing role in the stratum corneum it would seem plausible that an excessively high mitotic rate might disturb the cellular organization. Perhaps those factors which control the flattening of the keratinocytes during their differentiation into horny cells might also be of importance in producing the stacked arrangement.

Whether the disorganized arrangement of the horny cells in psoriasis and lamellar ichthyosis contributes to the reduced effectiveness of the stratum corneum as a barrier to transepidermal water loss cannot be established from this study. There is no doubt that transepidermal water loss is increased in psoriasis and lamellar ichthyosis (14, 27-29) and a good case may be made here for a causal relationship between the disturbance in the normal stacking pattern of the horny cells and their loss of barrier function. However, there are reports that transepidermal water loss may also be moderately increased in ichthyosis vulgaris (14, 27, 28) in which the stacking pattern is essentially normal. Since the normal development of the stratum corneum not only involves a complex cytological sequence beginning in the basal layer and ending with the mature horny cell, but also depends on a highly ordered

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**Fig. 12.** Horny cells from lamellar ichthyosis showing impressions left by the edges of randomly overlapping cells (arrows). Area outlined is magnified in figure below. × 1,163. 45°

**Fig. 13.** An enlargement of the area delineated in Fig. 12. The smooth edges of the horny cells line up precisely with the underlying groove-like depressions (arrows). Villus-like processes are not well developed, though there are many fine folds on the surface of the cells. × 4,292. 45°
FIGS. 14 and 15
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spatial arrangement of its constituent cells, significant alterations in either may impair barrier function.

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REFERENCES

Fig. 14. Cross-section of stratum corneum from the skin of a patient with ichthyosis vulgaris showing a well-organized pattern of stacked and interdigitating cells similar to normal skin. Phase contrast optics. × 810.0°

Fig. 15. A mosaic pattern of essentially hexagonal cells from ichthyosis vulgaris viewed with the scanning electron microscope. The highly organized stacked pattern is evident from the relatively even depression zone extending around the margin of each cell (asterisks) where it overlaps with cells in adjacent stacks. Villi are not well developed. × 1,810.0°