NOTES ON THE ANATOMY AND PATHOLOGY OF THE SKIN APPENDAGES

I. The Wall of the Intra-Epidermal Part of the Sweat Duct

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Most authors who studied the epidermal part of the sweat duct concluded that the duct loses its own lining epithelium when it enters the epidermis, and that the sweat flows through a channel formed by compression of the neighboring prickle cells.[1] It was thought for a long time that the intercellular spaces of the epidermis are in open communication with the passage-way for the sweat, but in a comprehensive study Hoepke[2] has shown that there is actually a closed tube because the lining cells are fused into a coherent membrane. Hoepke insists, however, that the wall is but a functional entity, and that its building stones are the prickle cells of the epidermis.

The standard object for all these studies was the thick epidermis of palms and soles because it supposedly offers the best

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[1] All recent American texts consulted express this opinion. Cf.:

a. Maximow, A. and Bloom, W.: A Textbook of Histology. Philadelphia and London 1931.

b. McCarthy, L.: Histopathology of Skin Diseases. St. Louis 1931.

c. Way, S. C. and Memmesheimer, A.: The Sudoriparous Glands. I. The Eccrine Glands. Arch. Dermat. **34:** 797, 1936.

[2] Hoepke, H.: a. Die Haut, in Handbuch der Mikroskopischen Anatomie des Menschen (W. V. Moellendorff), Vol. III, 1, p. 24. Berlin 1927.

b. Der epidermale Teil des Ausfuehrungsganges der ekkrinen Schweissdruesen. Ztschr. f. Anat. u. Entwicklungsgesch. **87:** 319, 1928. Extensive bibliography may be found in these articles.

opportunities for histological observations. Examination of the thin epidermis of the rest of the body, however, and particularly of certain pathologic specimens must raise considerable doubt as to the correctness of the teachings of the anatomists.

The purpose of this paper is to present various types of evidence to the effect that the sweat duct is lined by its own epithelium throughout, and to discuss the significance of this fact for some phases of the normal and pathological biology of the skin.

EVIDENCE

Figure 1a represents one of the relatively rare instances in which all the curves of a sweat duct are situated in one plane of space so that the entire course of the duct can be followed in one section. The photomicrograph illustrates most clearly the impression that one frequently gets when studying normal skin with thin epidermis. The sweat duct appears lined by two to three rows of epithelial cells which are different from the prickle cells of the epidermis and are separated from them by a layer of very flat cells. In some spots a "basal membrane" seems to be present.

The impression that the cells lining the sweat duct are different and are in their behavior independent from the rest of the epidermis is verified by instances in which the epidermal cells are altered experimentally or in the course of disease.

Figure 1d represents a sweat duct in a biopsy of acute vesicular dermatitis following a patch test with ragweed oil in a hypersensitive individual. Most of the vesicles in this case were periporal. The sweat ducts themselves, however, traversed the vesicles more or less unaffected by the edema which had completely dissolved the surrounding rete Malpighii. However, observations of this type may be interpreted as due to the fusing of the lining cells which does not permit them to take part in the spongiosis.

More conclusive is selective "vital staining" of the epidermis by means of pigment granules. Normal skin of white individuals contains melanin exclusively in the basal layer from where it is transported down into the cutis. In cases of increased pigment

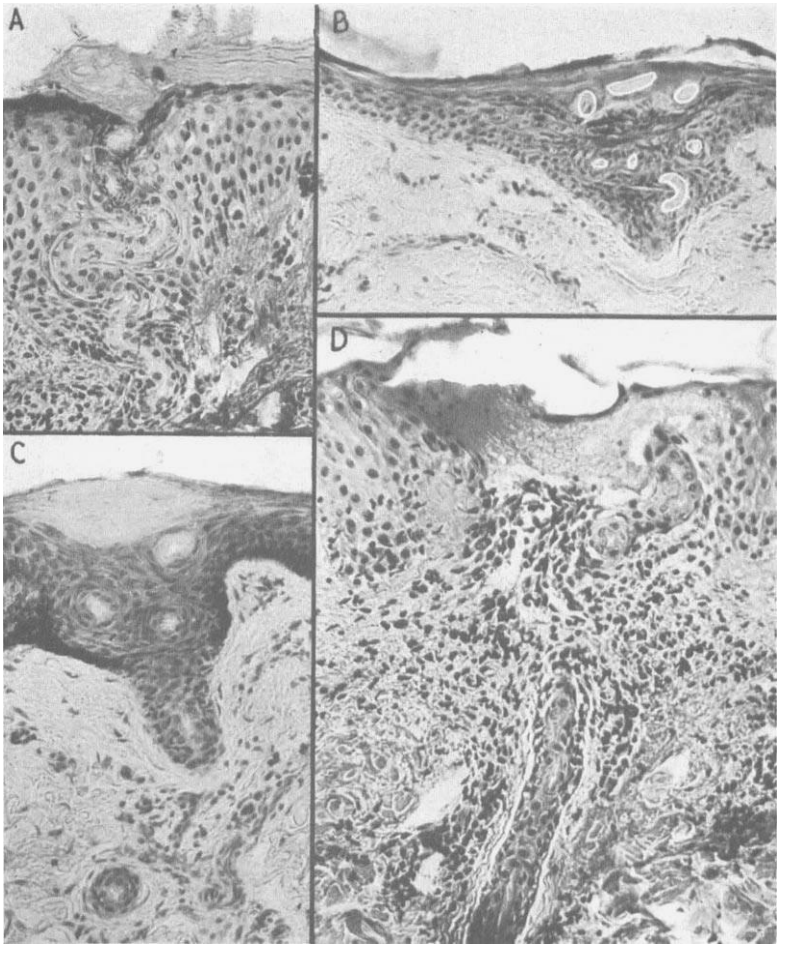

FIG. 1. a. Normal sweat duct showing intraepidermal wall and "basal membrane." Hematox.-van Gieson. × 225.

b. Coiled-up sweat duct in senile atrophic epidermis. Unna-Pappenheim. × 225. The lumen of the duct has been marked by white ink.

c. Absence of pigment from wall of sweat duct in epidermis of dark-skinned negro. Blue polychrome. × 225.

d. Sweat duct passing through periporal vesicle in case of acute dermatitis. H & E ×225.

formation following irradiation melanin granules are carried upward with the prickle cells, and may be found in all the strata of the epidermis. The same is true in Addison's disease and other pathological hyperpigmentations, and takes place normally in

the skin of negroes. In all these instances pigment granules are completely absent from the cells lining the sweat duct. The skin of dark colored negroes is a particularly good object for these observations (fig. 1c). The pigmented basal cells surround the sweat duct like a cuff, in some cases extending downward along the duct for a short distance. The distinction between pigmented and non-pigmented cells is always sharp, and throughout the entire thickness of the epidermis, including the horny layer, each single cell can be recognized as belonging either to the epidermis or to the duct. Defenders of the theory that the sweat duct has no wall would have to assume that the pigment is being totally destroyed by the sweat just as the tonofibrils are said to be dissolved in the lining cells.

This explanation, however, can not be applied to those instances in which the epidermal cells undergo anaplastic changes while the epithelium of the sweat ducts—and incidentally of the hair follicles—remains normal. Freudenthal[3] has called attention to the peculiar difference that exists in senile keratoses between the edematous irregular, parakeratotic epidermis and the dark-staining funnels of stratified epithelium which surround sweat ducts and hair follicles and which undergo normal keratinization (fig. 3a). Any well developed keratosis senilis furnishes ample evidence of the fact that the epithelial layers which line the appendages of the skin retain their normal structure even if the entire epidermis in between the ostia is converted into an atypical mass of anaplastic cells. Analogous pictures may be found in Bowen's disease. It is hardly conceivable that the sweat can restore anaplastic cells to their normal shape and function. Moreover, the fact that the follicular epithelium also remains normal bars any possibility of the sweat playing a rôle in this phenomenon. The conclusiveness of this demonstration of the wall of the intraepidermal duct can be disputed with only one argument, viz. that the conditions in a severely pathologic epidermis must not apply to the normal skin.

This argument can be refuted by taking into account the spiral

[3] Freudenthal, W.: Verruca senilis and Keratoma senile. Arch. f. Dermat. **152**: 505, 1926.

shape of the duct and its variations with varying thickness of the epidermis. Hoepke[2b] tried to explain the spiral by the action of inherent mechanical factors in the rete Malpighii (innere Gewebsspannung). He emphasizes that the duct always enters the thickest portion of the epidermis viz. the cristae intermediae of the palm, a particularly large "rete peg" at other parts of the body. The direction of an individual epidermal cell on its way toward the surface results from two components: (1) the push perpendicularly away from the epidermal-cutaneous junction, (2) the general mass movement toward the free surface. These two forces are likely to result in a spiral movement where the cells are crowded in a long and relatively narrow rete peg. If this reasoning is correct it follows that the tortuosity of the duct must be the more pronounced the thicker the epidermis and the longer the rete pegs. However, just the contrary is true. The sweat duct traverses the thick epidermis of the palms and soles as a steep spiral, while it is much more tortuous in the thin portions of the skin. Figure 2a illustrates how a sweat duct is practically straightened out in the acanthotic palmar epidermis of a chronic eczema, while figure 2b shows marked sinuosity in atrophic palmar epidermis. Most pronounced kinking is found in senile atrophy of the skin where the rete consists of only 4–6 layers of cells (fig. 1b). All these facts are consistent with the view that the intraepidermal part of the sweat duct is a separate entity of given length which adjusts its shape to fit various widths of the epidermis.

Some minor items of evidence can be cited which, although not conclusive in themselves, help to support the case. The cells which line the sweat duct in the epidermis do not contain tonofibrils. Hoepke assumes that these have been dissolved by the action of the sweat although he admits that there is no morphologic evidence of this taking place. This difficulty is eliminated if one grants that the lining of the sweat duct in the epidermis is of the same kind as in the cutis where tonofibrils are not usually present in the syringeal epithelium.

The ostia of the sweat ducts often continue to form kerato-

hyalin and normal keratin in cases of generalized exfoliative dermatitis in which the entire epidermis is parakeratotic. Hoepke cites convincing evidence that the formation of keratohyalin and keratin is entirely independent from the action of the sweat (keratinization in embryonic skin before the sweat glands begin to function; keratinization in the esophageal epithelium of ani-

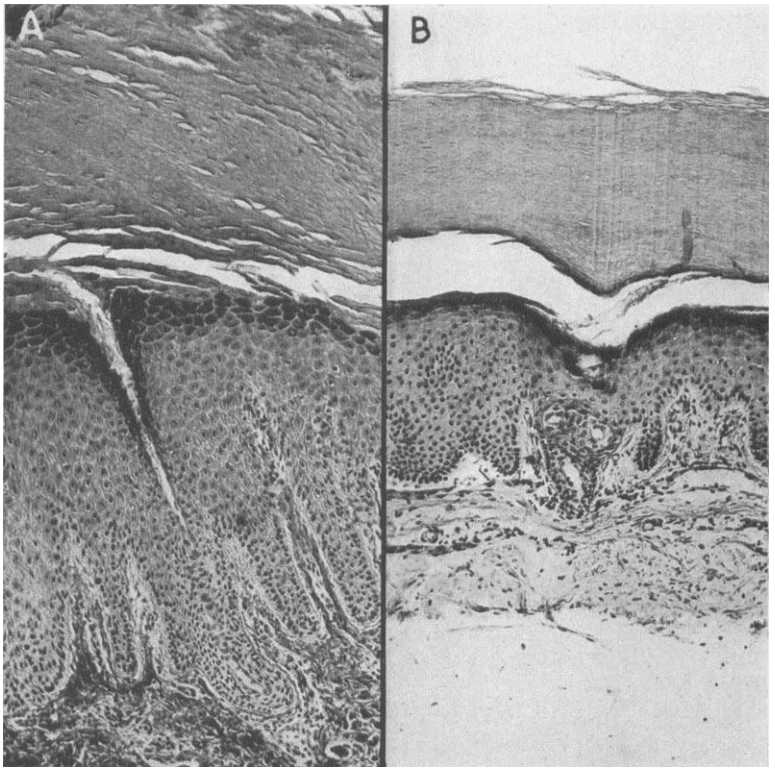

FIG. 2. a. Straight sweat duct in acanthotic palmar epidermis. H & E × 100.
b. Sinuous sweat duct in atrophic palmar epidermis. H & E × 100.

mals). His arguments can be supplemented with instances of pathologic occurrence of keratohyalin and keratin in sites remote from any sweat glands: leukoplakia of oral and cervical mucosa, hornpearls in seborrhoeic warts and epidermoid carcinomas. It is hardly possible, therefore, to make the sweat responsible for the normal keratinization of the ostia in exfoliative dermatitis.

It is much more likely that this phenomenon is due to biologic differences between epidermal and syringeal cells.

COMMENT

The significance of the issue under discussion is not at once obvious. It is, however, of more than scholastic interest. The view that the sweat duct retains its own wall within the epidermis changes our concept of the epidermal architecture to a certain degree. We must conceive of the epidermis not as a plate from which sweat ducts (and hair follicles) are suspended as its appendages, but as a cast which is pierced by biologically separate structures around which it is molded. Two questions immediately come to the mind: How is the connection maintained between the syringeal and the epidermal epithelia? And by which mechanism are the syringeal cells replaced, since they are constantly lost by cornification and desquamation on the surface?

Although the syringeal cells have no tonofibrils they are connected with each other and with the prickle cells by intercellular bridges. The connection apparently is not very firm—Hoepke mentions that the sweat ducts can be separated from the rest of the epidermis after maceration. It would seem, however, that the corkscrew shape of the duct together with specially arranged bundles of tonofibrils in the surrounding epidermis guarantees a safe coherence of the tissues under most circumstances. It is likely, therefore, that the sweat duct is carried upward at the same rate as the epidermis. According to Sutton[4] the horny layer of the normal epidermis is entirely replaced every seven to eleven days. Even if the rate is slower this means a constant loss of considerable amounts of syringeal epithelium particularly in those regions where the intraepidermal duct is kinked and coiled up. In addition, as Hoepke has pointed out, cells are constantly degenerating and dissolving into the lumen of the duct.

Where is the matrix for the replacement of these cells? In spite of rather extensive search in several hundred biopsy speci-

[4] Sutton, R. L., Jr.: Early Epidermal Neoplasia. Arch. Dermat. **37**: 737, 1938.

mens, I have never been able to find mitotic figures in the intraepidermal part of the sweat duct. It is well known that mitoses are rarely found in normal epidermis, so rarely indeed that some authors have held that amitosis is the common type of cell division in the epidermis. This contention, however, has not been proved,[5] and the small number of mitoses is usually explained as due to the rhythmical occurrence and relatively short duration of the process.[6] The same arguments can be applied to the sweat duct. However, the consistent absence of mitoses appears strange if any one level of the duct plays the rôle of matrix for the desquamating cells. Neither is there any other morphological indication that such a well defined matrix zone exists. The duct passes evenly from the cutis into the epidermis. There are two possibilities. Either the cells are replaced by amitosis, or the entire length of the sweat duct serves as matrix, and there is a continuous upward movement of cells from the deeper portions. Of the first mechanism there is no proof, and it is not even likely from what is known in general of the rôle of amitosis in cellular biology.[7] While the second possibility also is entirely hypothetical at present, there is at least evidence of considerable proliferative power of the deeper parts of the ducts. Adenomatous proliferation of the syringeal epithelium is not uncommonly found near lupus vulgaris, after roentgen-ray treatment of carcinomas, and in other chronic processes which destroy the upper end of the ducts. Another example is hidrocystoma of the face, in which the occluded ducts persist for a long time. The formation of the cysts apparently is not due entirely to the pressure of secretion but also to active proliferation of the epithelium.[8] In tissue cultures of human corium such fragments which contain parts of sweat glands often give rise to extensive epithelial growth.

[5] Pinkus, F.: Anatomie der Haut, in Handbuch der Haut- und Geschlechtskrankheiten (J. Jadassahn), Vol. I, 1, p. 89. Berlin 1927.

[6] Cooper, Z. K. and Schiff, A.: Mitotic Rhythm in Human Epidermis. Proc. Soc. Exper. Biol. and Med. **39**: 323, 1938.

[7] Macklin, C. C.: Binucleate and Multinucleate Cells in Tissue Cultures. Anat. Record **10**: 225, 1916.

[8] Kenedy, D. and Lehner, E.: Ein Fall von Hidrocystom. Arch. f. Dermat. **142**: 95, 1923.

The syringeal epithelium appears to be capable of more active proliferation than the epidermis under these conditions, and the mechanism of multiplication is mitosis.[9]

The proof of the existence of biologically independent structures in the epidermis would be of some significance in pathological conditions.

1. It would be of diagnostic value in the decision whether a given anaplastic process of the epidermis is "precancerous" (intraepidermal, preepithelioma[10]) or whether it has the destructive properties of the true carcinoma. As long as the malignant cells respect the basal membrane, they would in all probability also leave the sweat ducts untouched. Therefore, if sweat ducts (and hair follicles) were preserved within the altered epidermis of any biopsy it would not be likely that we were dealing with an invasive malignancy. If the appendages have been destroyed the carcinoma probably would also have transgressed into the corium.

2. Sweat ducts (and hair follicles) would become important as independent sources of cornifying epithelium when the epidermis proper had been eliminated.

It is a long recognized fact that remnants of the appendages help materially in the epithelization of granulating wounds. Sections of senile keratoses make it likely that the appendages play a similar rôle when the epidermis has become too anaplastic to fulfill its protective function of keratinization. Figure 3b shows a lesion in which a highly anaplastic basal layer is separated by a cleft from relatively normal upper strata. This constitutes the last step of a process the earlier stages of which are more commonly found in senile keratoses. Usually the ostia of the appendages are surrounded by inverted cones of normal epithelium which repress the anaplastic cells to a certain degree (fig.

[9] Pinkus, H.: a. Ueber Gewebekulturen menschlicher Epidermis. Arch. f. Dermat. **165**: 53, 1932.

b. Notes on Structure and Biological Properties of Human Epidermis and Sweat Gland Cells in Tissue Culture and in the Organism. Arch. f. exper. Zellforsch. **22**: 47, 1938.

[10] Satenstein, D. L.: Histologic Evidence of Epithelioma of the Skin. Arch. Dermat. **33**: 48, 1936.

3a). The area occupied by normal cells is greater on the surface than at the basal layer of the epidermis. If this process continues, the normal epithelium covers ever larger areas of the surface until the circles merge and the anaplastic cells remain

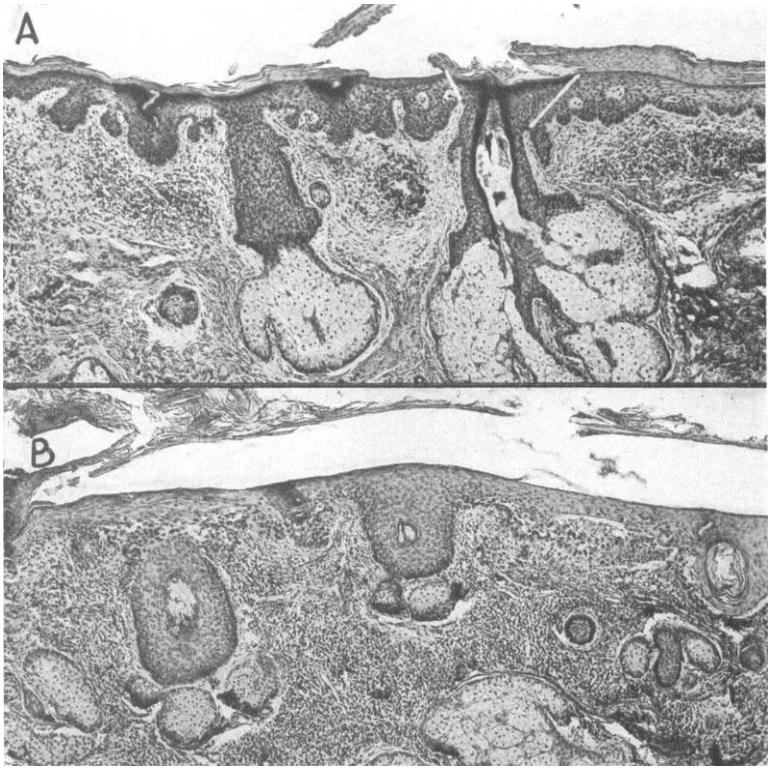

FIG. 3. a. Senile Keratosis. Inverted cones of dark staining epithelium with thick granular layer surround the ostia of sweat glands and hair follicles. The boundaries of one follicle have been outlined by white ink. Note that the broad bases of the cones almost touch each other in some spots. H & E × 50.

b. Senile Keratosis. Horny layer relatively normal because the anaplastic epidermis has been superseded by the normal lining of the appendages. H & E × 50.

in the depth. Thus the paradoxical picture of figure 3b is produced where an anaplastic basal layer seemingly gives rise to normal strata of prickle cells and keratin. An excellent example of this process is reproduced in figures 1a and 1b of Sutton's

article[4] on early epidermal neoplasia. While the center of the lesion shows parakeratosis arising on anaplastic epidermis the borders show the anaplastic cells buried under, and separated from, the normal epithelium that spreads from the hyperplastic ostia (in this instance mainly hair follicles).

3. While this paper deals with the ducts of the eccrine sweat glands exclusively, it has been shown elsewhere[11] that the concept of Paget's dermatosis as a mammary cancer which invades the epidermis secondarily may be aided materially by these findings. If the ducts of the apocrine glands and of their homologa, the milk ducts, are also lined by their own epithelium throughout, a carcinoma will be of extraepidermal origin even though it arises in the very ostia of the ducts.

CONCLUSIONS

Our understanding of the normal structures and life processes of the body has frequently been furthered by analyzing them under the abnormal conditions of experiment or disease, and by comparing them to entities of more or less different organization. It was the purpose of this paper to apply these methods to the end part of the sweat duct in order to correct a view based on most careful scrutiny of the normal anatomy of this structure. It appears that the tendency of the anatomists to consider the highly specialized skin of palms and soles as prototype of skin in general has contributed to establishing an erroneous concept. It is significant that Hoepke was inclined to accept the independence of the syringeal wall on the basis of observations made on the skin of the scalp.[2a] He reverted to the old view, however, after a painstaking study of palmar epidermis.[2b]

The author wishes to emphasize *that he considers the evidence for the existence of a wall of the intraepidermal sweat duct as conclusive*, while several of the points discussed in the commentary need further investigation and may be subject to correction.

[11] Pinkus, H. and Gould, S. E.: Extramammary Paget's Disease and Intraepidermal Carcinoma. Arch. Dermat. **39**: 479, 1939.

SUMMARY

1. Evidence is presented that the ducts of the eccrine sweat glands do not lose their walls where they enter the epidermis, but are lined by their own epithelium through all the strata of the skin.

2. The significance of this fact is discussed in regard to (a) the normal architecture of the epidermis, (b) the mechanism of replacement of the cells lost by desquamation, (c) the differential diagnosis of intraepidermal and invasive malignancies, (d) the pathology of keratosis senilis, (e) the concept of Paget's dermatosis as a malignancy of extraepidermal origin.

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