Experimental Production of Metaplasia in the Human Apocrine Sweat Gland*

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Any cell in the body may undergo a variety of changes. One of the most interesting of these is the morphologic transformation of a normal adult cell into another related, yet histologically distinct, type. Thus, the columnar epithelium of the bronchial tree may be transformed into squamous epithelium of a normal adult type. This process is known as metaplasia. It has recently attracted special attention because of its potential relationship to the growth problem of cancer.

Metaplasia has been described as occurring in numerous tissues and organs, e.g., the thyroid (1), the peritoneum (2), the uterus (3), the mucous membrane (6), the prostate (7), and the breast (9). In regard to the skin, Hempelmann, Lisco, and Hoffman (4), Nodi (8), Walther and Montgomery (11), and Weidman (12) have written concerning metaplasia in the eccrine sweat gland ducts and in an eccrine sweat gland tumor.

The generally held view is that metaplasia is a benign change in cells which are undergoing a reparative process. The transformation is within certain restricted limits, i.e., a differentiated columnar epithelial cell may undergo “squamous” metaplasia; an epithelial cell, however, never becomes a mesodermal cell, such as a histiocyte. The causes of metaplasia are as numerous and as nonspecific as the forms in which injury may appear. Many types of trauma may incite metaplasia. For example, chronic inflammation is a common antecedent of metaplasia. Metaplasia may be seen after vitamin A deficiency and occasionally after the administration of large amounts of estrogenic hormones. It would appear that metaplasia is possibly a reversion under stress to a more hardy type of cell.

Although nothing could be found in the literature regarding the occurrence of metaplasia in the apocrine sweat gland, our histologic studies of axillary skin (10) have convinced us that the secretory coil of the apocrine gland shows local areas of metaplasia under the stress of chronic inflammation. It was decided to study this process more closely by attempting to produce it experimentally.

MATERIALS AND METHODS

A variety of damaging or irritating technics was employed in treating the axillary skin of normal human male subjects:

(1) Formaldehyde, aqueous solutions, 5, 10, 25, 50 per cent applied topically for 5 minutes, once daily for 2 weeks.
(2) Procaine, 4 per cent aqueous solution, injected once.
(3) Talcum, aqueous suspension, injected once.
(4) Milk, pasteurized, injected once.
(5) Electrocoagulation, variable intensity.
(6) Silk thread, in incision site for 2 weeks.
(7) Hair, in incision site for 2 weeks.
(8) Epidermis excised.
(9) Axillary tissue, wedge buried in situ by suturing adjacent skin over it.
(10) Simple incision.
(11) Superficial undercutting of axillary epidermis.
(12) Deep undercutting of axillary epidermis.
(13) Deep excision of skin followed by scarring.

Biopsy specimens were taken 2 weeks after the noxious stimuli or traumatic procedure. In the case of the scar excisions, specimens were obtained at the following intervals: 1, 2, 3, 5, 7 weeks, and 6 months. All of the specimens were serially sectioned and stained with hematoxylin and eosin.

RESULTS

The only process which led to the appearance of squamous metaplasia in the secretory coil of the apocrine gland was scar formation after excision of axillary skin. The technics other than deep excision either had no effect on the gland or, as in the case of the electrocoagulation, produced only occasional metaplastic cells.

In the scars of healing wound sites, diffuse inflammatory changes were found, and certain apo-
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crine glands showed desquamating cells which were highly pigmentated with yellow-brown granules. In others, the lumen was partially or completely filled with large, pale staining, finely granular, and at times vacuolar cells (Fig. 1). These cells had small pyknotic nuclei and in certain glands could be seen to arise from the wall of the damaged apocrine gland (Fig. 2). The contrast between these vacuolar squamous cells and the normal columnar secretory cells of the apocrine gland (Fig. 4) is remarkable. Comparison of these metaplastic cells (Fig. 3) with those of the normal sebaceous gland (Fig. 5) shows striking similarities. Actually, some of the metaplastic apocrine coils were identified as normal sebaceous gland on cursory inspection.

These metaplastic cells showed no anaplastic changes and their growth was strictly confined to the cavity of the gland. Abnormal mitotic figures were not seen.

A study of biopsy specimens of scars present in the axilla for over 1 month failed to reveal metaplasia of the apocrine secretory coils.

DISCUSSION

The epidermis and all of the epidermal appendages appear to arise embryonically from a single ectodermal cell which has the potential of forming all of the highly specialized cells of the adult epidermis and the appendages. In areas of local trauma of appropriate intensity, the adult cells are destroyed, and regenerative processes are called into play. At times metaplasia may result. In this experiment, metaplasia of the apocrine cells occurred. This process is in no way limited to the apocrine gland, and has been seen in the eccrine gland, the sebaceous gland, and elsewhere in skin, by us and by other observers.

The metaplastic change in the apocrine gland offers special opportunities for the study of the growth processes of primitive epidermal cells. No other area in the skin affords this opportunity; elsewhere, metaplasia is not associated with hyperplasia.

Further studies on the histochemistry of these metaplastic apocrine cells should prove rewarding. Recent work (5) would suggest that mucin may be present in these more elementary glandular cells.

SUMMARY

Proliferative squamous metaplasia of the secretory cells of the human apocrine sweat gland has been experimentally induced by inciting a low-grade local inflammatory change in the axillary skin. The metaplasia is interpreted as a process of cellular de-differentiation occurring during the regenerative and reparative process.

REFERENCES

FIG. 1.—Squamous metaplasia and hyperplasia occurring in an apocrine secretory coil as seen in an axillary scar 2 weeks old. X140.
Fig. 2.—Origin of metaplastic cells from apocrine cell wall. Note granular, squamous character of cells. ×370.

Fig. 3.—Squamous metaplasia filling lumen of apocrine gland. Note pyknotic nuclei and complete absence of normal apocrine cells. Compare with Figures 4 and 5. ×240.

Fig. 4.—Normal apocrine cells for comparison. ×240.

Fig. 5.—Normal sebaceous gland for comparison. ×240.
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