

CELL TRANSITION IN HUMAN SEBACEOUS GLANDS

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Abstract. Cellular transition in human sebaceous glands was analysed by means of ^3H -thymidine autoradiography. 20 biopsies from 8 healthy young men were taken 2 to 14 days after injection of the tracer. Observations on 3 proliferative portions of the sebaceous gland (sebaceous duct, fundus with differentiating cells and undifferentiated cell pool) showed marked differences. The duct displayed fast cellular migration with a renewal time of 2 to 4 days. Similarly, a fast migration (4-7 days) was observed in the undifferentiated cell pool. The differentiating (lipid-producing) cells in the glandular fundus, however, showed slow cell movement with a replacement time of more than 14 days. It is concluded that, despite a high labelling index, the lipid-producing parts of the sebaceous gland have a long renewal time.

Germinative cells in human sebaceous glands are located at the basement membrane as revealed by ^3H -thymidine (^3H -TdR) autoradiography (2-4). Their proliferative activity is region-dependent. Furthermore, there is a distinct labelling distribution within the gland itself (4). These findings prompted us to divide the proliferative cell pool of the sebaceous gland into two portions, namely the differentiating cell pool (DCP) and the undifferentiated cell pool (UCP). The differentiating cell pool includes (germinative) basal cells and differentiating lipid cells of the glandular fundus. The undifferentiated cell pool comprises several layers of epithelial cells and is located primarily at the tips of connective tissue protrusions, bordering single bland lobules or adjacent to the keratinizing cells of the sebaceous duct. In serial sections, these undifferentiated cells appear as a coral-reef or sponge-like skeleton throughout the gland (4). Differences in new cell formation in these two portions of the sebaceous gland, which were described in a previous paper (4), led us to study the fate of ^3H -TdR-labelled post-divisional daughter cells and to re-examine the renewal time of the gland.

MATERIALS AND METHODS

Twenty biopsy specimens from uninvolved skin of caucasian men, age 21-34, were examined. Some of these men served in previous studies of new cell formation in the human sebaceous gland (4).

Excisional biopsies were secured from:

the *mid-scalp* of two subjects, 2, 4, 6, 7, 10 and 14 days after injection of ^3H -TdR and of two subjects 3 days after the injection;

the *forehead* of two subjects 7 days after the injection;

the *back* of two subjects 4 and 7 days after the injection.

Injection of the tracer and preparation of autoradiographic slides followed previously described techniques (4). Evaluation of specimens included position of labelled cells and estimation of grain density over individual cells.

RESULTS

The results of this study will be given separately for each portion of the sebaceous gland: sebaceous duct epithelium, undifferentiated cell pool (UCP) and differentiating cell pool of the glandular fundus (DCP).

Sebaceous duct epithelium

Two days after injection of the tracer, labelled cells could be seen moving towards the lumen of the sebaceous duct. They were at right angles to the basement membrane and had reached the innermost cell layer of the epithelial lining by day 4 to 7 (Fig. 3). By this time they had passed through a thin granular layer, above which shedding of keratinized cells took place (Fig. 4b). No labelled material was seen in the ductal lumen at this time or later. Cells with fewer silver grains could still be seen in the middle or upper portion of the ductal epithelium.

Undifferentiated cell pool (UCP)

Labelled cells had traversed this accumulation of cells within 2 to 4 days. There was basically no

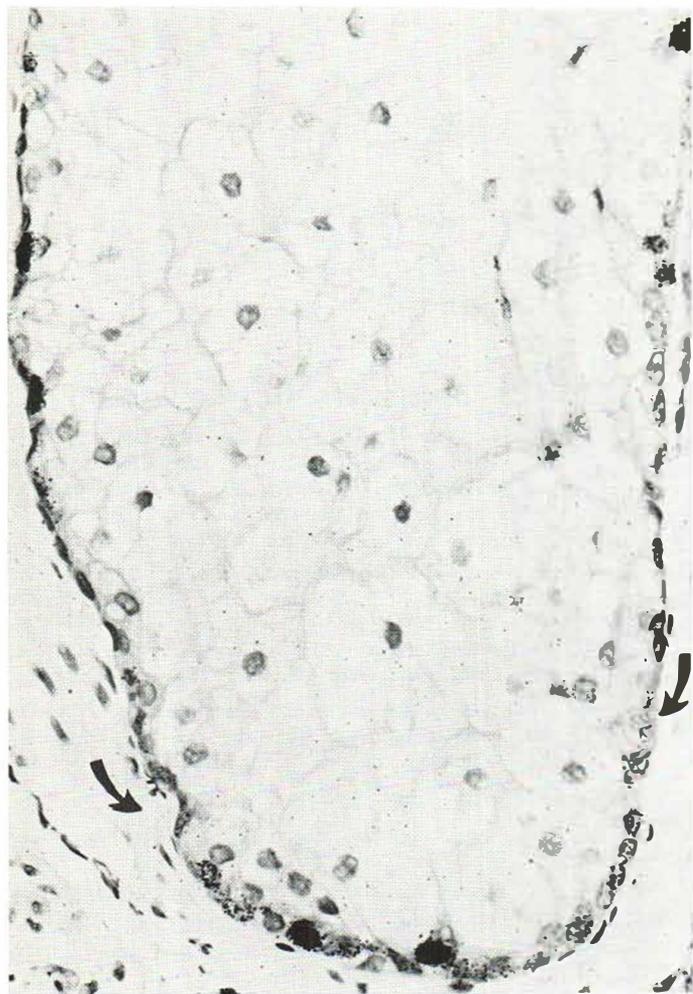


Fig. 1. Sebaceous gland. Scalp, 31-year-old man, 4 days after $^3\text{H-TdR}$ injection. Rosary-bead-like arrangement of labelled cells, which are still confined to the basement membrane (arrows). Hematoxylin, $\times 410$.

difference whether the UCP was thick (up to 8 cells, Figs. 2 and 3), or consisted of fewer cell layers. Where the UCP was adjacent to the sebaceous duct, clusters of cells with many labelled nuclei were often seen being shed into the lumen (Fig. 4a). These cells were flattened and contained basophilic nuclei. No lipid droplets or signs of keratinization could be found in the cytoplasm. After 7 days there were still some slightly labelled cells within the buds of undifferentiated cells. No labelling of this compartment could be detected after 14 days. However, a large number of labelled lipid cells was present in the central portion of the glandular fundus. It could not be decided whether these labelled cells stemmed from the germinative cells of the UCP or the DCP.

Glandular fundus (DCP)

During the first 7 days labelled cells remained in the basal cell row (Figs. 1 and 3), or in close proximity. This observation was true for all three regions studied (forehead, scalp, back). No attempt was made to elaborate on regional variations in transit time or gland renewal time because of the small number of specimens under study.

A repeated finding was the occurrence of an almost continuous rosary-bead-like band of labelled cells 3 and 4 days after injection of the tracer (Fig. 1). In 7-day specimens there was but little movement towards the lumen of the glands (Fig. 2). The central parts of the acini did not contain labelled cells before the 14th day. At this point silver grains were no longer seen in the basal cells (Fig. 5).

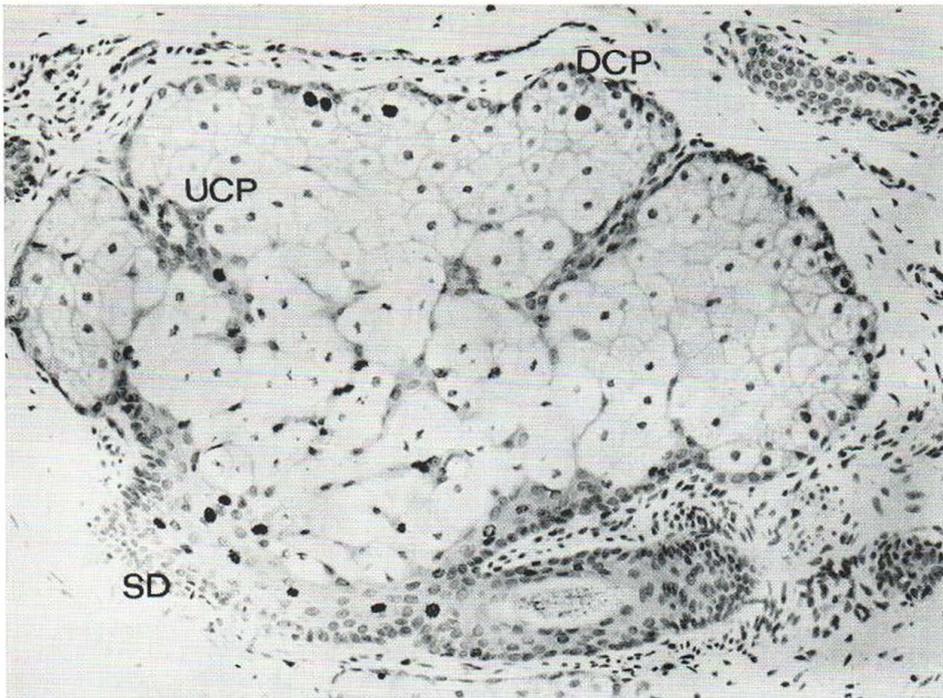


Fig. 2. Sebaceous gland with differentiating cell pool (DCP), multiple clusters of undifferentiated cell pool (UCP), sebaceous duct (SD) and hair shaft. Scalp, 21-

year-old man, 7 days after $^3\text{H-TdR}$ injection. Slow migration of labelled lipid cells (top) and rapid migration of UCP and SD cells (bottom). Hematoxylin, $\times 150$.

For comparison, the slow migration of sebaceous cells from the basement membrane was demonstrated together with cell migration of the overlying adjacent epidermis. In the epidermis, pairs of labelled cells had migrated some distance within 3 days, whereas in the underlying sebaceous gland, even 4 to 7 days after injection of the tracer, labelled cells were still located in the basal cell row (Fig. 1). After 7 days they had moved only 1 or 2 cell positions off the basement membrane (Fig. 2). With the data available from this study, however, no direct comparison of epidermal and sebaceous gland transit time was possible: reference-points, such as the granular layer or horny layer, where cells are trapped for observation, are not available in the sebaceous gland.

DISCUSSION

It became obvious in this study that cellular kinetics in the sebaceous gland were not homogeneous, but exhibited distinct differences depending on the portion of the gland. In defining glandular

turnover one should therefore specify the group of cells to be discussed.

Cells with the clear-cut task of producing an end-product (sebum or keratin) are those in the glandular fundus or those in the duct. Both types of cells exhibited marked differences in their migratory activity: whilst ductal epithelial cells migrated towards the lumen in 4 to 7 days (Fig. 4 *b*), the lipid cells from the periphery of the acini reached this objective usually later than 14 days after the injection of $^3\text{H-TdR}$ (Fig. 5). This is considerably longer than previously described (2, 3).

Certainly the fate of post-divisional cells of the UCP depends on their place of origin. UCP cells located near the sebaceous duct were found either to produce lipid cells or were emptied through the duct as clusters of undifferentiated cells (Figs. 3 and 4 *a*). It is possible that their anatomical position (close vicinity to the keratinizing duct, increased sebum flow rate) affects the ultimate fate of these cells. On the other hand, UCP cells in the glandular fundus behaved differently. They were devoid of labelling after 7 days, whereas

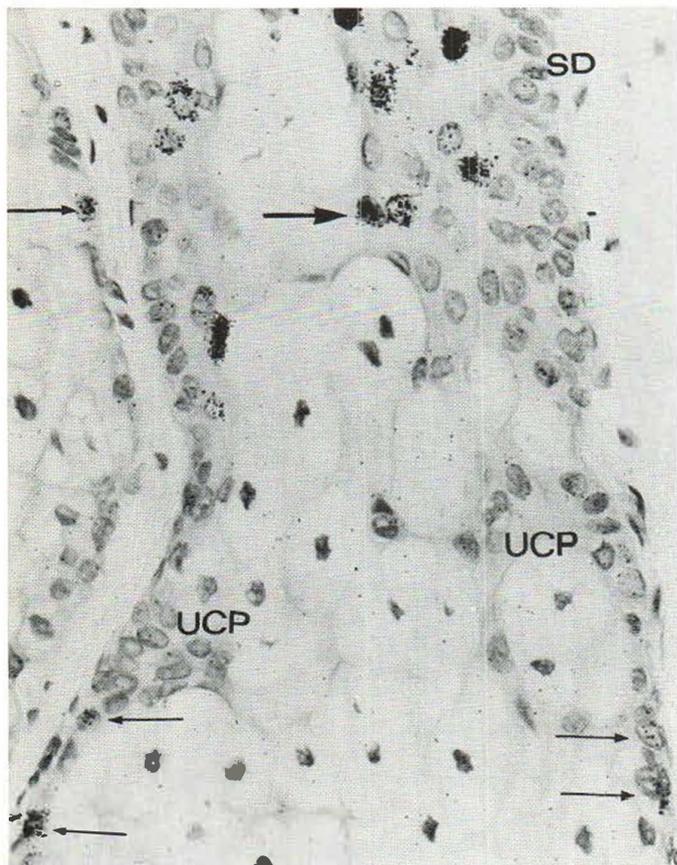
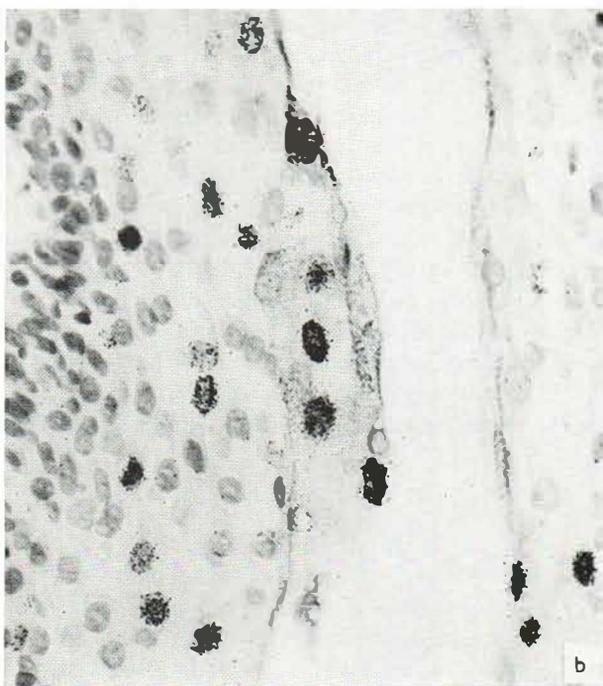
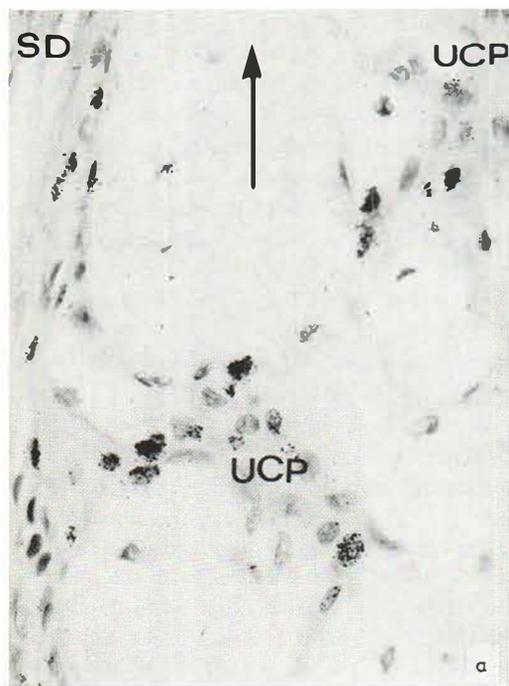


Fig. 3. Sebaceous duct (SD) and upper portion of the sebaceous gland with undifferentiated cell pool (UCP). Scalp, 27-year-old man, 7 days after $^3\text{H-TdR}$ injection. Labeled cells have moved through the entire SD towards the sebaceous duct lumen (bold arrows). Note labeled cells are still positioned at the basement membrane of the sebaceous gland (fine arrows). Hematoxylin, $\times 430$.



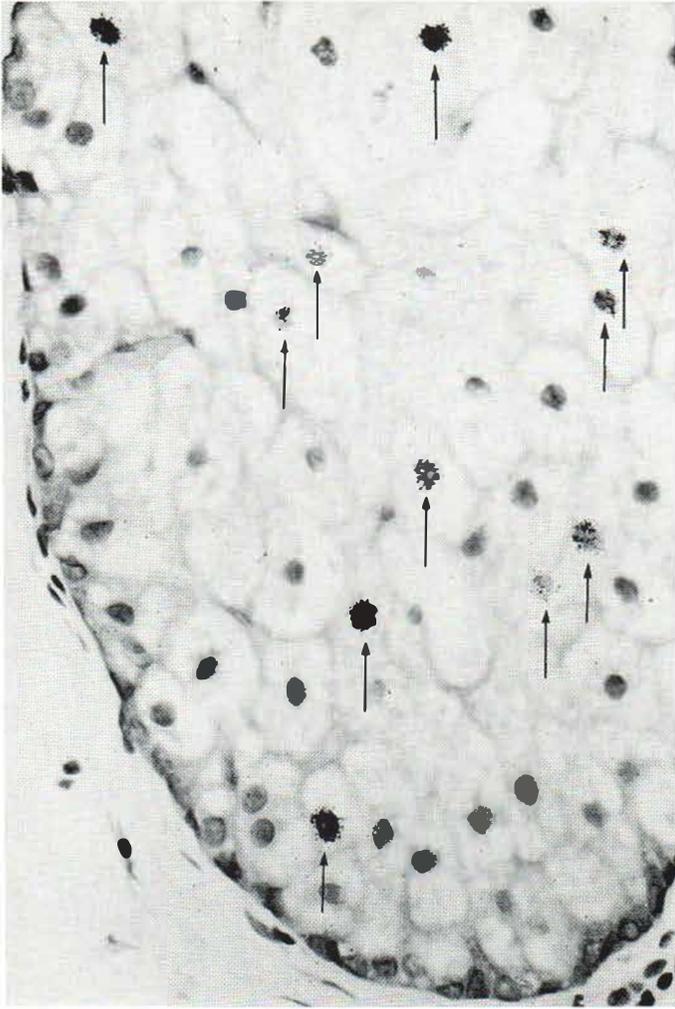


Fig. 5. Fundus of sebaceous gland (same subject as in Figs. 2 and 3). 14 days after $^3\text{H-TdR}$ injection. Labeled cells (arrows) have moved into the centre of the fundus. No more labelling over basal cells. Hematoxylin, $\times 455$.

many lipid cells adjacent to it were labelled. This shows that the UCP cells finally transform into lipid cells. Thus the UCP rather seems to be an accumulation of rapidly proliferating basal cells as suggested in the foregoing paper (4).

Our report clearly indicates that this cell-portion plays a significant role in the new cell production of the sebaceous gland. However, the separate

characterisation of the two cell populations of the sebaceous gland (DCP and UCP) seems to be justified on the basis of their histological features and their proliferative activity.

The slow migratory activity of the lipid cells in the fundus is in contrast to the comparatively high labelling index described in the foregoing paper (4). The reason for this discrepancy between the high labelling index and a slow cell transition in the sebaceous gland is not clear. However, a considerable lengthening of the time during which DNA is synthesized might be a factor.

From the data of this study it seems unlikely that stimulation of the sebaceous gland by physiologic or induced stimulators results in an immediate increase of sebum output. The circadian rhythm of sebum output in man (1) and fluctua-

Fig. 4 (a) Upper portion of the sebaceous gland. Scalp, 21-year-old man, 7 days after $^3\text{H-TdR}$ injection. Clusters of undifferentiated cells (UCP) are located between fully differentiated lipid cells. These clusters are evidently emptied into the sebaceous duct (SD). Large arrow marks direction of sebum flow. Hematoxylin, $\times 450$. *(b)* Sebaceous duct within the same section. $^3\text{H-TdR}$ -labelled daughter cells have reached the granular layer and are shed into the lumen. Hematoxylin, $\times 450$.

tions of the casual sebum level are more likely to be due to environmental factors than to cell division in the periphery of acini. Furthermore, stress factors, emotions and unsuitable diet, claimed to cause a sudden increase in sebum output, are difficult to explain by our kinetic observations.

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