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NEONATAL SEBACEOUS GLANDS: FINE STRUCTURE OF SEBACEOUS AND DENDRITIC CELLS

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Abstract. Ultrastructural features of sebaceous glands in newborns were examined in adnexal polyp lesions of neonatal skin. Material for electron microscopy was obtained from the nipple areola of 10 Japanese newborn babies of both sexes, less than 8 days of age. The cell organization of the neonatal sebaceous acini consisted of undifferentiated, differentiating, and mature sebaceous cells, and the sequence of sebaceous transformation seemed to be consistent with that described in the postnatal acini. The sheet of continuous basal lamina covering the sebaceous acini was neither distorted nor convoluted. This configuration in the basal lamina revealed no convincing evidence for physiological involution of the neonatal sebaceous cells were identified at the outer periphery of the sebaceous glands. Melanocytes in symbiosis with the sebaceous acini in concurrent presence of Langerhans cells.

Key words: Newborn; Adnexal tumour; Sebaceous cells; Melanocytes; Langerhans cells

The ultrastructural features of postnatal sebaceous glands in man have been investigated by many workers (4, 5, 17). In comparison with circumstantial studies performed on the early fetal sebaceous gland (4, 7), no information has as yet been obtained on that in newborn babies. This fact may primarily reflect certain restrictions attendant upon obtaining biopsy specimens from neonates.

The adnexal polyp of neonatal skin described by Hidano & Kobayashi (10) is a tiny polypoid tumour occurring on the nipple areola of neonates. One of the characteristic histopathological features of the skin lesions is the presence of adnexal elements including hair follicles, eccrine sweat glands, and sebaceous glands. We found the skin lesions a suitable material for the ultrastructural study of human sebaceous glands at the beginning of extra-uterine life.

MATERIALS AND METHODS

Lesions of adnexal polyp of neonatal skin were removed from the nipple areolae of 10 Japanese newborn babies of both sexes, less than 8 days after birth. The materials were fixed for 2 hours in cold 4% glutaraldehyde with cacodylate buffer at pH 7.4. After washing, they were post-fixed for 2 hours in 1% osmium tetroxide adjusted to pH 7.4 with buffer containing sucrose. The specimens were dehydrated in ethanol, passed through propylene oxide and embedded in Epon 812. Ultrathin sections cut on a Porter-Blum ultramicrotome MT-2 were stained with uranyl acetate and lead citrate. They were examined in a Hitachi HU-12A electron microscope.

RESULTS

Human neonatal sebaceous glands were small in size, and consisted of a small number of sebaceous acini. The outer surfaces of the acini were separated from the dermis by a smooth and continuous layer of basal lamina. Within the sebaceous acini, five cell types were readily discernible. Three of these were undifferentiated, differentiating, and mature sebaceous cells. The other two were dendritic cells of melanocytes and Langerhans cells.

Undifferentiated sebaceous cells

This type of cell was composed of two or more layers of cells at the immediate periphery of the sebaceous acini. The cells were oblong in shape and smooth in outline. Wrinkled, finger-like cytoplasmic projections were observed on the lateral surfaces of the cells. The apposed cells were joined together so tightly that the intercellular space was seen to be obliterated. When neighbouring cells formed contact by means of prominent, interlocking microvilli, few desmosomes were noted along the cell membrane.

Cuboidal nuclei contained nucleoli with nuclear bodies, and showed a large nucleo-cytoplasmic ratio. Varying numbers of mitochondria with opaque granules embedded in the matrix, glycogen particles aggregated into a small glycogen area, ribosomes and tonofilaments, were found scattered

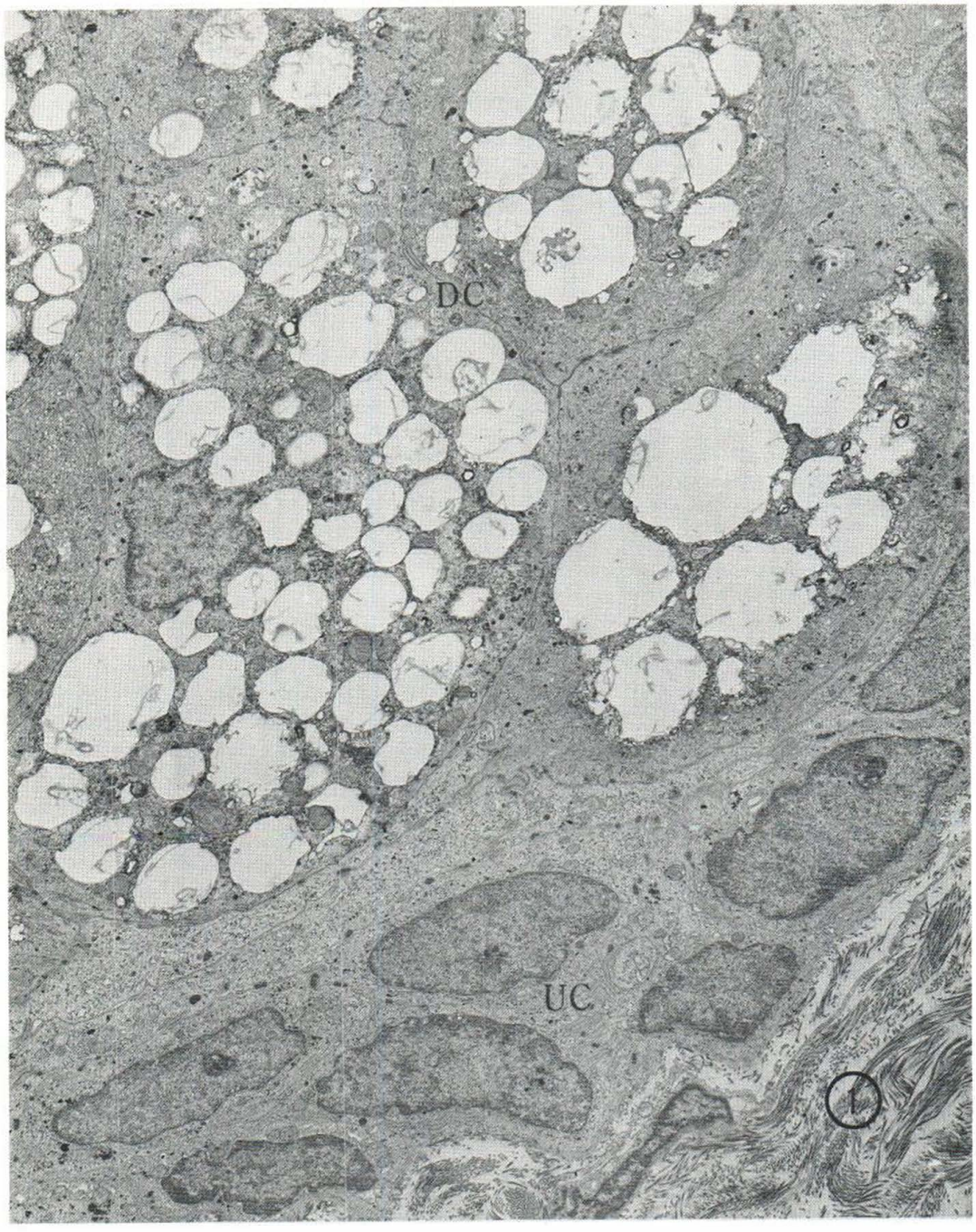

Fig. 1. Low-power electron micrograph of sebaceous acinus, showing layers of undifferentiated (UC) and differentiating sebaceous cells (DC). No intercellular space is visible. ×4000.

throughout the scanty cytoplasm. Frequently, the Golgi apparatus and endoplasmic reticulum were poorly developed or scarce. No lipid droplet was encountered in the cytoplasm (Figs. 1, 3 and 6).

Differentiating sebaceous cells

Drastic morphological alterations in the differentiating sebaceous cells were found from the inner periphery toward the centre of the sebaceous acini.

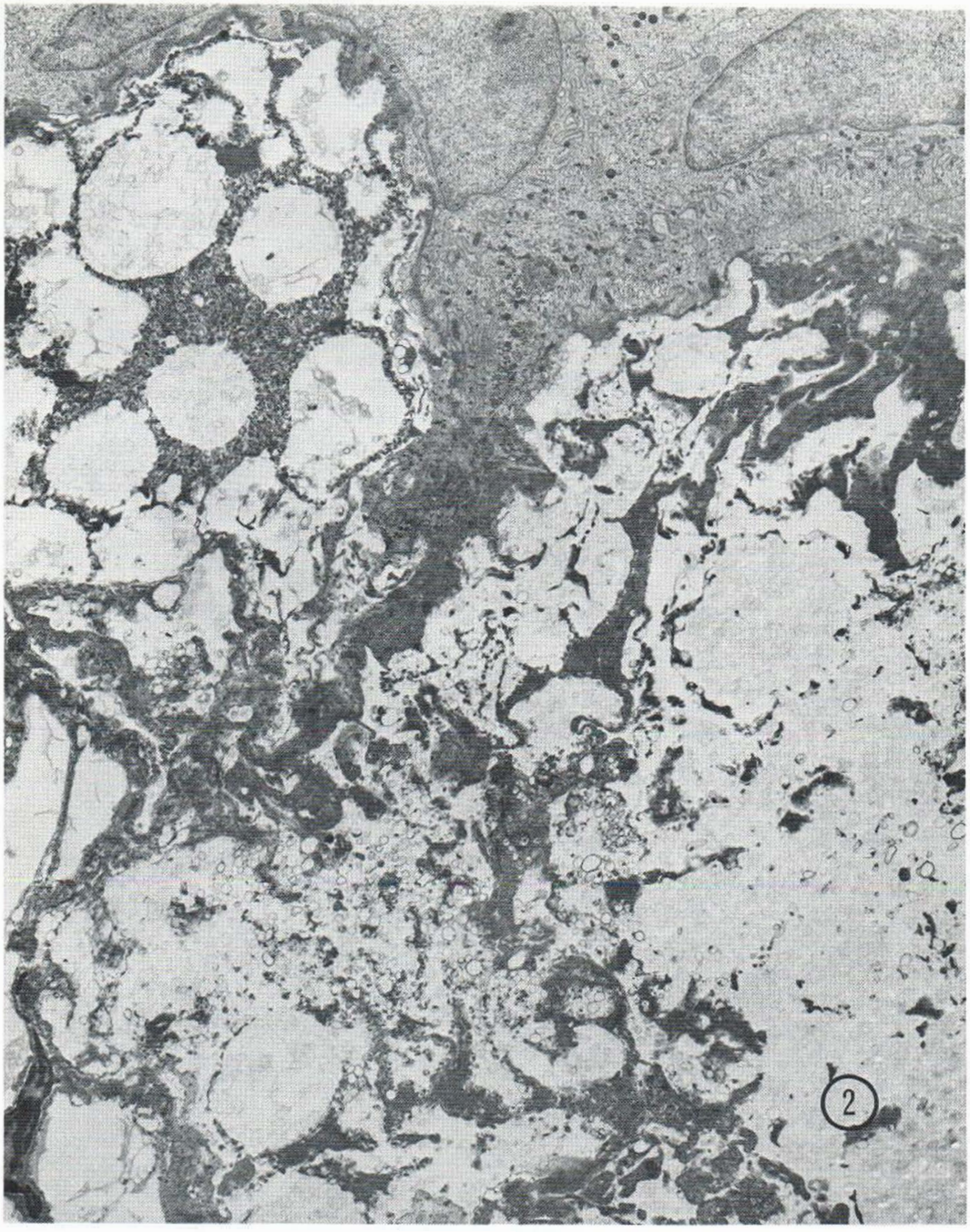

Fig. 2. Electron micrograph showing lumen of sebaceous duct. The sebaceous cell membrane is disrupted and the lumen is occupied by fused lipid droplets with remnants of disorganized organelles. In upper part of micrograph, membrane-coating granules are seen in duct epithelial cells. ×6000.

The cells gradually became large in size and ovoid in appearance, and the abundant cytoplasm was observed to contain the first visible lipid droplets. The nuclei were spherical with shallow undulations and were located in the cell centre. In contrast to the surrounding large cytoplasm, the nuclei remained small in size, giving a low nucleo-cytoplasmic ratio.

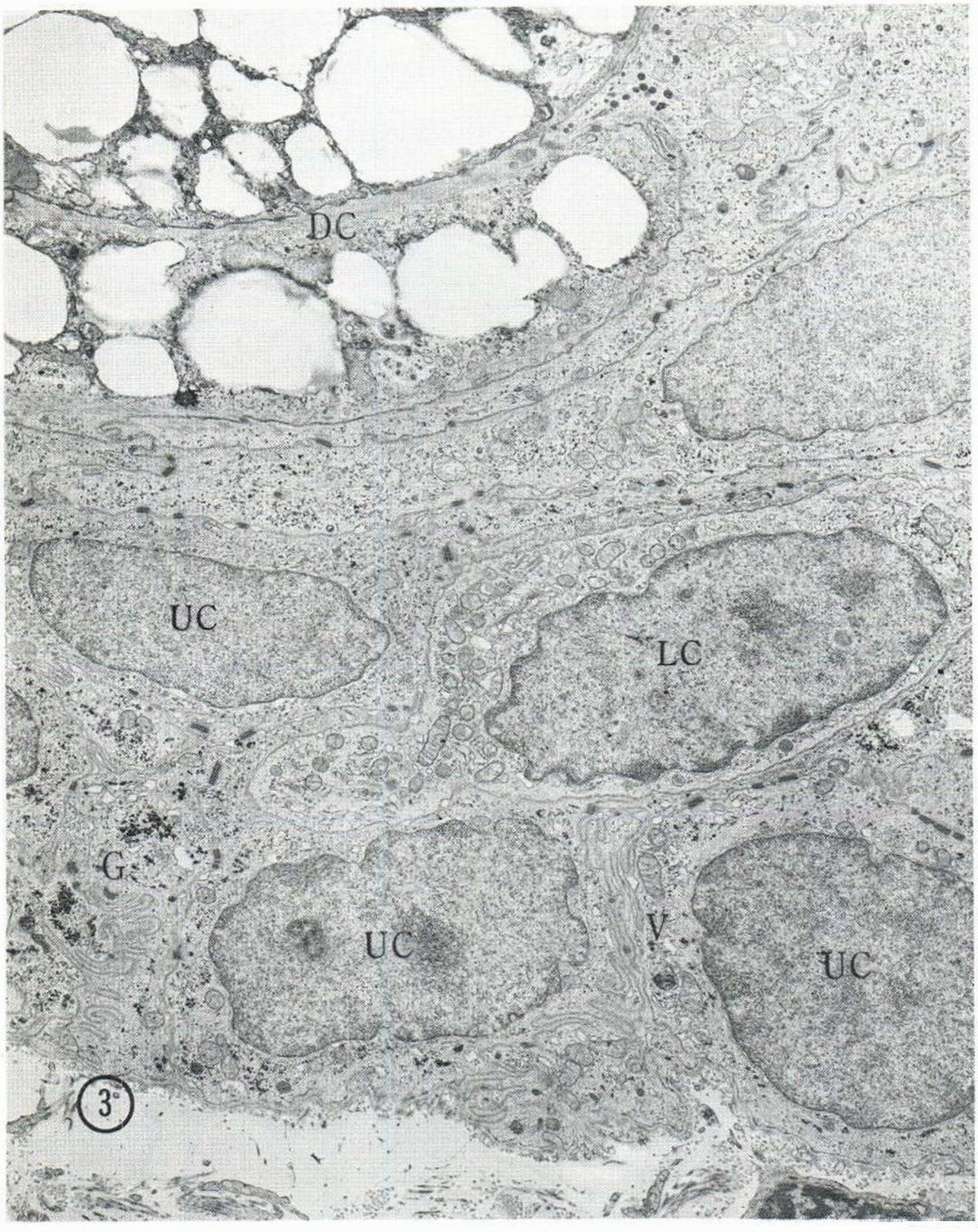

Fig. 3. Electron micrograph of undifferentiated sebaceous cell (UC) in outer periphery of acinus. Cells have a large nucleo-cytoplasmic ratio with moderately developed cytoplasmic organelles. *DC*, differentiating sebaceous cell; *G*, small glycogen area; *LC*, Langerhans cell; *V*, microvillous projection. ×6 000.

The differentiating sebaceous cells had disproportionally few desmosomes and microvillous projections along the cell membrane. The usual feature of the cells was the presence of the developed endoplasmic reticulum free of ribosomes, and the Golgi apparatus associated with many vesicles. Extensively dilated endoplasmic reticulum, ellipsoid or tubular in outline of nearly uniform diameter,

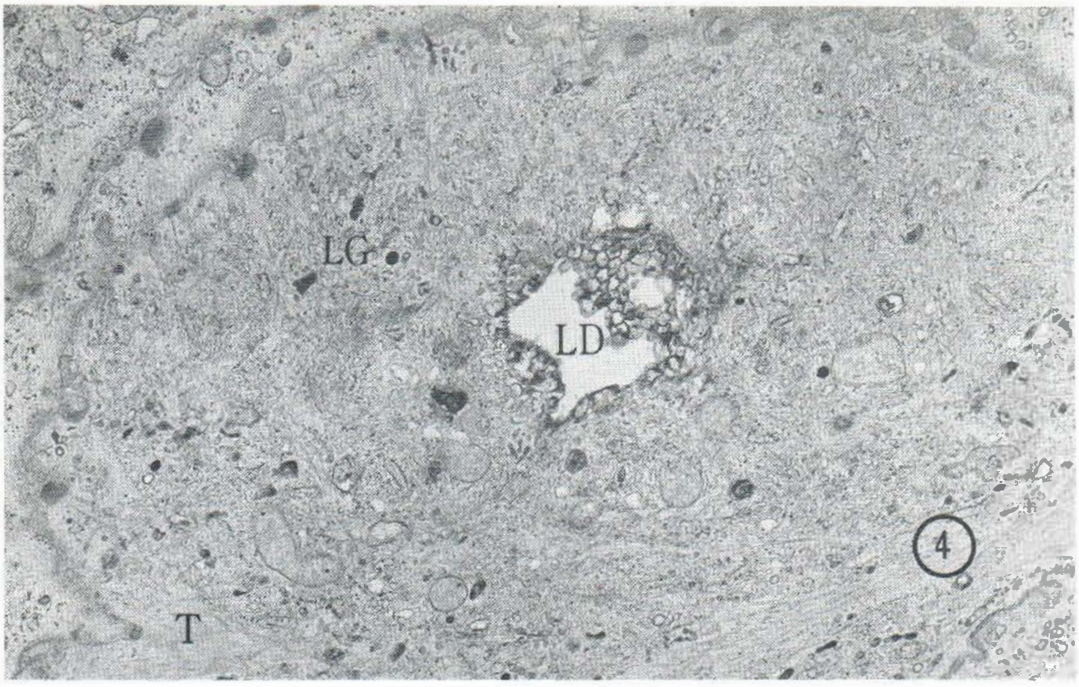

Fig. 4. Part of differentiating sebaceous cell. Expanded cytoplasm has tonofilaments (*T*) and lysosomal granules (*LG*). First lipid droplet (*LD*) is irregular in shape and surrounded by smooth vesicles. Endoplasmic reticulum is poorly developed. ×10000.

pervaded the cytoplasm, but contained no electron-opaque material.

A small number of the first lipid droplets were seen to occur in the central portion of the cytoplasm. They were either irregular or ovoid to round in shape and of varying size. As the sebaceous transformation progressed, the lipid droplets increased progressively in diameter and number to fill the cytoplasm. Though their limiting membrane was obscure, their circumference was usually encompassed by smooth vesicles, polyhedral in shape, which were arranged into distinct palisade formation. The interior of the droplets was observed to contain amorphous or flocculent material of low electron density intermingled with a clear component, of mottled appearance.

Initially, mitochondria were scattered at random within the cytoplasm. During the sebaceous transformation, they tended to enlarge and their matrix increased in electron density. Finally the mitochondria came into close contact with the lipid droplets. At this stage, the intramitochondrial granules could no longer be perceived. Over a period of active sebaceous transformation, the overall numbers of glycogen particles, ribosomes and tonofilaments were inversely proportional to the apparent increase in size and number of lipid droplets and lysosomal granules (Figs. 1, 3, 4, 5 and 6).

Mature sebaceous cells

Around the centres of the acini and in the sebaceous ducts, the sebaceous cells ultimately matured. Markedly expanded cytoplasm was further crowded with a large accumulation of multiple, huge lipid droplets occurring singly or fused with each other. This configuration seemed to be related to the deep nuclear indentations in order to produce a bizarre profile.

Swollen mitochondria were found disintegrated, and Golgi apparatus, endoplasmic reticulum, ribosomes, or tonofilaments were significantly reduced in number and finally disappeared from the cytoplasm. Deformed pyknotic nuclei, dense bodies resembling lysosomes, and electron-opaque strands possibly derived from the residue of the disorganized organelles were dispersed in the intracytoplasmic space between the lipid droplets. The cell membranes of both differentiating and mature sebaceous cells looked alike and were slightly thickened. None of membrane-coating granules were

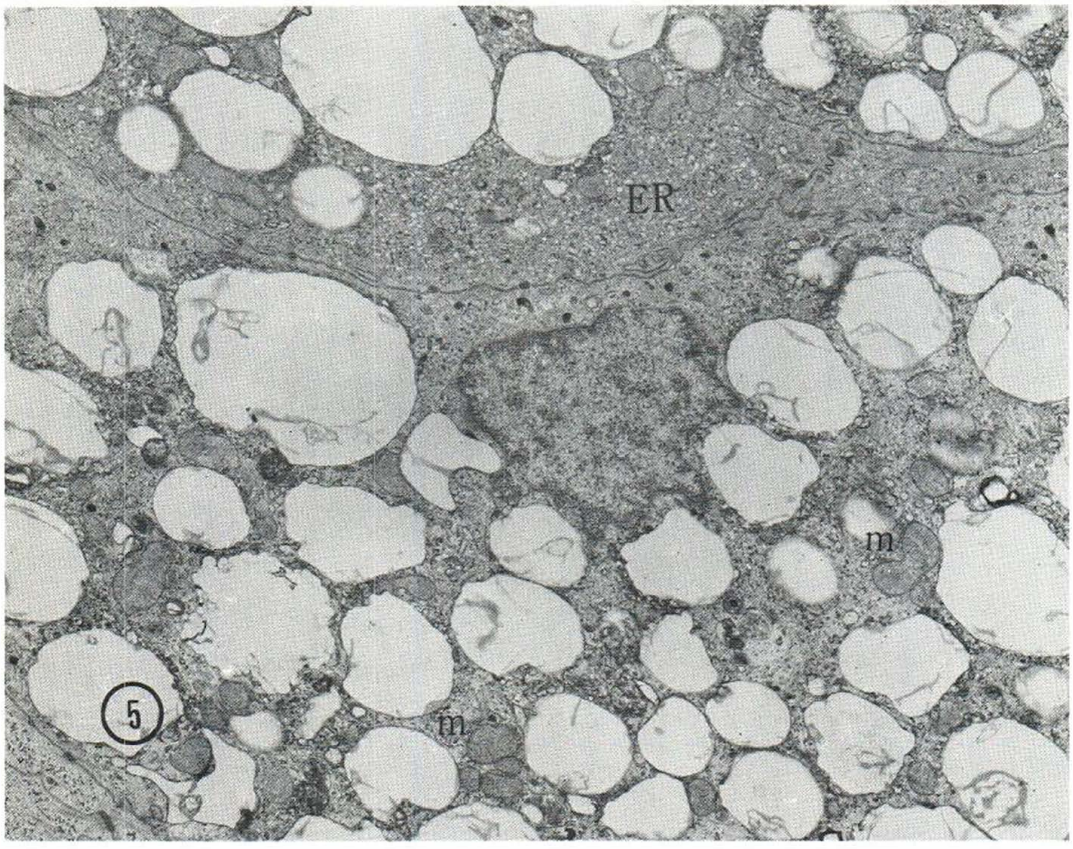

Fig. 5. Electron micrograph showing part of 3 differentiating sebaceous cells illustrated in Fig. 1. Note the developed endoplasmic reticulum (*ER*). *m*, mitochondrion closely apposed to lipid droplet. ×6 000.

noted. In the sebaceous ducts, the outline of the mature sebaceous cells seemed disrupted, leading to a breakdown of cell integrity (Fig. 2).

Melanocytes

Melanocytes were found distributed exclusively in the outer periphery of the sebaceous acini and in topographical relation to the basal lamina. When the perikaryon was directly apposed to the basal lamina, dense plates were clearly observed. As compared with the epidermal melanocytes, melanin-containing organelles synthesized by the sebaceous melanocytes were small in size and number, displaying incompletely melanized premelanosomes. Remote from the perikaryon, only few premelanosomes were present in the dendritic processes. Premelanosomes that had transferred into the sebaceous cells were only rarely encountered (Fig. 6). A preliminary report of the sebaceous melanocytes has been published elsewhere (11).

Langerhans cells

Langerhans cells in the sebaceous acini were more easily identified than were melanocytes. Langerhans cells were noted to be in close relation to the undifferentiated sebaceous cells but not preferentially to the basal lamina as were melanocytes. Nuclei of Langerhans cells were generally elongated and indented in appearance and had prominent nucleoli with nuclear bodies. Abundant cytoplasm contained a moderately developed Golgi apparatus, a number of mitochondria, scattered ribosomes, and small lysosomal structures round or tubular in profile. The cells were dendritic in shape, but the dendrites were mostly characterized by a cytoplasm which was devoid of recognizable cytoplasmic organelles (Figs. 3 and 7).

DISCUSSION

Previous electron microscopic observations on postnatal sebaceous glands have demonstrated that,

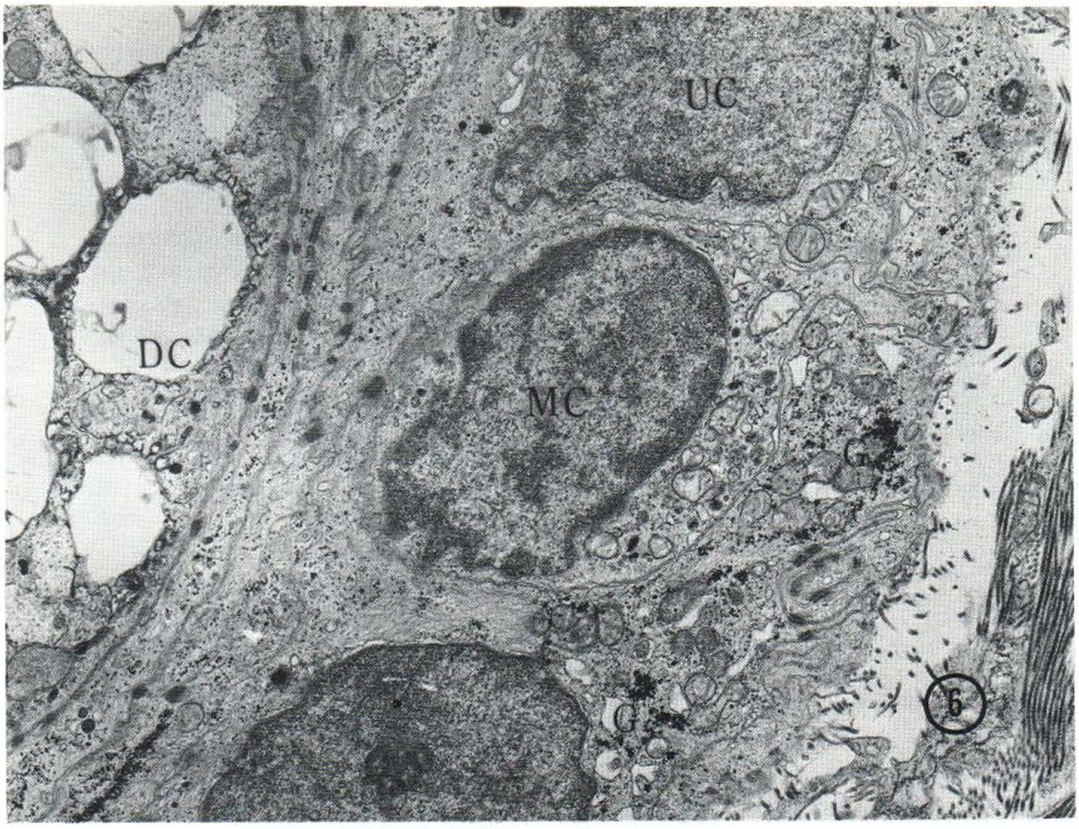

Fig. 6. Electron micrograph of melanocyte (*MC*) in sebaceous acinus. Note the melanin-containing organelles in developmental stages. *DC*, differentiating sebaceous cell; *G*, glycogen particle; *UC*, undifferentiated sebaceous cell. ×8 000.

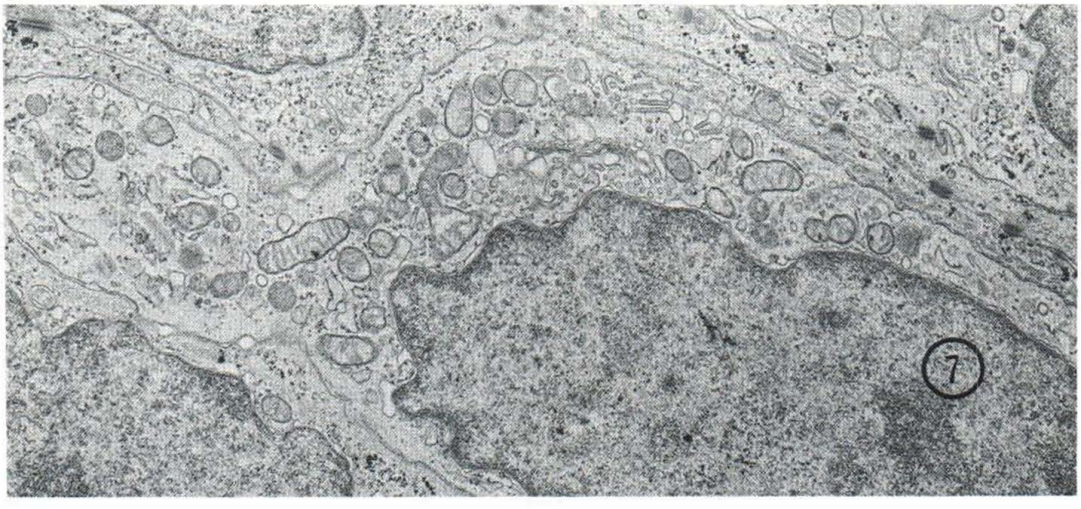

Fig. 7. High-power electron micrograph showing part of Langerhans cell illustrated in Fig. 3. Cytoplasmic organelles including characteristic Langerhans granules are seen. ×10 000.

with regard to age and site of the body, there is no substantial difference in sebaceous cell organization or in the cytoplasmic organelles (2, 4, 5, 6, 17). In the present study, the fine structure of the neonatal sebaceous glands also differed little from that of the postnatal ones.

The primary site of lipid synthesis in the sebaceous cells has been a controversial subject for many years. Several studies on the human sebaceous gland postnatally have shown that the smooth membrane system, consisting of endoplasmic reticulum and Golgi apparatus, is associated with the formation of lipid material (6). In contrast to the postnatal sebaceous glands, on the other hand, the lipid droplets appear free in the cytoplasm at an earlier, prenatal stage of development when the smooth membrane system is hardly observable in the sebaceous cells (4). Similar findings have been reported in the embryonal sebaceous glands of subhuman primates (1).

In the present study, the dilated sacculi of the Golgi apparatus, accompanied by developed endoplasmic reticulum, is the significant early intracytoplasmic event of lipogenesis. The continuity between the lipid droplets and smooth vesicles, probably endoplasmic reticulum in origin, is another common finding in the differentiating sebaceous cells. The latter configuration is similar to the 'husk' as termed by Palay (16). This peculiar pattern of the association of the lipid droplets and vesicles may be indicative of the ultimate coalescence of the two. In the differentiating sebaceous cells, attention is drawn to the tendency for glycogen particles to diminish in number and that mitochondria are tightly apposed to the lipid droplets. These findings most probably suggest the high energy requirement in the process of the sebaceous transformation. Thus, the morphological evidence reported is generally compatible in many respects with the proposed sequence of lipogenesis in human postnatal sebaceous glands (6).

The microvillous cell surface observed predominantly in the undifferentiated sebaceous cells may be suited to an increase in the cell surface in order to absorb the materials necessary for metabolism. In addition, the interdigitation between the adjoining cells may possibly facilitate cell-to-cell adhesion, as the desmosomes are found mainly on the relatively straight portion of the cell membrane. The slight thickening of the cell membrane in the sebaceous cells has been reported by Morohashi (15). The absence of distinct membrane-coating granules responsible for membrane thickening is in marked contrast to the situation noted in the epithelial cells of the sebaceous ducts. The way in which the membrane thickens remains uncertain.

The sebaceous glands regress shortly after birth and remain small in size through infancy and childhood. Nevertheless, it is still not known when this physiological involution of the sebaceous glands occurs. In order to elucidate this problem, it would be of value to examine the relation of the basal surface of the acini to their surrounding basal lamina. A popular view is that once the development of the basal lamina is completed, this structure may have the ability to maintain a relatively permanent and stable integrity (19). The basal lamina itself is remarkably flexible, but is is not suited to conform to altered surface conditions in cells or tissues. By 8 days after birth, the configuration of the basal lamina examined is neither distorted nor convoluted, but its major portion is in intimate association with the sebaceous cell surface. Thus, no convincing explanation for involutional change in the sebaceous glands was obtained.

In histochemical observations on human sebaceous glands, Montagna et al. (13, 14) emphasized the presence of varying numbers of melanocytes in the acini. Nevertheless, no actual confirmation of presence of absence of the cells at the electron microscopic level has been made. Our previous (11) and present reports demonstrate for the first time the typical melanogenic melanocytes in the human sebaceous acini. As early as 13 weeks of gestational age, when the sebaceous buds become apparent on the posterior wall of the hair pegs, melanocytes distribute randomly in the developing hair follicles as well as in the perifollicular mesenchymal tissue (9). It may be plausible, therefore, that the intrafollicular melanocytes are eventually carried into the sebaceous buds as they extend into the dermis. The migration of the mesenchymal melanocytes into the sebaceous buds cannot be excluded.

It is worth mentioning that the neonatal sebaceous glands which have not been exposed to visible or ultraviolet light for any length of time actively synthesize the melanin-containing organelles, and allow their transfer. The physiological role of the melanocytes in the human sebaceous glands remains to be investigated.

Histochemically, Breathnach (3) suggested the presence of Langerhans cells in the human sebaceous glands. But no confirmative observation has been carried out at the electron microscopic level. The present study would appear to be the first to confirm Breathnach's findings (3), and also extends the data that the cells are demonstrated in normal human sebaceous ducts (12). A similar description was made by Hashimoto & Tarnowski (8) in sebaceous acini and ducts in patients with Letterer-Siwe's disease. Nevertheless, the Langerhans cells found were, as the authors mentioned, actually the exocytotic histiocytes of Letterer-Siwe's disease.

The identification of both melanocytes and Langerhans cells in the neonatal sebaceous acini may provide some basis for further clarification of their physiological and biological significance. As far as the human pilosebaceous system is concerned, the same symbiotic relation of the two dendritic cells to the epithelial cells has been demonstrated in black and grey hair matrices in man (18).

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