Electron Microscopic Study on Human Eccrine Sweat Glands*

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Electron microscope observations on eccrine sweat glands have been carried out by many workers, namely on human eccrine sweat glands by Hibbs (1958), Iijima (1959), Chrales (1960), Kurosumi et al. (1960), and Munger (1961) and on those of animals by Kitamura (1958), Munger et al. (1961), Ellis et al. (1961), Matsuawa et al. (1963), Kurosumi et al. (1964) and Terzakis (1964). Already by means of light microscopy, it has been established that the secretory epithelium of the eccrine sweat gland is composed of two types of secretory cells, the superficial or dark cells and the basal or clear cells (Ito 1949 and Montagna 1956). By electron microscopy this finding has been confirmed by almost all investigators mentioned above, but Hibbs (1958) alone proposed the existence of the third cell type or intermediate cells located between secretory cells and myoepithelial cells; these cells, however, were regarded by several authors as modified myoepithelial cells. Although the ultrastructural characteristics of the three cellular components of the secretory portion, the superficial and basal secretory cells as well as myoepithelial cells, have been examined by previous investigators, several important ultrastructural problems on these cells remain unclarified or in dispute. In the present study the authors have attempted electron microscopic observations on the eccrine sweat glands in human axillary skins obtained operatively from young women to contribute some new findings to the electron microscopic knowledges of the eccrine sweat gland.

Materials and Methods

The material used was the axillary skin taken surgically from the axillary region of four Japanese women aged 17, 22, 23 and 32 years. The tissue was cut into small pieces and, as fast as possible, immersed in the 1% osmic acid solution of Caulfield (1957). The dermis and the subcutaneous tissue containing the sweat glands were then isolated from the epidermis and cut with razor blades into many small tissue blocks of about 1—2 cm³ to be fixed in the same fixative for about 90 minutes at 0°C. After fixation the specimens were immediately dehydrated with an ascending series of ethanol and then embedded in Epon of Luft (1961). Ultrathin sections for electron microscopy were cut with glass knives on the Leitz's ultramicrotome. Prior to ultrathin sectioning, somewhat thicker sections were made to examine, under the light microscope, the existence of the sweat glands in the given specimens. Ultrathin sections were mounted on copper grids and stained with lead hydroxide or with a double staining of uranyl acetate and lead hydroxide. The stained sections were examined with the JEM-5G type and JEM-7 type electron microscope. Electron micrographs were taken at

* This work is dedicated to the memory of Prof. Masaji Seki.
Observations

1. **Two types of secretory cells**

   In the coiled tubular secretory portion of the human eccrine sweat gland we can distinguish three kinds of epithelial cells lining usually small glandular lumen, i.e. the myoepithelial cells and two types of secretory cells. The myoepithelial cells make the outermost layer lying on the basement membrane of the secretory portion. The two types of secretory cells are arranged irregularly inside the discontinuous myoepithelial layer. They are both irregular in shape and named by most of the electron and light microscopists who studied this gland as “dark” and “clear” cells because of their staining reactions against certain basic dyes (Montagna, Chase and Lobit 1953, Terzakis 1964). In the present study, however, we would like to designate the dark cells as “superficial” and the clear cells as “basal” cells respectively, since the characteristic arrangement of both secretory cells has been confirmed also by electron microscopy. The former cells namely occupy the superficial position in the secretory epithelium bordering with their luminal surface on the main glandular lumen and the latter in general are present in the basal part without facing directly on the main lumen, although they enclose the intercellular canaliculi which may empty somewhere into the main gland lumen after running between the basal cells. Both in the superficial and the basal cells the basal ends or surfaces rest on the internal surface of the myoepithelial cells or, passing through the gaps in the myoepithelial layer, on the basement membrane (Fig. 1). The light microscopic terms “dark” and “clear” do not coincide with the electron microscopic appearances of the both types of the secretory cells of the eccrine sweat gland, since they are scarcely different in electron density of cytoplasm as can be seen in several electron micrographs in this paper. In the light microscopy of the eccrine sweat gland Ito and his co-workers (Ito 1943, 1949, Ito and Iwashige 1951) have presented the terms “superficial” and “basal” cells instead of the nomenclature “dark” and “clear” proposed by Montagna and his co-workers (Montagna, Chase and Lobit 1953, Montagna 1956)on the basis of the distinct difference in location of the both cell types in the secretory epithelium as confirmed afterwards also by electron microscopy. In the electron microscope observation on the eccrine sweat gland, Hibbs (1958) used the designations “clear, superficial” and “dark, basal” cells and Iijima (1959) the terms “superficial” and “basal” cells.

   In the present electron microscopic work we mainly observed the superficial and basal secretory cells and the ultrastructures of the myoepithelial cells and the eccrine duct will be treated in following separate articles.

   a. **Superficial secretory cell (dark cell)**

   In cross sections of the secretory epithelium the tall superficial secretory cells frequently show complicated irregular shapes (Fig. 1); the cell bodies with the wide luminal surface cap the basal cells sending slender cytoplasmic processes between the latter to reach the myoepithelial cells or the basement membrane (Fig. 1, 6). The elliptic nuclei of the superficial cells are situated in the border between the apical cell body and the basal thinner part, so that they are generally located more or less higher than those of the basal cells.

   The free surface of the superficial cell lining the main glandular lumen is generally provided with scanty microvilli which are not uniform in shape and size (Fig. 2, 3); in some
In the main gland lumen the cytoplasmic projections protruded from the superficial cells are seen. These projections may presumably be brought about by the tension dealt on the luminal surface.

The opposed lateral surfaces of the adjacent superficial cells show, abuting on the luminal surface, the typical junctional complex composed of a zonula occludens (tight junction), zonula adhaerens (intermediary junction) and a macula adhaerens (desmosome) (Fig. 2); in other cases they disappear almost completely making the free surface smooth (Fig. 4).
addition, there occur toward basal part not infrequently several desmosomes (Fig. 2-6). Towards the desmosomes the tonofilaments are converged as seen in the figures. The plasma membranes of the lateral surfaces of the adjoining superficial cells are interdigitated in several portions, but these intercellular interdigitations are not so prominent as between adjacent basal cells. Though they scarcely occur in the uppermost parts of the lateral cell borders, conspicuous interdigitations are sometimes recognized in the supra- and paranuclear regions of the superficial cells (Fig. 2-6). Here it must be noted that in the interdigitations between neighboring superficial cells the extracellular space is in general scarcely dilated, being as narrow as in other parts having no interdigitations, and the vesicle formation of the interdigitating plasma membranes is rarely observed (Fig. 4, 6).

In the narrow basal surfaces of the superficial cells resting either on the myoepithelial cells or the basement membrane the folding of plasma membrane is generally so poor, that the basal infoldings are often absent in them (Fig. 6).
One of the striking ultrastructural characteristics of the superficial cells consists in their richness in tonofilaments. The occurrence of tonofilaments in eccrine sweat gland cells has been noted only by a few workers (Hibbs 1958 and Kurosumi et al. 1960). In this study we could demonstrate in the superficial secretory cells of axillary eccrine sweat gland from young women a large amount of well-developed long tonofilaments distributed in whole cytoplasmic areas especially in the apical cytoplasm (Fig. 2-6). Most of them make prominent bundles of different thickness which run in various directions (Fig. 19). In the apical cytoplasmic area the majority of the bundles are oriented approximately parallel to the luminal surface (Fig. 2-4), and in the supra- and paranuclear areas there may occur several bundles running along the boundary of the Golgi apparatus located near the nucleus or along the nuclear membrane (Fig. 5). As described above, the tonofilaments are converged to the desmosomes at the lateral cell boundaries.

The mitochondria of the superficial cells were round or rod-shaped, but a few irregular shaped ones may be mixed among them. Their distribution in cytoplasm is not always uniform, though they are widely distributed in the entire cytoplasm except for the narrow apical cytoplasmic layer subjacent to the luminal surface, where the secretory vacuoles usually accumulate as described below. The matrix of the mitochondria is somewhat electron denser than that of the cytoplasm of the superficial cells. The moderately numerous cristae mitochondriae are oriented approximately transversely though in fairly irregular and tortuous
In the eccrine sweat gland cells the Golgi apparatus has been observed by many investigators with the electron microscope (HIBBS 1958, IIJIMA 1959, KUROSUMI et al. 1960, MUNGER 1961, MUNGER et al. 1961, etc.). In the superficial cells of the human axillary eccrine sweat gland a prominent Golgi apparatus is recognized in the supranuclear region close to the apical surface of the nucleus; it consists of well developed lamellae, numerous vesicles and several vacuoles of various sizes. The Golgi lamellae are composed of flattened agranular membrane sacs arranged in lamellar form, they are curved along the boundary of the Golgi area surrounding incompletely the latter (Fig. 3, 5, 19). Numerous Golgi vesicles and vacuoles are seen along the lamellae. Within the Golgi area there occur not infrequently large vacuoles with finely granular or fibrillar content of electron lucidity similar to that of secretory vacuoles described below. Between these vacuoles which seem to correspond to the prosecretory vacuoles of MUNGER (1961) and the Golgi vacuoles, gradual transitions are present suggesting the possibility that the secretory vacuoles of the superficial cells might originate from the vacuoles in the Golgi area. Among Golgi vesicles there are those containing dense materials;
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such dense vesicles may presumably fuse together to form dense bodies or granules of various
shapes and sizes which are often found within and in the vicinity of the Golgi area (Fig. 5). Possible relationship between these dense bodies and the lipid droplets will be discussed below. As seen in Fig. 5, a membrane bounded, fairly large dense body containing membranous structures and vesicles rarely occurs in the Golgi area; it may probably represent the complex dense body.

The secretory vacuoles or granules of the gland cells were reported by many investigators of human and animal eccrine sweat gland. According to our electron microscope observations the majority of superficial cells contain more or less numerous small secretory vacuoles measuring about 0.25—0.3 μ in diameter and this finding represents one of the important ultrastructural characteristics of the superficial cells which may be available for the differentiation of them from basal cells. The majority of secretory vacuoles of the superficial cells are gathered in the apical cytoplasmic area (Fig. 1—4), except for a few which may be dispersed in the para- and infranuclear regions. In a cell with numerous secretory vacuoles, they are closely packed in the apical cytoplasm subjacent to the luminal surface making large accumulations. The secretory vacuoles of the superficial cells are bounded by a well-defined limiting membrane, and contain electron lucent fibrillar or granular material (Fig. 2, 4, 19). We
encounter, however, among these electron lucent secretory vacuoles more or less dense ones usually in small number (Fig. 2, 3) which contain coarse granular material similar to the so-called secretory granules in several other secretory cells.

The majority of electron microscopic investigators of the eccrine sweat glands have agreed in the finding that the both types of the secretory cells have poorly developed granular endoplasmic reticulum. The free ribosomes have been observed by Hibbs (1958), Iijima (1959) and Kurosumi et al. (1960); and especially Munger (1961), Munger et al. (1961) and Terzakis (1964) have paid attention to the fact that the cytoplasm of the dark or mucoid cells (superficial cells) are rich in them. The present study could confirm, concerning the rough surfaced endoplasmic reticulum and the free ribosomes, the findings reported by above authors. Fairly numerous cisterns of the granular endoplasmic reticulum studded by ribosomes, irregular in shape and size, are scattered in the whole cytoplasm of the superficial cells. Small vesicles studded by ribosomes may also be found. Sometimes these cisterns are concentrated
around the Golgi area (Fig. 5) and sometimes associated with the mitochondria (Fig. 2—6). The free ribosomes are remarkably numerous and scattered in the entire cytoplasm of the superficial cells; especially abundant ribosomes are distributed among the secretory vacuoles accumulated in the apical cytoplasm (Fig. 2—4). The free ribosomes usually exhibit the tendency to aggregate into clusters of irregular shape and size.

In the present study we could scarcely identify the components of the agranular endoplasmic reticulum in the cytoplasm of the superficial cells. Only a few glycogen granules were occasionally demonstrated randomly in the cytoplasm.

Though the centriole of the eccrine sweat gland cells was first demonstrated by Zimmermann (1898) with the light microscope in the monkey and then by several investigators in man (literature cited by Ito 1949), it has never been demonstrated, so far as we know, with the electron microscope; this is also the case with the cillum (central flagellum) and the
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Associate basal corpuscle. In this study we could not reveal the centriole in the superficial cells; the basal corpuscle, however, was not infrequently identified in the apical cytoplasm of them (Fig. 4). The longitudinal profile of a basal corpuscle illustrated in Fig. 4 measures about 450 mμ in length and 200 mμ in width, it sends out a satellite at right angle from the apical or distal end and contains a vesicle in the basal or proximal end similar to the centriole basal body of fibroblasts described by SCHUSTER (1964). To our regret, we did not succeed in demonstrating the basal corpuscle and the associate cilium cut simultaneously in one section.

Multivesicular body, a vacuole containing several small vesicles, was occasionally observed in the apical cytoplasm of the superficial cells, but in general less frequently than in the basal cells (Fig. 4, 7, 10). The occurrence of the multivesicular bodies in eccrine sweat gland cells was reported by MATSUZAWA and KUROSUMI (1963) and KUROSUMI and MATSUZAWA (1964) in their electron microscopic studies on the eccrine gland of the rat foot pad. According to their observations the favorite location of the multivesicular bodies is the cytoplasmic area near the Golgi apparatus.
The theory of the apocrine secretion in eccrine sweat gland cells was advanced by Ito and his co-workers (ITO and IWASHIGE 1951, Ito 1949) on the basis of the findings obtained by light microscopy. In the present electron microscope study on human axillary eccrine glands, we often obtained, in the superficial cells, pictures which support the view of apocrine secretion in eccrine sweat gland. In the survey picture of low magnification in Fig. 1 we can find several cytoplasmic processes protruded from superficial cells into the main gland lumen which may suggest the secretion discharge by apocrine mechanism. In Fig. 7 a large, papillary cytoplasmic process of a superficial cell is observed in a higher magnification. This process is covered by the plasma membrane continuous with that of the apical surface of the superficial cell, microvilli having completely disappeared on the surface of the process. The electronlucent cytoplasm of this apocrine process appears almost homogeneous and finely granular, containing no cell organelles and inclusion bodies except for moderately numerous ribosomes scattered in the whole area and sparse small vesicles. At the base of this process a constriction is observed and just beneath the constriction along the borderline between the apical cytoplasm of the superficial cell and the base of the process there appears a transversely oriented tubular structure which seems to be formed by coalescence of vesicles aligned side by side (Fig. 7, arrows). Corresponding to the tubular structure a paired demarcation membrane may seemingly be formed to separate the base of the process from the apical cytoplasm of the superficial cells. In this way the apocrine process may probably be detached at the constricted portion from the cell body and liberated as a spheroidal secretion droplet into the lumen.

On the contrary to the apocrine process, the apical cytoplasm of the superficial cell subjacent to the above mentioned tubular structure contains mitochondria, tonofilaments, cisterns of the granular endoplasmic reticulum, free ribosomes, vesicles and secretory vacuoles. The numerous secretory vacuoles accumulated in the apical cytoplasm may be in part discharged in the gland lumen seemingly by means of the eccrine secretion mechanism or the reversed pinocytosis; namely they move toward and come into contact with the plasma membrane of the luminal surface, and at the contact place of the plasma membrane and the limiting membrane of the secretory vacuoles an opening is created, through which the vacuole content may be emptied into the gland lumen. In the present study we could not satisfactorily trace the entire process of this secretion mode, but frequently observed several secretory vacuoles being in contact with the luminal plasma membrane, a finding that may suggest the occurrence of eccrine secretion release (Fig. 2).

On the other hand, the contents of the secretory vacuoles might escape through the interrupted part of their limiting membrane into the surrounding cytoplasm to accumulate in the apical cytoplasm. This accumulation of secretion fluid might protrude the luminal plasma membrane toward the gland lumen, eventually making the papillary apocrine process. The finding gained in the present study that numerous secretory vacuoles exhibited discontinuities in their limiting membranes seems to support the above mentioned view. In the pictures shown in Figs. 2—4 the cytoplasmic areas surrounding the secretory vacuoles appear extraordinarily electron transparent and watery; this transparency may presumably be induced by the watery contents emptied from the secretory vacuoles.

In addition to the above described voluminous apocrine projection, small papillate or bullate cytoplasmic processes were sometimes observed on the luminal surface of the superficial cells which may correspond to the microvilli with polypoid swellings at their tips. The swollen portions of the processes may probably be liberated as small droplets into the lumen by being pinched off at the constricted base of the processes. This finding seems to support
b. Basal secretory cell (clear cell)

As described above, the basal cells are covered by the cell bodies of the superficial cells from the luminal side, so that they usually do not face directly on the main gland lumen. They generally possess, however, a wide basal surface which rests on the myoepithelial cells or, through the discontinuous part of the myoepithelial layer, immediately on the basement membrane of the secretory coil (Fig. 1). The narrow surface lining the intercellular canalculus is the free surface of the basal cell and corresponds to the apical surface of the superficial cell lining the main gland lumen. As recently reported by MUNGER (1961), MUNGER et al. (1961) and others, from the free surface facing to intercellular canalculus numerous, closely packed microvilli of uniform size and shape are protruded into the small canalicular lumen (Fig. 8—10, 12, 13, 17). The population density of microvilli in the canalicular surface of the basal cells is higher than in the luminal surface of the superficial cells. But sometimes they diminish in number and occasionally even almost completely disappear (Fig. 1, 11); this state may

Fig. 9. Intercellular canalculus (is) with closely packed microvilli (mv) and junctional complexes between adjoining basal cells which are composed of zonula occludens (zo), zonula adhaerens (za) and macula adhaerens (ma) and close the canalicular lumen from the extracellular space of the complicated intercellular interdigitations (ig). In the apical cytoplasm of the basal cells, cisterns and tubuli of the smooth surfaced endoplasmic reticulum (sER), tonofilaments (f), glycogen granules (gly), clusters of free ribosomes (rb) and mitochondria (M) are observed. ×30,000

the view of the microapocrine secretion mechanism of KITAMURA (1959) and KUROSUMI (1961).
probably be due to the dilatation of the canaliculi caused seemingly by intensive retention of secretion. Such a dilated intercellular canaliculus shown in Fig. 11 is filled with a moderately dense, finely granular material. Besides, several factors responsible for the dilatation of the intercellular canaliculi were proposed by previous authors; in their electron microscopic study on the eccrine sweat gland from an aged man KUROSUMI et al. (1960) confirmed dilatation of canaliculi caused by atrophy or retraction of gland cells, in their case, however, well preserved microvilli were observed. Recently, MUNGER (1961) reported in his electron microscope study on human eccrine sweat glands the dilatation of canaliculi induced by experimental stimulation.

In human eccrine sweat gland we have found, in accordance with MUNGER (1961), well defined intracellular canaliculi neither in the basal nor in the superficial cells, but pocket-shaped or tubular extensions of the canalicular lumen into the basal cell cytoplasm were occasionally observed (Fig. 11, arrow).

Besides the free surface lining the intercellular canaliculus and the basal surface resting on the myoepithelium or the basement membrane, the basal cells have surfaces which are
opposed either to the adjoining basal cell or to the neighboring superficial cell (Fig. 1). The plasma membranes covering the contact surfaces of two adjoining basal cells exhibit usually well-developed and most complicated intercellular interdigitations (Fig. 1), however, abutting on the canalicular surface they are in certain length straightened, where we find the same junctional complex as found between the superficial cells; it is composed of the zonula occludens (tight junction), zonula adhaerens (intermediary junction) and macula adhaerens (desmosome) (Fig. 9). The prominent intercellular interdigitation between adjacent basal cells consists of long slender cytoplasmic processes protruded from either side. The plasma membranes bordering these cytoplasmic processes are closely arranged in parallel with each other and appear lamelliform. Between these plasma membranes the inter- or extracellular spaces are considerably dilated as compared with those found in the interdigitations between superficial cells (Fig. 9, 12, 14, 16). This finding is worthy of particular attention and should not be

Fig. 11. Dilation of intercellular canaliculus (is) induced probably by retention of fine fibrillar material in canalicular lumen. A pocket-like part (†) of canalicular lumen protruded into the basal cell cytoplasm is observed. Microvilli disappeared almost completely, but a large cytoplasmic droplet found in the lumen suggests the occurrence of the so-called micro-apocrine secretion process in the basal cell. Basal corpuscle (bb) is observed subjacent to the canalicular surface of the basal cell. The basal cell cytoplasm is characterized by the closely packed agranular endoplasmic reticulum (SER) and numerous glycogen granules (gly). d Desmosome, f tonofilaments scattered evenly in entire cytoplasmic areas, jc junctional complex, M mitochondria, n nucleus, ncl nucleolus. ×15,000
put aside as a mere artifact. In his electron microscope study on eccrine sweat gland of monkey Terzakis (1964) was also of same opinion concerning the remarkably wide extracellular spaces between interdigitating clear (basal) cells.

Between the adjoining basal and superficial cell, less prominent interdigitations are observed than between two basal cells (Fig. 6, 10). In this case the majority of interdigitating cytoplasmic processes are mainly included in the marginal zone of the basal cell showing similar wide extracellular spaces as found in the interdigitations between two basal cells (Fig. 6).

In the both types of intercellular interdigitation mentioned above in which the basal cells participate, the plasma membranes frequently show vesiculations or vesicle formation; several periodical constrictions on a pair of plasma membranes in the lamelliform interdigitation give rise to formation of vesicles which are frequently aligned in a beaded row (Fig. 6, 10, 14); they seem to be pinched off to be liberated into the cytoplasm. In the both types of interdigitation, the vesiculation usually occurs in the marginal zones of the basal cells and vesicles thus formed seemingly migrate into the internal cytoplasmic areas of them (Fig. 6, 10, 14).

The occurrence of extensive intercellular interdigitation and frequent vesiculations in the above mentioned sites may support the view that the basal cells, as discussed below, may be involved

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**Fig. 12.** Well-developed agranular endoplasmic reticulum (SER) in the basal cell. Cisterns and tubuli bounded by the smooth limiting membrane anastomose with each other and make a continuous reticular system spread almost evenly in the whole cytoplasm; among these elements are scattered glycogen granules (gly), free ribosomes and tonofilaments. d Desmosome, jc junctional complex, ig intercellular interdigitation, is intercellular canaliculus ME myoepithelial cell. mv microvilli. ×21,300
in the function of the active transport of water and solute from extracellular space to intercellular canaliculus.

In the basal cells intensive basal infoldings of the plasma membrane are observed, especially in the part facing directly on the basement membrane, but in the part resting on the plasma membrane of the myoepithelial cells the infoldings of the plasma membrane are in general as poor as in the basal surface of the superficial cells, sometimes even absent at all (Fig. 1, 14, 15). In the former part the well developed and closely packed complex foldings of the plasma membrane are directed almost perpendicularly to the basement membrane, while in the latter sparse foldings are oriented approximately in parallel with the surface of the myoepithelial cell (Fig. 14, 15), as described by Hibbs (1958), Iijima (1959), Munger (1961) and others. In both cases the extracellular spaces are in general wide and similar vesiculations of plasma membrane are observed as seen in the interdigitations between two basal cells (Fig. 14, 15). The same functional significance as afforded to the vesiculation in the intercellular interdigitations of the basal cells may be expected in these cases.

Ultrastructural properties of the nuclei and nucleoli of the basal cells are scarcely different
from those of the superficial cells. The nuclei of the basal cells are round or oval in shape and contain small nucleoli composed of nucleolonema; they may, however, show some foldings of the nuclear membrane. They are located in the center of the cell bodies. Moderately numerous nuclear pores are found in their nuclear envelope (Fig. 1, 11).

In contrast with the superficial cells, the basal cells contain generally smaller amount of poorly developed short tonofilaments which are distributed irregularly in the entire cytoplasm without making distinct bundles, though they may be densely gathered in some areas. In the vicinity of desmosomes they are converged to them (Fig. 9, 12).

As to the Golgi apparatus of the basal cells, most workers of the eccrine sweat gland reported that it is small or poorly developed in comparison with that of the superficial cells (Iijima 1959, Mungur 1961, and Mungur et al. 1961). According to our observations the basal cells possess well defined Golgi apparatus which is composed mainly of elongated lamellae and vesicles; the vacuoles are in general sparse. In the basal cells the intimate topographic relationship between Golgi apparatus and nucleus is not observed, as the former often lies near the intercellular canaliculus extending its lamellae along the canaliculus (Fig.
In the present study, however, any sign indicating the elaboration of secretory granules or vacuoles could not be recognized within the Golgi area of the basal cells. The mitochondria of the basal cells coincide in all ultrastructural properties with those of the superficial cells (Fig. 6, 8, 14—8). Their distribution in cytoplasm is not uniform; they are often concentrated in perinuclear regions (Fig. 1, 6), sometimes are distributed along the intercellular interdigitations or the basal infoldings (Fig. 6, 8, 15). However, the apical cytoplasmic areas surrounding the intercellular canaliculi generally lack the mitochondria (Fig. 1, 8, 10—13).

The most conspicuous cytological characteristic of the human basal cells is that they have well-developed, complex agranular endoplasmic reticulum which is composed of closely packed cisterns, vesicles and tubuli bounded by smooth limiting membrane (Fig. 8—14). They seemingly anastomose with each other to form a continuous reticular system spread almost uniformly in the entire cytoplasm (Fig. 8, 10—14). In the peripheral parts of the cytoplasm, vesicles derived from membrane vesiculation either in the intercellular interdigitation or in the basal infolding may presumably join to this agranular endoplasmic reticulum. In the apical cytoplasm, on the other hand, cisterns, vesicles and tubuli of the smooth endoplasmic reticulum approach to the plasma membrane lining the intercellular canaliculi and some of them may come into contact with the plasma membrane to empty in the lumen of the intercellular canaliculi by means of the mechanism of reversed micropinocytosis. These findings
suggest the means by which water and solutes might be taken up from the extracellular spaces of the interdigitations and basal infoldings into the basal cells and be transported through the channel system of the agranular endoplasmic reticulum into the intercellular canaliculi. We often encounter, among the components of the smooth surfaced endoplasmic reticulum, variable numbers of cisterns, vesicles and tubuli dilated to some extent and occasionally so intensively dilated vesicles which resemble in size and shape the secretory vacuoles of the superficial cells (Fig. 10, 12, 13). They are bounded by a distinct limiting membrane and contain a finely granular or fibrillar material of electron transparency similar to the latter. They are, however, in general somewhat smaller than the latter and do not show conspicuous accumulation in the apical cytoplasm just beneath the intercellular canaliculus. Besides these large vesicles described now, there appear in the basal cell cytoplasm no other particular formations which may be identified as secretory vacuoles or granules.

In contrast with the prominent agranular endoplasmic reticulum the elements of the granular endoplasmic reticulum are sparse; it is difficult to identify them among the numerous cisterns and tubuli of the former. In spite of this, relatively numerous free ribosomes are found among them, scattered in the entire cytoplasm. They tend to aggregate in clusters of
irregular shapes (Fig. 9, 16, 21).

It is one of the important morphological characteristics of the basal cells that they generally contain a considerable amount of glycogen. The cytological evidence of this was first gained by ITO and OTA (1949) in their light microscopic study on human eccrine sweat glands. Though, in their early electron microscopic studies on human eccrine sweat gland, HIBBS (1958), IJIMA (1959) and CHARLES (1960) could not confirm this finding, KURSUMI et al. (1960) and MUNGER (1961) in human eccrine sweat glands and MUNGER et al. (1961) and TERZAKIS (1964) in cat and monkey respectively have revealed that the basal cells (clear cells) contain large amounts of glycogen granules of electron opacity, and according to TERZAKIS they measure 200—400Å in diameter.

In the present electron microscope study on human eccrine sweat gland we were able to identify in the basal cells without exception the glycogen granules scattered irregularly in the whole cytoplasm (Fig. 8—17, 20, 21); they are intermingled with the free ribosomes. The amount of glycogen granules varies from cell to cell. In the basal cells considerably rich in glycogen, the granules show a tendency to aggregate to numerous small clusters; in some of the clusters the aggregation is so dense that the individual glycogen granules are scarcely discernible (Fig. 16). The individual glycogen granules measure about 200—400Å in diameter, so we can distinguish them on the basis of difference in size from free ribosomes measuring about 150Å in diameter. As mentioned above, the glycogen granules are scarcely demonstrated in the superficial cells even by electron microscopy, and therefore the occurrence of glycogen granules may be available as a cytological criterion of the basal cells.

In this study an interesting finding concerning the glycogen granules was obtained that they occasionally appeared in cisterns of the agranular endoplasmic reticulum. As observed in Fig. 13 several glycogen granules are found in somewhat dilated cisterns whose matrix appears moderately dense. This finding may presumably support the view that the smooth surfaced endoplasmic reticulum may participate in the intracellular metabolism of glycogen.

As mentioned above, the basal cells do not face as a rule with their free surface immediately on the main gland lumen, since they are situated in the basal part of the secretory epithelium and line with their narrow free or apical surface the small lumen of the intercellular canaliculi which take their way between the basal cells toward the main gland lumen.
to empty through the gap between superficial cells into the latter. But it has been pointed out by ITO and IWASHIGE (1951) in their light microscope observation that the basal cell can occasionally border directly on the main gland lumen. The same exceptional location of the basal cell was also occasionally confirmed in the present electron microscopic observation as shown in Fig. 18. In such cases the ultrastructural characteristics of the basal cells, namely numerous microvilli on the apical surface, well-developed agranular endoplasmic reticulum, absence of the secretory vacuoles, inconspicuous tonofilament bundles and occurrence of a considerable amount of glycogen granules, are maintained, so that the transformation of such basal cells into the superficial cells seems to be impossible. In this respect, we do not agree with TERZAKIS (1964), who found in his electron microscope observation on the eccrine sweat gland of the monkey also exceptional basal cells (clear cells) facing directly to the main gland lumen. He observed, between such basal cells and the ordinary superficial cells (dark cells), intermediate forms and postulated the transformation of the basal cells into the superficial cells.

So far as we know, the centriole and the basal corpuscle associated with the cilium have...
been demonstrated by means of the electron microscopy neither in the superficial cells nor in the basal cells of the eccrine sweat gland. In this study we succeeded in demonstrating centrioles and basal bodies of the basal cells in the apical cytoplasm just beneath the intercellular canaliculus. Their long axes were obliquely or almost perpendicularly oriented to the canalicular surface (Fig. 11, 17). The longitudinal profile of the centriole measured about 450 m in length and 200 m in width and that of the basal body about 450 m and 200 m respectively. The submicroscopic structure of the basal body coincided with that of the basal body seen in the superficial cell. We did not, however, encounter the profile of a cilium projected from the basal body into the canalicular lumen. The detailed tubular structures in the wall both of the basal body and the centriole could not be clarified, since we had no opportunity to observe their transverse sections.

In the basal cells the multivesicular bodies were encountered more frequently than in the superficial cells. They were found in various portions of the cytoplasm, for example in the apical cytoplasm near the intercellular canaliculus (Fig. 13), in the neighboring area of the...
Golgi apparatus and so on. The multivesicular bodies, namely vacuoles containing small vesicles, are variable in shape and size; they are sometimes crescent in shape (Fig. 8). The number of the internal vesicles are also widely variable. In some cases numerous closely packed vesicles fill up the lumen of the vacuole (Fig. 20), while in others only a few vesicles are scattered in it (Fig. 21). This structural variability of the multivesicular bodies suggests that they might participate in the function of the cell.

In the lumen of the dilated intercellular canaliculus seen in Fig. 11, a large droplet of cytoplasm bounded by plasma membrane is observed which may probably be formed by pinching-off from a large polypoid swelling at the tip of a microvillus protruded from the apical surface of the basal cell. Such a prominent polypoid swelling of the microvillus was actually confirmed in this study on the free surface of a particular basal cell bordering directly on the main gland lumen. This finding may correspond to the mechanism of the microapocrine secretion introduced by Kitamura (1958) and Kurosuni (1961) into the
secretory cell cytology, and in this study was also observed in the superficial cells as already described above. The evidences that the epithelial cells which show no signs of ordinary secretory phenomena can sometimes display pictures of the apocrine secretion have been reported by some authors in the light microscopy and recently by Hayward (1966) in the electron microscope observation on foetal gall bladder epithelium in the rabbit.

2. Lipid droplets in eccrine sweat gland cells

The morphological evidence that the human eccrine sweat gland cells, both basal and superficial cells, contain various amounts of lipid droplets which increase in aged individuals has already been reported in light microscopic observations by some investigators (Ito 1943, Ito and Iwashige 1951, Iwashige 1952 and others). According to their observations the lipid droplets are either solid or mono- or polyvesicular, and in the latter case they contain within them clear vacuoles of variable size and number. Recently, this finding was confirmed by several workers by means of electron microscopy (Hibbs 1958, Iijima 1959, Kurosuni et al. 1960, Munger 1961, and Terzakis 1964). Among them especially Iijima carried out detailed observations of lipid globules in the superficial and basal secretory cells in human axillary eccrine sweat gland. According to him the lipid globules measuring about 1—4 μ in diameter are solid or vesicular (vacuolated), and bounded by the dense limiting membrane. He was of the opinion that at the end stage of the maturation the vesicular lipid droplets release the vacuoles through the interrupted portions of the limiting membrane into the surrounding cytoplasm.

In the present electron microscopic study on eccrine sweat gland in axillary skins taken from young healthy women, spherical lipid globules were observed in the majority both of the superficial and basal cells, though generally in a small number. The frequency of occurrence and the amount of these cytoplasmic inclusions are not remarkably different between the both cell types. They are found in the majority of cases in intimate topographic relationship with the Golgi apparatus and sometimes also with mitochondria (Fig. 1, 6, 8, 19): so they appear frequently in contact with the Golgi area and sometimes seem as if included within it. In addition, the lipid globules are not infrequently intermingled within the cluster of mitochondria as observed in Figs. 1 and 18. The size of the spherical lipid droplets is variable ranging from 0.5 μ to 2 μ in diameter. A smooth limiting membrane is identified in every lipid droplet. In this study, however, multivesicular or multilocular lipid droplets which contain, as described by Iijima, in the dense matrix various number of electron lucent vesicles or vacuoles are only rarely encountered (Fig. 19). The majority of lipid droplets found either in the superficial or in the basal cells contain a single large vacuole, namely they are monovacuolated or monolocular. In most of them the single vacuoles are as large as to occupy almost entirely the droplets, so that the dense matrix remains as dense narrow layer or rim surrounding the electron lucent large vacuole (Fig. 20, 21). Thus, in low power electron micrographs the majority of lipid droplets appear electron lucent. In several lipid droplets, however, the narrow rim of high electron density is partially thickened and in some cases the thickening becomes so extensive that it forms an electron dense crescent or demilune covering the lipid droplet from one side (Fig. 19).

Pictures which suggest the fusion of the monovacuolated lipid droplets are occasionally observed as shown in Fig. 19.

The dense matrix of the lipid droplets is not homogeneous; it contains numerous electron dense particles or granules and vesicles distributed almost evenly. The contents of the vacuoles in the lipid droplets are also not uniformly electron lucent, they show faintly vesicular or
vacuolar structures of variable electron opacities (Fig. 19—21). The margin of the single large vacuole opposed closely to the limiting membrane of the lipid droplet is electron dense and, in profile presents dense line similar to the limiting membrane (Fig. 19—21). Thus, the lipid droplets containing a single large vacuole look erroneously as if they were bounded by a double or paired limiting membrane. The dense narrow matrix rim of the monolocular lipid droplets is in fact sandwiched between the limiting membrane and the dense borderline of the single large vacuole and displays the same fine structures of dense granular and vesicular appearance as just described above (Fig. 19—21).

As for the origin of the lipid droplets of the eccrine sweat gland cells IIJIMA (1959) and KUROSUMI et al. (1960) are of opinion, that they may arise from dense granules derived from Golgi vesicles. As has been mentioned above, we also have revealed especially in the superficial cells that by fusion of the Golgi vesicles with dense material the dense bodies of various sizes and shapes may arise in the Golgi area. Such dense bodies appear also in the vicinities of the lipid droplets and this evidence may suggest that they have migrated from the Golgi area into the surrounding cytoplasm (Fig. 19, 21). By detailed observations it was determined that the dense bodies possess a distinct limiting membrane and their dense matrix almost coincide in fine structure with the dense matrix of the lipid droplets. But the dense bodies show, besides the dense granular and vesicular structure, occasionally the membranous, concentrically lamellar structure as mentioned above (complex dense body). As to the formation mechanism of the lipid droplets the following processes are presumed: The membrane bounded dense bodies may gradually grow and increase in size to transform into the solid lipid globules. In the lipid globules of considerable size appear vesicles or vacuoles which may probably be derived from small vesicles contained in the dense matrix. Vesicles may grow or fuse with each other to vacuoles, in this way the multilocular lipid droplets may finally convert into the monolocular lipid droplets containing a single large vacuole. On the other hand, we occasionally encountered the pictures which actually indicate the fusion of the dense bodies to large monolocular lipid droplets (Fig. 21). This cytological evidence may suggest one of the growing processes of the lipid droplets. The functional significance and the fate of the lipid droplets remain despite of the present study unexplained. We could not confirm the finding of IIJIMA (1969) that the multivesicular lipid droplets may release vesicles or vacuoles contained in them into the surrounding cytoplasm,
Discussion

By light and electron microscopy it has been revealed that the secretory epithelium of the eccrine sweat gland is composed of the two different secretory cell types which were named by many electron and light microscopists as the "dark" and the "clear" cells; the former were termed by MUNGER (1961) and MUNGER et al. (1961) "mucoid" cells because of the histochemical properties of the secretory vacuoles elaborated in them. In the present study we have designated the dark cells as "superficial" cells and the clear cells as "basal" cells, since we could reveal by the electron microscope observations that the former cells occupy a superficial position in the secretory epithelium directly lining the main gland lumen, whereas the latter cells take their places in the basal part of the secretory epithelium without facing directly to the main gland lumen. These basal cells, however, line the intercellular canaliculi which may, through the gaps between superficial cells, empty into the main lumen. The narrow free surface of the basal cells lining the intercellular canaliculi thus corresponds to the apical surface of the superficial cells. In addition, the terms "dark" and "clear" do not coincide with the electron microscopic appearances of the both cell types, since they show no remarkable difference in the electron density of their cytoplasm.

Several distinct ultrastructural differences were confirmed between these two cell types. The development of the microvilli is fairly different between the both cell types: from the narrow apical surfaces of the basal cells facing to the intercellular canaliculi numerous closely packed microvilli of uniform shape and size are protruded into the narrow lumen, while in the apical surfaces of the superficial cells bordering on the main gland lumen they are less numerous and irregular in shape, size and distribution. The same differences in microvilli were already remarked by some authors as cited above. The population density of microvilli is consequently higher in the canalicular surface of the basal cells than in the luminal surface of the superficial cells.

Occasional dilatation of the intercellular canaliculi was observed: in such cases the microvilli diminished in number and size and sometimes even disappeared at all. The dilatation in the canaliculi seems to be caused by intensive retention of finely granular content in the canalicular lumen and the reduction and disappearance of microvilli may be due to the tension dealt as the result of the dilatation on the canalicular surface. Several factors responsible for the dilatations of the canaliculi and associated alterations of the microvilli were discussed by some investigators as already cited above. Also in the luminal surface of the superficial cells the reduction and disappearance of microvilli caused probably by the same factor were occasionally observed. In the apical cytoplasm both of the superficial and basal cells either a single centriole or a basal corpuscle was occasionally found near the free surface. The basal corpuscle with associated cilium, however, was not demonstrated.

On the junctions between secretory cells of the eccrine sweat gland, several investigators have made merely short observations (HIBBS 1958, MUNGER 1961, MUNGER et al. 1961 and KURSUMI and MATSUZAWA 1964). Between the juxtaposed surfaces of two superficial cells and of two basal cells there occurs, abuting on the luminal and the canalicular surface respectively, the junctional complex with its typical composition, i.e. zonula occludens (tight junction), zonula a\textasciitilde haerens (intermediary junction) and macula adhaerens (desmosome). In addition, between two adjoining superficial cells there occur randomly several desmosomes toward the basal ends, but they are in general scant between two adjoining basal cells and between adjoining basal and superficial cells.
The intercellular interdigitations seen between secretory cells of the eccrine sweat glands have been described in detail by many investigators (Hibbs 1958, Kitamura 1958, Iijima 1959, Charles 1960, Munger 1961, Munger et al. 1961, Matsuzawa et al. 1963, Kurosumi et al. 1964 and Terzakis 1964). According to these investigators especially to Iijima, Munger and Terzakis the intensive complicated interdigitations are found between two adjoining basal cells while they are in general less prominent between two neighboring superficial cells. The similar ultrastructural differences in the interdigitations were also confirmed in this study between the both cell types. Between adjoining basal cells there occur extensive and complicated interdigitations as described above. Between the finger-like cytoplasmic processes in these interdigitations the inter- or extracellular spaces are in general more or less widened. These intensive, closely packed intercellular interdigitations are distributed in the entire contact surfaces between basal cells, except for the short straightened part subjacent to the canalicular surface where the above mentioned junctional complex occurs. The basal cells, when juxtaposed with a superficial cell, however, show intercellular interdigitations which are less prominent and include dilated extracellular spaces only on the side of the basal cell. Between the adjoining superficial cells there occur least prominent interdigitations without dilatation of the extracellular spaces.

To the vesicle formation in the intercellular interdigitation of the eccrine sweat gland cells, no special attention as far as we know, has been payed until now. The frequent vesiculations in the interdigitating plasma membranes have been demonstrated in this study especially in the extensive intercellular interdigitations in which the basal cells participate, namely in those between two basal cells and between a basal and a superficial cell. Interdigitations between adjoining superficial cells rarely displayed the pictures of vesicle formation. In the interdigitation the closely packed slender cytoplasmic processes protruded from the opposite cell surfaces are interdigitated in parallel with each other, so the plasma membranes bordering the cytoplasmic processes are closely arranged side by side in parallel showing the lamellar structures. Several periodical constrictions on these lamelliform interdigitating plasma membranes give rise to formation of vesicles lined up in beaded rows.

In the infolding of the basal plasma membranes some differences were also observed between both cell types. The basal infoldings in the eccrine sweat gland cells were first reported by Kurosumi and Kitamura (1958), Kitamura (1958), and Hibbs (1958), then by Iijima (1959), Kurosumi et al. (1960), Munger (1961), Matsuzawa et al. (1963) and Kurosumi and Matsuzawa (1964). Among them Kurosumi, Kitamura, Iijima and Matsuzawa observed also the vesiculations in the folded membrane and postulated their functional significance as related to the uptake and the transcellular transport of water and solutes. Kurosumi et al. (1960) observed the reduction of the basal infoldings in an aged man and Matsuzawa et al. (1963) and Kurosumi and Matsuzawa (1964) confirmed in their histogenetic studies on the eccrine glands of rat foot pad the correlation between the initiation of sweating and the development of basal infoldings as well as intercellular interdigitations; in addition, they could cytochemically demonstrate the activities of alkaline phosphatase and adenosine-triphosphatase in the basal infoldings.

We observed intensive basal infoldings in the basal cells of the eccrine sweat glands from young women especially in the part where the basal surface of the cell faced directly to the basement membrane; in the part facing to the myoepithelial cell the infoldings were poorly developed. The basal infoldings in both of these cell parts generally resemble the intercellular interdigitations in their fine structure, Wide extracellular spaces are included between the
plasma membranes arranged in a lamellar array and the vesiculations of the plasma membrane similar to those seen in the intercellular interdigitations frequently occur. On the contrary, the generally narrow basal surfaces of the superficial cells resting either on the basement membrane or the myoepithelial cell show no or only poorly developed, simple infoldings. Here the membrane vesiculations are almost absent.

The above mentioned differences in the intercellular interdigitations and basal infoldings between the basal and superficial cells seem to indicate the functional difference between both cell types. The well-developed and extensive intercellular interdigitations and basal infoldings including dilated extracellular spaces as well as the associated vigorous membrane vesiculations confined approximately to the basal cells may suggest a particular and essential role in the special sweat production of the basal cells.

Though the tonofilaments in eccrine gland cells have been remarked merely by a few investigators, we could confirm in this study that the superficial cells contain a large amount of long tonofilaments forming prominent bundles especially in the supranuclear region. In the basal cells, however, only poorly developed short tonofilaments were recognized in the entire cytoplasm without making well-defined bundles. This difference in development of the tonofilaments may imply mechanical differentiation in the cytoplasm of the both cells.

The Golgi apparatus and the mitochondria of the eccrine sweat gland cells were described by all investigators mentioned above in their electron microscope observations. As to the mitochondria no differences were seen between both cell types. As cited above, some differences between the Golgi apparatus in both cell types were proposed by several authors. The Golgi apparatus in both cell types consists of well-developed Golgi lamellae, numerous vesicles and a small number of vacuoles. The localization of the apparatus is, however, remarkably different between both cell types: in the superficial cells it is recognized in the supranuclear region close to the nucleus, while in the basal cells in the apical cytoplasmic zone along the intercellular canaliculi without showing any intimate topographic relationship with the nucleus. The participation of the Golgi apparatus in the elaboration of the secretory vacuoles and the dense bodies will be discussed below.

As remarked by several investigators, the granular endoplasmic reticulum is generally poorly developed in the both cell types of the eccrine sweat gland. The superficial cells, in contrast to the basal cells, are provided with moderately numerous cisterns of the rough-surfaced endoplasmic reticulum studded by ribosomes and with considerably abundant free ribosomes aggregated frequently in clusters. In the basal cells, however, the rough endoplasmic reticulum is scant and scarcely identified among those of the smooth endoplasmic reticulum, although the free ribosomes in small clusters are relatively numerous.

One of the most conspicuous ultrastructural differences between the superficial and the basal cells consists in that the extraordinarily well-developed smooth-surfaced endoplasmic reticulum is present in the latter, while in the former this organelle is scarcely identified. This important cytological evidence has not been remarked by most investigators of the eccrine sweat gland. The reticulum in the basal cells is composed of numerous cisterns, vesicles and tubuli bounded by smooth limiting membrane. These elements seem to anastomose with each other to form a closely packed reticular system spreading uniformly in the entire cytoplasm. In the apical zone of the cell some of these elements seem to approach to the plasma membrane lining the intercellular canaliculus to be fused with the latter and empty into the canalicular lumen. In the peripheral zones of the cell, on the other hand, the vesicles derived from the plasma membrane in the extensive intercellular interdigitations and the prominent basal
infoldings seem to join the agranular endoplasmic reticulum. These findings support the view of several authors (Kurosuni, Kitamura, Iijima and Matsuzawa) that in the basal cells the water and solutes are absorbed by means of the basal infoldings and intercellular interdigitations from the extracellular spaces and transported through the continuous channel system of the agranular endoplasmic reticulum to the intercellular canalculus to be emptied into the canalicular lumen. The finding that the cisterns and tubuli of the agranular endoplasmic reticulum are in some cases considerably dilated may represent a morphological change corresponding to a state of functional activity.

Munger (1961) felt in his electron microscope study on human eccrine sweat gland that the two distinct secretory cell types might correspond to the two types of sweat; it seems as if he might presume the secretion of the sweat rich in water and solutes by the clear (basal) cells. Terzakis (1964) agreed with Munger and proposed, referring to the paper of Fawcett (1962) on the avian salt gland and that of Adams and co-workers (1958) on the two loci of human sweat production, that the clear (basal) cells produce sweat which is high in Na and Cl content. According to him this idea is strengthened by the consideration that the avian salt gland is a salt-excreting organ and that the clear cells of the eccrine sweat gland can show a striking resemblance to salt gland especially in their complicated cytoplasmic processes. Doyle (1962) who recognized in his electron microscope study on the rectal salt-gland of the Urolophus that the gland cells contain abundant 350–400Å vesicles and numerous multivesicular bodies and are rich in lateral interdigitations running deeply into adjacent cells, postulated that the abundant vesicles derived from the tubular extensions of the interdigitating plasma membranes might probably transport sodium from extracellular space to the gland lumen. Referring to the above mentioned reports and on the basis of our own results obtained in this study, we came to the conclusion that the basal cells with their complicated interdigitations and basal infoldings are the production site of the watery sweat which is high in Na and Cl concentrations and that the vesicles derived from the interdigitating and folding plasma membrane may participate in the transport of water and probably of sodium (Nolte 1966) via closely packed agranular endoplasmic reticulum from extracellular space into the intercellular canalculus. The role played by the multivesicular bodies was not clarified, though they were more numerous in the basal cells than in the superficial cells.

The secretory vacuoles or granules of the eccrine sweat gland cells were reported by many electron microscopists (Hibbs 1958, Iijima 1959, Munger 1961, Munger et al. 1961, Terzakis 1964, Kurosuni and Matsuzawa 1964 and others). Especially Munger (1961) demonstrated in the dark (superficial) cells of the human eccrine sweat glands the secretory vacuoles with fibrillar and granular content which might be elaborated in the Golgi zone and migrate to the apical cytoplasm; in the clear (basal) cells, however he observed merely numerous small vesicles instead of secretory vacuoles. On the basis of the histochemical properties of the secretory vacuoles, he designated the dark cells as the mucoid cells. The small vesicles found by Munger in the basal cells seem to us to be the components of the agranular endoplasmic reticulum; he regarded them as the structures responsible for the transport of the watery fluid to the intercellular canalculus. Terzakis (1964) recognized similar secretory vacuoles in the monkey dark cells, but he did not agree with Munger in designating the dark cells as mucoid cells from the resemblance to the goblet cells.

In the present study we could demonstrate in the basal cells neither secretory vacuoles nor secretory granules except for the dilated vesicles and tubuli of the agranular endoplasmic
reticulum which are in some respects similar to the secretory vacuoles of the superficial cells. It is likely that the basal cells do not have such an ordinary secretory activity as the majority of secretory cells have. This presumption is also supported by the evidence that the Golgi apparatus of the basal cells displays no signs of production of secretory vacuoles or granules in it. In the superficial cells, however, the secretory activity was morphologically proved; namely the prosecretory vacuoles similar to those described by Munger (1961) arise in the Golgi area from the Golgi vacuoles, are transformed gradually into the secretory vacuoles, the majority of which then migrate to the apical cytoplasm to be accumulated there. As revealed by Munger and Terzakis the prosecretory and secretory vacuoles enclosed by the limiting membrane contain the electron lucent fibrillar and granular material. The apical accumulation of the secretory vacuoles represents one of the conspicuous morphological characteristics of the superficial cells which can be utilized for the identification of the cells. Munger (1961) and Munger et al. (1961) observed in the dark cells, especially following experimental stimulations, the eccrine mode of extrusion of the secretory vacuoles; we also confirmed in this study the pictures which may suggest the eccrine secretion of the superficial cells, namely some of the secretory vacuoles approach to the apical surface and their limiting membranes come into contact with the plasma membrane lining the apical surface. The Japanese authors, IIIMA (1959), Kurosumi et al. (1960) and others proposed in their electron microscope studies the apocrine secretion of the superficial cells seeing large electron lucent papillary cytoplasmic projection from their apical surface into the gland lumen. They further paid special attention to the disappearance of the microvilli from the covering plasma membrane of these so-called apocrine projections. Charles (1960) also observed the similar papillary projection protruded from the eccrine sweat gland cell, though he did not regard it as the feature of the apocrine secretion. In this study the present authors frequently found large papillary cytoplasmic projection on the luminal surface of the superficial cells and could trace the mode of its detachment from the apical end of the superficial cell. As revealed by IIIMA and others the microvilli have completely disappeared from the covering plasma membrane of the papillary projection which is constricted at the base of them. The clear cytoplasmic content of the projection is finely granular but devoid of cell organelles and inclusion bodies except for a number of free ribosomes and few vesicles, in striking contrast to the apical cytoplasm of the superficial cells just beneath the base of the projections which contains cell organelles and inclusions especially secretory vacuoles and smooth vesicles. At the base of the projection, just beneath its constriction, transversely oriented tubular structure is observed which seemed to be composed by coalescence of vesicles aligned side by side in a row. This evidence may suggest the occurrence of a paired demarcation membrane corresponding to the transverse tubular structure mentioned above, which may separate the projection from the apical end of the superficial cell. In this manner the projection seems to be detached at the constriction from the superficial cells and liberated as spherical droplet into the gland lumen. This mode of detachment of the cytoplasmic portion from the cell body resembles that of the blood platelets from the megakaryocytes reported by Yamada (1957), Han and Baker (1964), De Bruyn (1964) and others. These investigators observed the formation mechanism of the demarcation membrane which separate the blood platelets from the megakaryocytes and confirmed that the fusion of the vesicles aligned in rows give rise to the paired demarcation membranes in the cytoplasm of the megakaryocytes. In this manner the present authors who believe in the existence of the apocrine mode of secretion discharge have acquired a strong morphological support. In his light microscopical study on the axillary apocrine sweat gland,
MINAMITANI (1941) has already proved the occurrence of the demarcation line stained by iron hematoxylin between the base of the apocrine projection and the apical end of the secretory cell.

As to the formation mechanism of the apocrine projection of the superficial cell, the present authors are of opinion that the contents of the secretory vacuoles in the apical cytoplasm may probably escape through the interrupted parts of the limiting membranes into the surrounding cytoplasm to accumulate in the apical cytoplasm. The accumulation of the secretion fluid may gradually protrude the plasma membrane toward the gland lumen forming finally the papillary apocrine projection which consequently contains secretion fluid derived from the secretory vacuoles. The microvilli may be smoothed out by stretch dealt on the plasma membrane.

The pictures of the microapocrine secretion introduced by KITAMURA (1958) and KUROSUMI (1961) into the secretory cell cytology were observed not only in the main gland lumen but also rarely in the intercellular canalculus; they may probably correspond to the liberation by pinching-off of the polypoid swellings at the tips of the microvilli of the superficial and basal cells.

As mentioned above, the finding of KUROSUMI et al. (1960), MUNGER (1961), MUNGER et al. (1961) and TERZAKIS (1964) that the clear or basal cells of the eccrine sweat gland contain a large amount of glycogen granules could be confirmed in the present study. The most interesting finding in this study concerns the occurrence of a part of glycogen granules within the cisterns of the agranular endoplasmic reticulum which were somewhat dilated and showed moderately dense matrix. This finding may support the view that the smooth surfaced endoplasmic reticulum participates in the intracellular glycogen metabolism, but the question whether it might indicate the glycogen synthesis in the smooth endoplasmic reticulum or the glycogen mobilization in it, is still to be solved. Recently ROSE et al. (1965) postulated, in the study on hepatic glycogen depletion in Amphiuma during induced anoxia, the participation of the smooth endoplasmic reticulum in the mobilization of glycogen from hepatic cells by demonstrating greater development and changes in the density of this organelle during the depletion of hepatic glycogen. COIMBRA and LEBLOND (1966) further studied the site of glycogen syntheses in the liver cell of the rats treated with tritiated glucose by means of electron microscope radioautography and revealed the possibility that smooth membranes play a role in glucose uptake at an early stage in de novo formation of glycogen granules.

From the comparative observations on the ultrastructural characteristics of the both secretory cell types in human eccrine sweat gland the present authors could summarize the main cytological properties of the basal cells as follow: 1. They possess a number of closely packed microvilli protruded into the intercellular canalculus, 2. the well-developed agranular endoplasmic reticulum, 3. the poorly developed tonofilament bundles, 4. no secretory vacuoles and 5. considerable amounts of the glycogen granules. ITO and IWASHIGE (1951) have revealed in their light microscopic study on human eccrine sweat glands that the basal cells can occasionally border directly on the main gland lumen, and the same evidence was also confirmed in the present electron microscopic study. It is worthy to note that even in such a particular case the cytological properties of the basal cells are maintained, and no transitional forms between the basal and superficial cells are found. The present authors thus came to the conclusion that the transformation of basal cells into the superficial cells does not occur. In this respect the present authors do not agree with TERZAKIS (1964), who observed in the monkey eccrine
sweat glands occasional clear (basal) cells facing on the main gland lumen which sometimes appear intermediate between dark (superficial) and clear cells.

On the large lipid droplets found in the both types of human eccrine sweat gland cells have been already described and discussed in the chapter of Observations. It is an interesting finding that they are encountered in most cases in the direct neighborhood of the Golgi complex and sometimes within the cluster of the mitochondria. As described above, the lipid droplets are variable in appearance and internal structure, though the majority of them found in this study were large monolocular ones containing a single large vacuole. The formation mechanism of such monolocular lipid droplets may presumably be as follows: a small solid droplet may become monovesicular and then multivesicular as it grows to be finally transformed into a large monovacuolated one containing a single large vacuole which is believed to be induced by fusion of the vesicles or smaller vacuoles found in the multivesicular droplets. It seems very likely that the vesicles and smaller vacuoles of the mono- and multivesicular droplets may probably originate from small dense granules and vesicles scattered in the dense matrix of the lipid droplets. In this study the authors could not, however, confirm the finding reported by IIJIMA (1959) that the vacuoles are discharged into the surrounding cytoplasm. On the other hand, the view of IIJIMA (1959) and KUROSUMI et al. (1960) that the dense granules or bodies which arise from Golgi vesicles may participate in the formation of the lipid droplets has been supported by this study. The authors observed the membrane bounded dense bodies of various sizes which had been probably derived from the Golgi vesicles with dense material. These dense bodies were also sometimes found in the vicinity of the lipid droplets and occasionally displayed pictures of fusion with the latter. A figure suggesting a direct transformation of the dense bodies into the lipid droplets, however, was not obtained. The fate and functional significance of the lipid droplets have not been clarified in this study.

Summary

In this electron microscopic study on human axillary eccrine sweat gland, the so-called dark and clear cells composing the secretory epithelium were designated as “superficial” and “basal” cells respectively, because of their different location in the secretory epithelium.

The cell bodies of the tall superficial cells occupy the superficial portion and line the main gland lumen with their apical surface, whereas the slender basal parts are extended in between the basal cells to reach either to the myoepithelial cell or to the basement membrane. The superficial cells are characterized by poorly developed microvilli protruded into the gland lumen, well-developed abundant tonofilament bundles oriented in various directions, poorly developed intercellular interdigitations as well as basal infoldings, and the accumulation of the secretory vacuoles in the apical cytoplasm.

The rounded basal cells occupy the basal portion of the secretory epithelium without bordering directly on the main gland lumen. They enclose, however, the intercellular canaliculi between them which seem to empty in the main gland lumen; their wide basal surface rests either on the myoepithelial cell or the basement membrane. The basal cells are characterized by a number of closely packed microvilli protruded into the intercellular canaliculus, lacking secretory vacuoles, large content of glycogen granules, extraordinarily well-developed agranular endoplasmic reticulum, and extensive and complicated intercellular interdigitation and basal infolding both of which show vigorous vesiculation of the plasma membrane.
The transformation between both secretory cell types was never proved. The occurrence of two secretory cell types with distinct cytological differences suggests the existence of two loci of different kinds of sweat production in the secretory epithelium of the human eccrine sweat gland.

The concordance in certain cytological features of the basal cells with the salt-gland cells of some animals and birds supports the view that the basal cells are probably the production site of sweat which is high in water, Na and Cl content. The agranular endoplasmic reticulum closely packed in the whole cytoplasm of the basal cells is supposed to participate in the transport of water and the solutes from extracellular spaces to the intercellular canaliculus.

The agranular endoplasmic reticulum in the basal cells sometimes contain a small amount of glycogen granules within its dilated cisterns, a finding which suggests that the agranular endoplasmic reticulum may probably play a role also in intracellular glycogen metabolism.

The secretory vacuoles elaborated from the Golgi vacuoles in the superficial cells are discharged into the main gland lumen by means of either eccrine or apocrine mode of secretion. In the process of the latter, it was discovered that the paired demarcation membrane was formed at the neck of the papillary apocrine projection. The opinion of the present authors concerning the formation mechanism of the apocrine projection was also presented.

The ultrastructural properties of the membrane bounded lipid droplets found in both cell types were described and the formation of large monolocular lipid droplets and the correlation between the lipid droplets and the dense bodies elaborated in the Golgi area were also discussed.

ヒトのエックリン汗腺の電子顕微鏡的研究（内容自抄）

ヒトの腋窩エックリン汗腺を電子顕微鏡で観察した。腺上皮を構成するいわゆる暗調細胞と明調細胞を、その腺上皮内における位置から各々 表層細胞と基底細胞と呼んだ。

表層細胞は高く、その細胞体は腺上皮の表層部を占め、自由表面をもって腺腔を開むが、細い基底部は基底細胞間にあって、その狭い基底面は筋上皮細胞または基底膜につく。表層細胞の特徴としては、1）腺腔へ出された発達の悪い微絨毛、2）種々の方向に向う発達した多数の張微原線維束、3）細胞形成をあまり示さない著明でない細胞間架合と基底陥入、4）腺腔面下の分泌空胞の密積などがあげられる。

他方、円い基底細胞は腺上皮の基底部を占め、腺腔には直接臨まないが、結局腺腔へ開口する細胞間細管を閉み、その狭い自由表面は細管にのぞみ、広い基底面は筋上皮細胞または基底膜にのる。基底細胞の特徴は1）細胞間細管へ出される多数の密生する微絨毛、2）分泌空胞がないこと、3）多量のグリコゲン顆粒を含むこと、4）非常によく発達して密に配列する滑面小胞体。5）旺盛な小胞形成を示す広範囲にわたる複雑な細胞間架合と基底陥入などである。両細胞間の移行は認められない。

以上のような明確な細胞学的相異をもつ2種腺細胞の存在は、ヒトのエックリン汗腺の腺上皮には異なる汗の産生を行なう2つの部位があることを暗示する。上述のように基底細胞は他の動物や鳥類の塩類腺と一致して、旺盛な小胞形成を示す複雑な細胞間架合と基底陥入を形成する多数の著明な細胞質突起を備えるという特徴をもつが、このことは基底細胞がおそらく水分と Na および Cl に富む汗の産生部位であろうという見解を支持する。
さらに基底細胞の細胞質内に広く密に分布する滑面小胞体は、水と溶質を細胞内を通して細胞外腔から細胞間細管へ運搬するに与かるであろう。また滑面小胞体の拡大した小囊内に時に少数のグリコゲン顆粒が含まれる所見が証明されたが、おそらく滑面小胞体が他方において細胞内グリコゲン代謝に関与することを暗示する。

表層細胞内で形成される分泌空胞はエックリンまたはアポクリン分泌によって腺腔へ排出される。アポクリン分泌過程において、表層細胞の先端とそこから腺腔へ出された乳頭状のアポクリン突起の基底との間に対をなす分離膜の形成が観察され、またアポクリン突起の形成機構に関する著者の見解が述べられた。両種細胞に認められる、限界膜をも特異な球形の脂質滴の特性が詳細に観察され、大なる単一空胞をもつ脂質滴の形成機構について、またゴルジ装置で形成される dense body と脂質滴との関係について検討した。

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