From:
The Department of Oral Surgery,
University of Umeå,
Sweden

AN ELECTRON MICROSCOPE STUDY OF NORMAL HUMAN PALATAL EPITHELIUM

by

HOLGER THILANDER

INTRODUCTION

Knowledge of the fine structure of the normal oral soft tissues is of the greatest importance in order to understand physiological and pathological processes in these tissues. In the last decade several investigations have been published concerning the ultrastructure of human oral epithelium, especially the buccal gingiva and the lining oral mucosa. These studies were focused either on some details of interest (*Sognnaes & Albright*, 1956, 1958; *Albright* 1960; *Melcher*, 1965; *Stern*, 1965; *Frithiof & Wersäll*, 1965; *Listgarten*, 1966), or on a more or less complete description of the appearance of the epithelial layers (*Kurahashi & Takuma*, 1962; *Zelickson & Hartman*, 1962; *Heim*, 1964; *Listgarten*, 1964; *Schroeder & Theilade*, 1966).

Detailed descriptions of the ultrastructure of human palatal epithelium are, however, very sparse. One abstract has been published recently (*Weinstock & Albright*, 1966). The aim of the present study is, therefore, to give a survey description of the ultrastructure of normal human palatal epithelium, the specimens of which were taken under standardized conditions (randomized, well defined regions and healthy tissue).

MATERIAL AND METHODS

The material consisted of biopsies from the palatal gingiva of 10 adult patients (between 20—30 years old) who were referred for the removal of im-

pacted upper canines. The biopsies were obtained from normal non-inflamed palatal gingiva randomly taken about 1 to 1.5 mm from the incisors by excision with scalpel. The absence of inflammation was determined by clinical scoring and by lack of exudate from the adjacent gingival crevices. The latter was ascertained by the extra-crevicular filter paper strip method described by *Brill & Krasse* (1958) and *Löe & Holm-Pedersen* (1965).

The specimens were immediately immersed in ice-cold one per cent osmium tetroxide buffered to pH 7.6 with phosphate buffer (*Milloning*, 1961) and cut into smaller pieces. The fixation time was 2—3 hours in the osmium fixative. The specimens were then dehydrated in graded ethanols and finally embedded in Epon.

Sections for orientation were obtained by cutting 1—2 micron thick sections in an ultramicrotome. These sections were then placed on ordinary glass slides and were stained in toluidin blue.

After final trimming the specimens were sectioned in an LKB ultrotome using glass knives. The thin sections were stained with uranyl acetate or double stained with uranyl acetate and lead citrate. The examination of the sections was performed in a Zeiss electron microscope EM 9 or a Philips electron microscope E M 200.*

RESULTS

Border zone epithelium — connective tissue

The border between epithelium and connective tissue was irregular with a wavy course (Fig. 1). The two tissues were separated by a 400—700 Å thick osmiophilic layer, the basement membrane or the lamina densa. This lamina densa consisted of a finely granular or sometimes filamentous substance (Fig. 2). Between the cell membranes of the basal cells and the lamina densa, there was a less electron dense, homogenous zone of about 300—500 Å in width. This clear zone has been named lamina lucida. At irregular intervals hemidesmosomes with a typical lamellated appearance were present. Filamentous structures were seen to extend to the lamina densa from the peripheral density of the hemidesmosomes and often even from areas of the cell membrane between the hemidesmosomes.

At the connective tissue side of the lamina densa there was a zone (about 0.5 μ wide) where connective tissue fibrils were rather sparse. Here the fibrils were fine and ran without apparent organisation. Blood vessels were abundant and capillaries were often seen close to the lamina densa (Fig. 3).

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* The electronmicroscopes were kindly put at the author's disposal by the Departments of Pathology and Anatomy, University of Umeå.

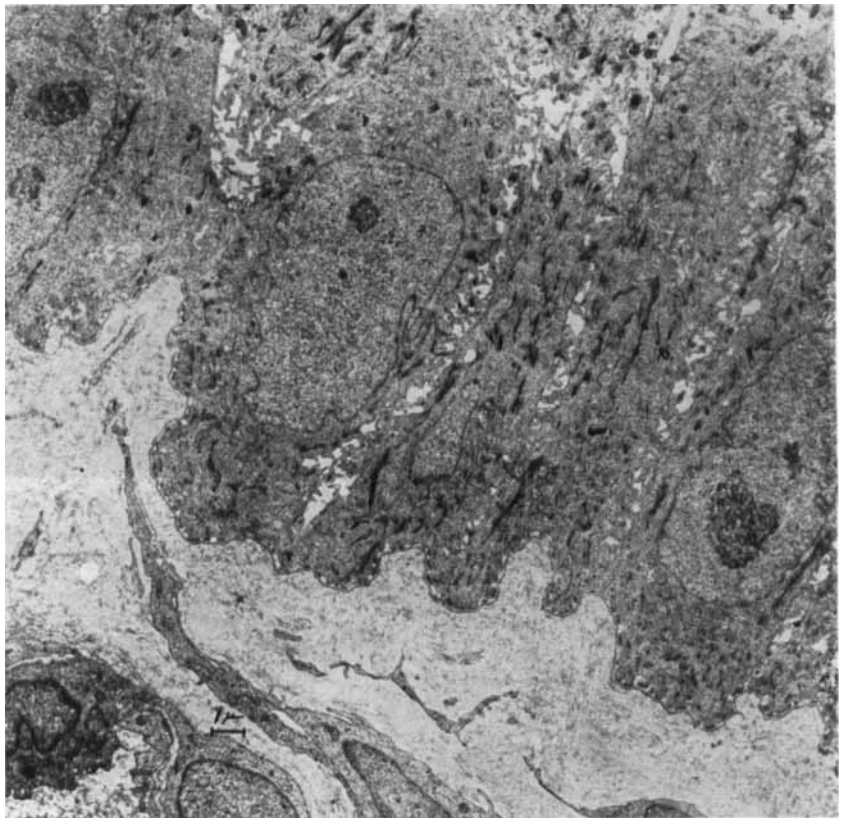

Fig. 1. Survey picture of the basal cells. The cells are columnar in shape. Intercellular space is rather wide. The border between epithelium and connective tissue is irregular with a wavy course. The lamina densa (basement membrane) can clearly be seen. × 6.000.

Stratum basale

The cells in this layer were more or less columnar when the specimens were sectioned perpendicularly to the lamina densa, (Fig. 1), but with a slightly oblique cutting they seem to be more rounded in appearance. The nucleus was round or oval and had often shallow infoldings. The various organelles (mitochondria, Golgi complex, endoplasmic reticulum etc.) could clearly be seen, as the tonofilaments were rather sparse and did not mask them as in higher strata (Fig. 5). The mitochondria were distributed randomly in the cytoplasm possibly with a slightly greater number at the base of the cell. The rough surfaced endoplasmic reticulum was rather well developed but numerous ribosomes were free in the cytoplasm (Fig. 5).

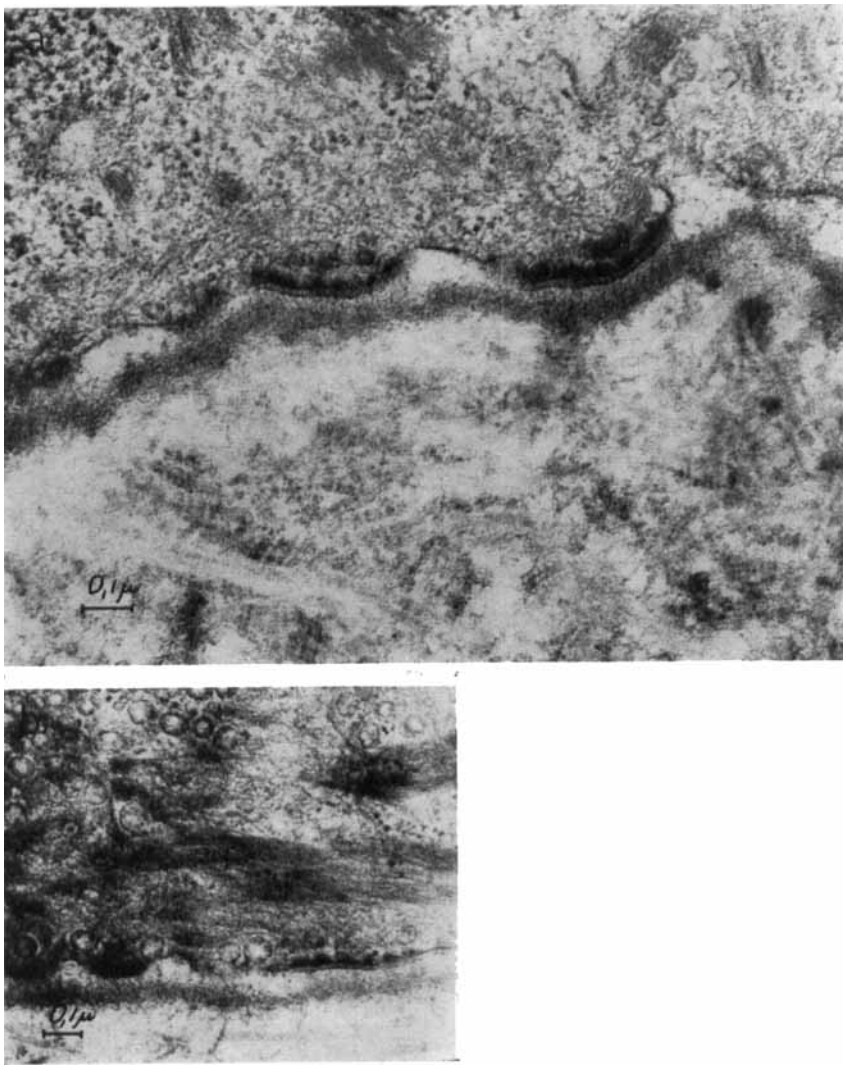

Fig. 2. *a*. Border zone epithelium-connective tissue. Hemidesmosomes and lamina densa are seen. Filamentous structures extend from the cell membrane and the peripheral density of the hemidesmosomes to the lamina densa. At the connective tissue side of the lamina densa *there is a rather* narrow zone, sparse in fibrils. ×100.000. *b*. Border zone epithelium-connective tissue. Small vesicles are present in the cytoplasm near and at the cell membrane. × 70.000.

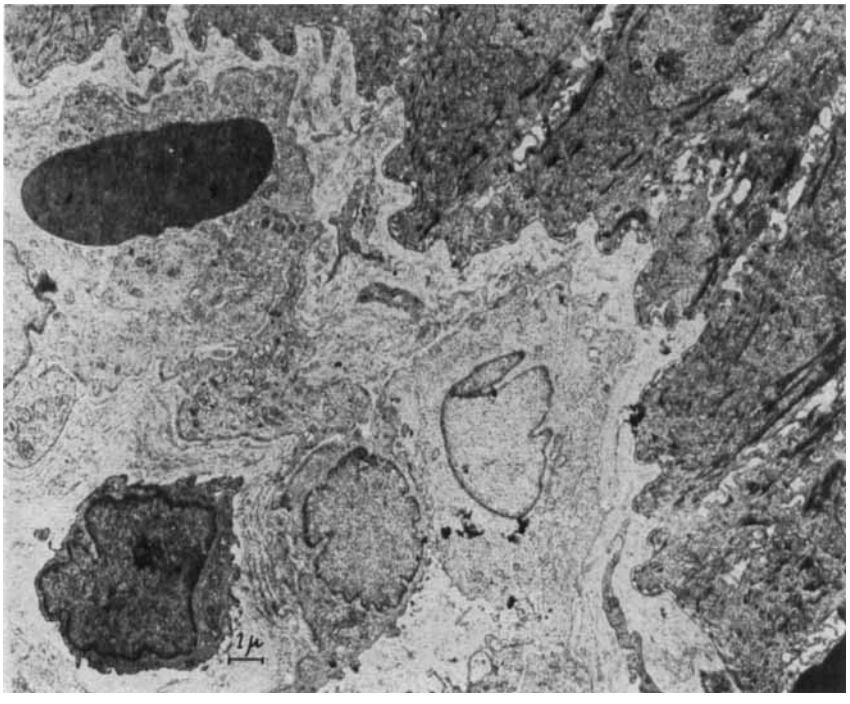

Fig. 3. Survey picture of the basal layer. Capillaries run close to the lamina densa. × 6.000.

The tonofilaments were, as mentioned above, rather sparse and crossed the cytoplasm in various directions in bundles (tonofibrils). Some of them were connected with the attachment plaques of the desmosomes and the hemidesmosomes. Sometimes they changed direction perpendicularly close to the attachment plaques (Fig. 4).

In the cytoplasm near and at the basal part of the cell membrane small vesicles occurred frequently (Fig. 2). Often there was an infolding in the cell membrane with the same vesicle appearance. The vesicles were partially filled with a rather electron dense substance.

The intercellular space was rather wide and is, therefore clearly seen even at low magnification (Fig. 1). The cell peripheries were very uneven, and cytoplasmic processes of different size and shape frequently interdigitate. Desmosomes were evenly distributed around the cells and showed a typical lamellated structure (Fig. 4). Tight junctions (zonula occludens) could be observed frequently. In this layer they were rather short and followed a straight or slightly wavy course. Intermediate junctions were also frequently observed. Between the epithelial cells, so-called clear cells were frequently

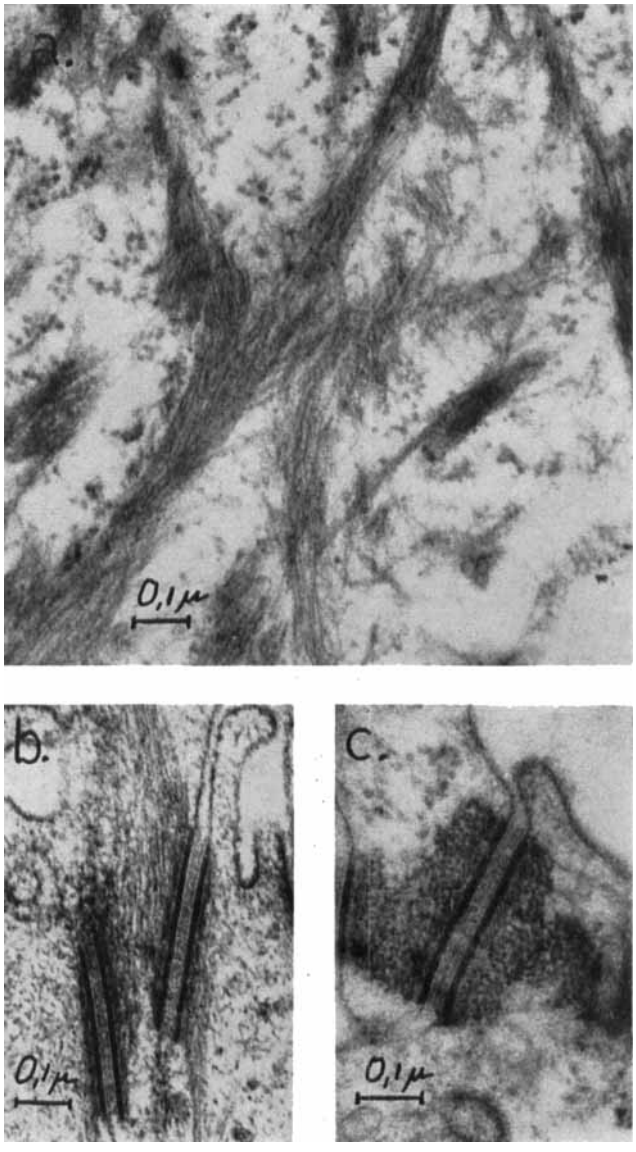

Fig. 4. *a*. The arrangement of tonofilaments in the basal cells. The bundles (tonofibrils) are rather thin and cross the cytoplasm in various directions. × 65.000. *b*. and *c*. The attachment of tonofilaments to the attachment plaques of a desmosome. In *b* they follow a straight course, in *c* they change direction perpendicularly close to the attachment plaques. × 67.000 (*b*). × 89.000 (*c*).

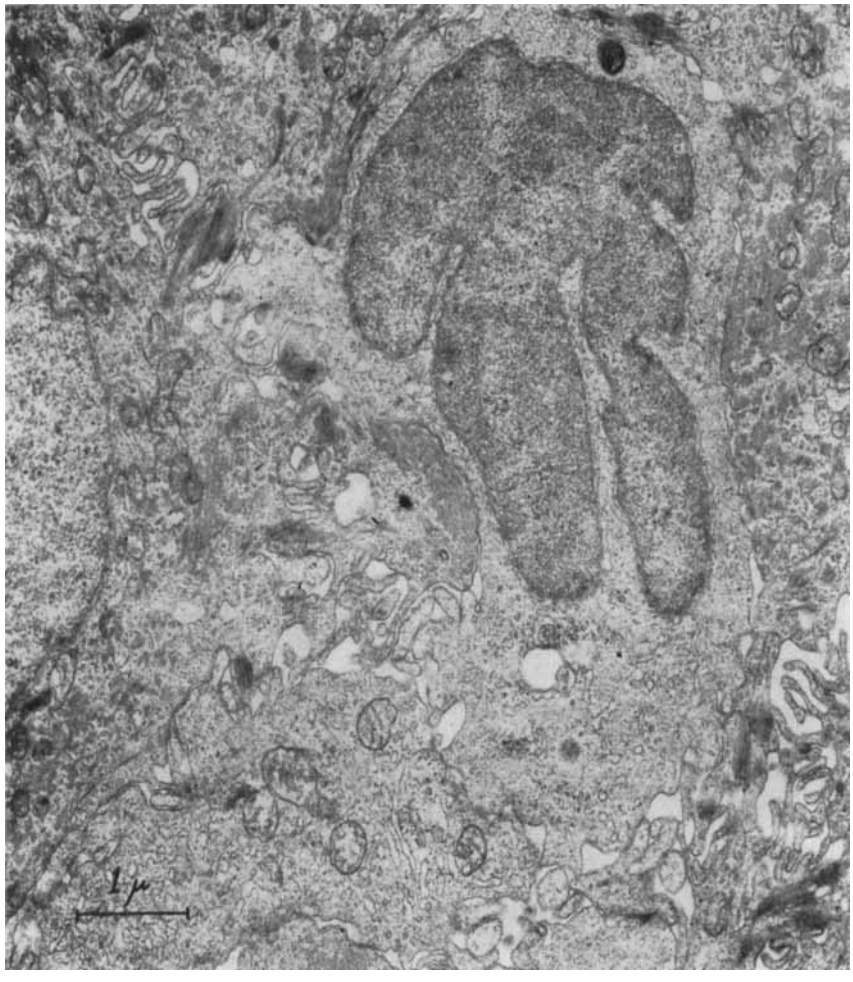

Fig. 5. From the basal layer. A clear cell between epithelial cells. In the clear cell: chromatin rich nucleus with deep infoldings; in the cytoplasm no tonofilaments, many small vesicles and granules; The osmiophilic granula in the upper part of the cell is matured melanin. In the epithelial cells: the conventional set of organelles, free ribosomes in the cytoplasm. × 20.000.

interspersed (Fig. 5). They have a very characteristic appearance, and it was easy to distinguish them from epithelial cells. The clear cell lacked tonofilaments in the cytoplasm, and the chromatin-rich nucleus had deep infoldings. In the cytoplasm there were many small vesicles and granules of varying electron density, the latter representing premelanosomes and melanosomes. Mature melanin granules were observed in the cytoplasm in most cases

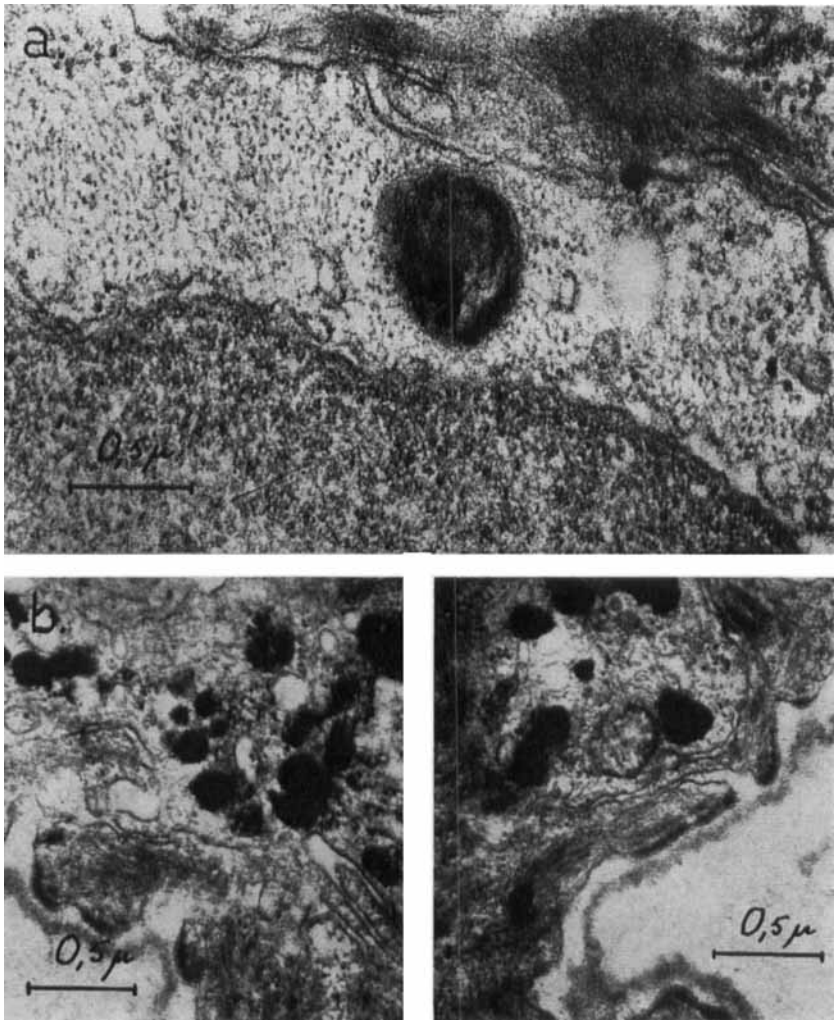

Fig. 6. Melaningranules from clear cells in the basal layer. In 6a a higher magnification of the melanin granula seen in fig. 5. × 34.000 (*a*); × 30.000 (*b* and *c*).

(Fig. 5, Fig. 6). Occasionally rod-shaped bodies were observed in this layer. Cytoplasmic projections from these cells were often found between epithelial cells in higher strata (Fig. 7). The cell membrane of this cell type was more even than in the epithelial cell, and the intercellular space was in most places rather narrow (Fig. 5). No desmosomes or tight junctions were observed in connection with these cells, only attachment devices of the intermediate type.

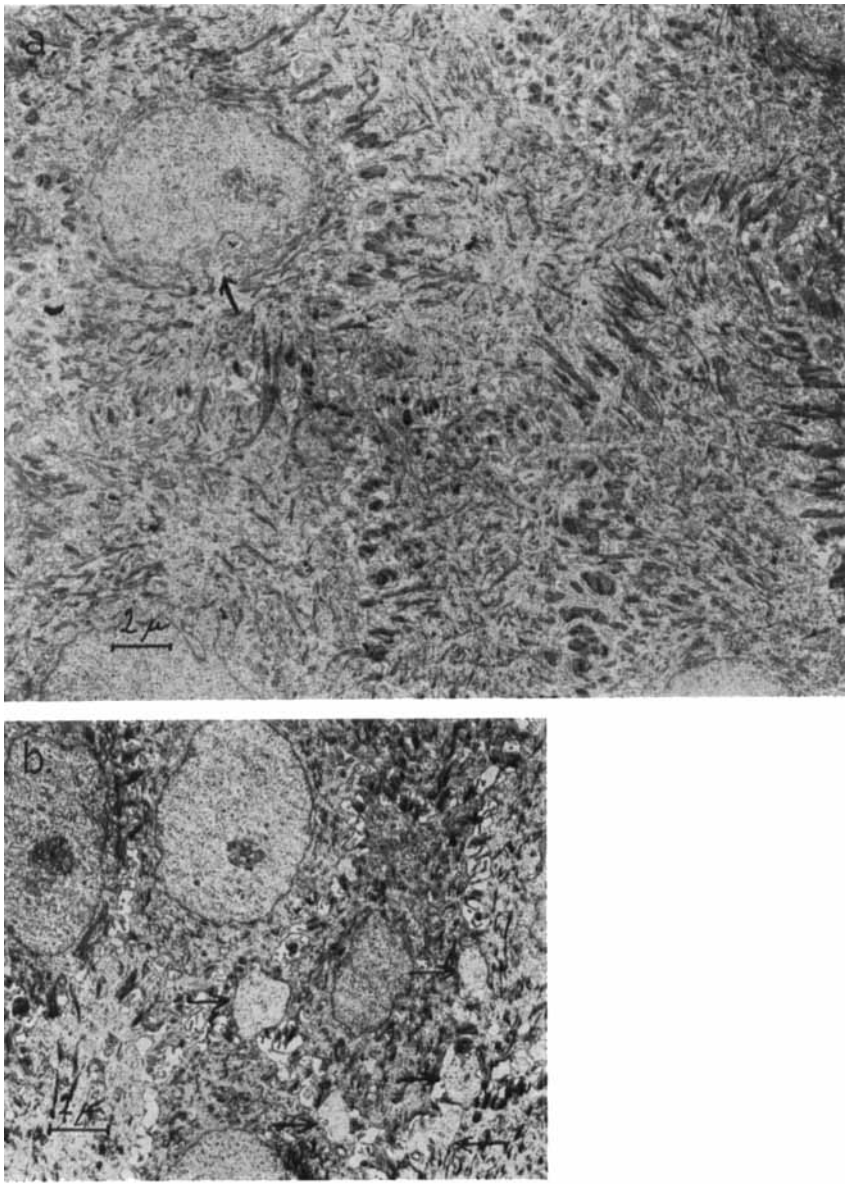

Fig. 7. Survey pictures of the stratum spinosum. *a*. The spinosum cells are relative spherical. The nuclei have deeper infoldings than in the basal layer. In the wider infoldings often mitochondria are situated (arrow). × 4.800. *b*. Between the spinous cells cytoplasmic projections from clear cells in the basal layer are seen (arrows). × 4.800.

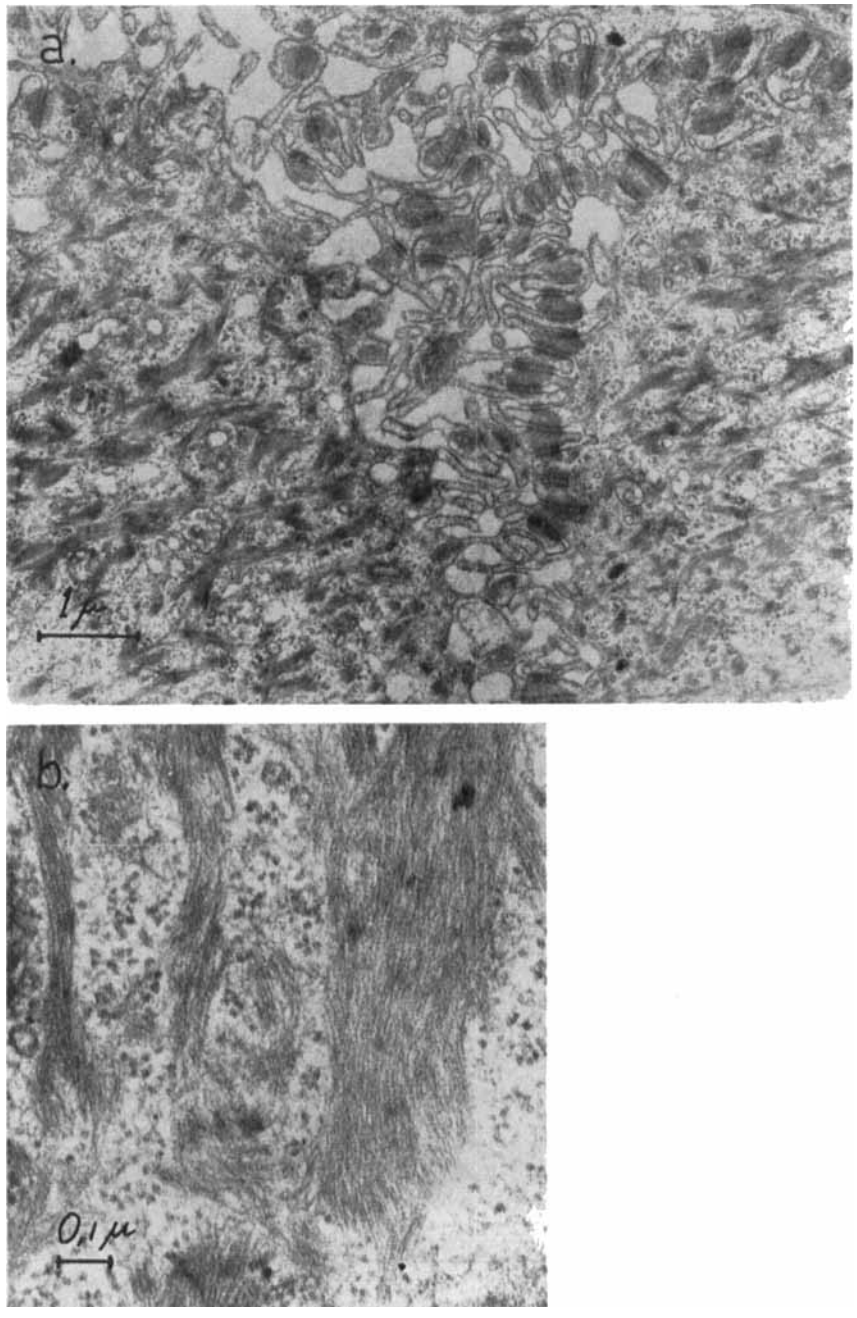

Fig. 8. From the spinous layer. *a*. The intercellular space is rather wide. The cellmembranes are highly convoluted. The desmosomes are numerous. × 14.000. *b*. The tonofilaments are arranged in rather thick bundles. There seem to be a real increase in the number of filaments in this layer compared to the basal layer. × 72.000.

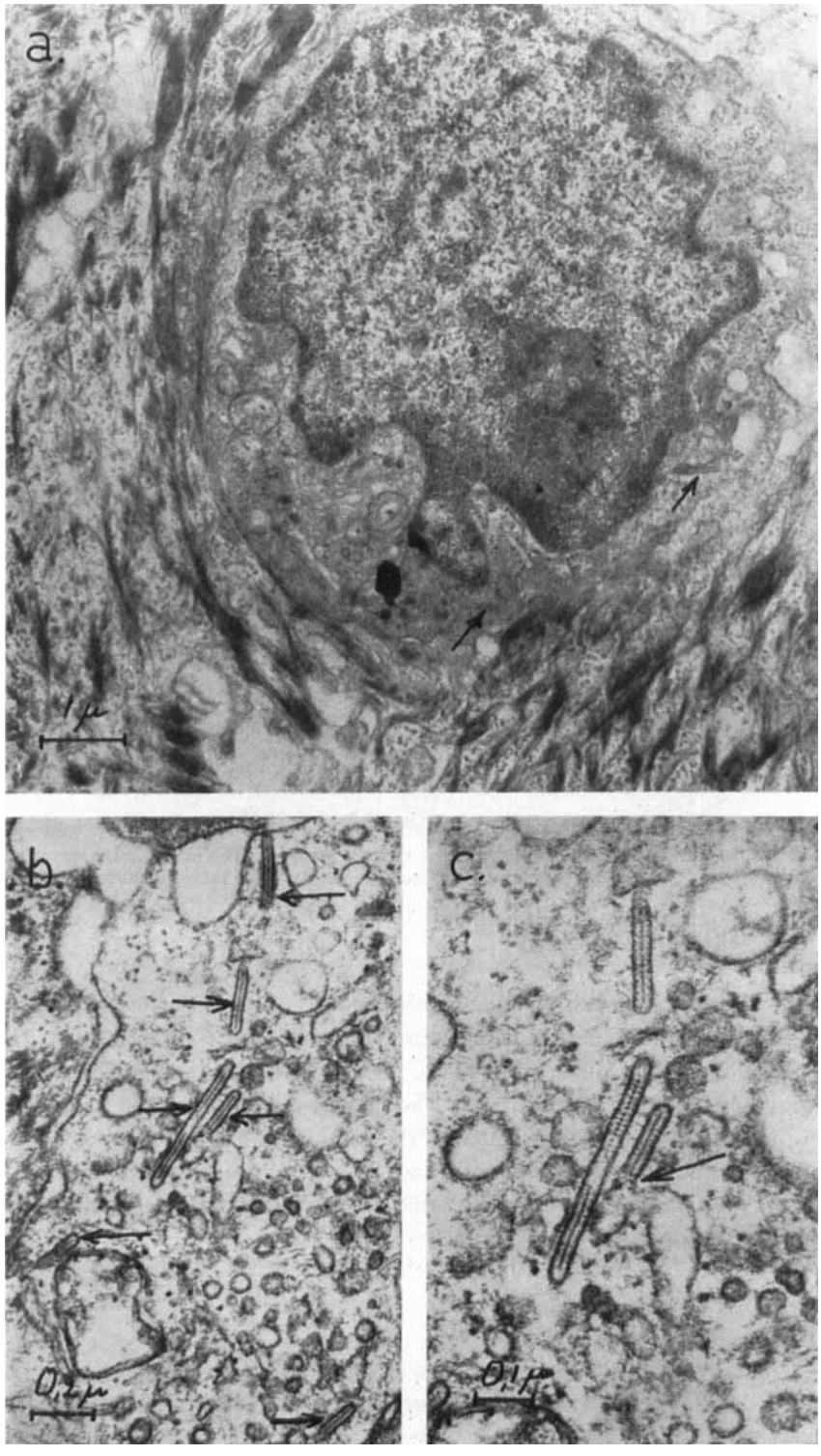

Fig. 9. *a.* Clear cell (Langerhans cell) in the spinous layer. No matured melanin granules are present. (The very strong osmiophilic spots are artefacts). Two rodshaped bodies can clearly be seen (arrows). × 12.000. *b.* Part of a clear cell in the spinous layer. Six rod-shaped bodies can clearly be seen (arrows). × 43.000. *c.* Higher magnification of some of the rod-shaped bodies in 9b. Their characteristic structure is clearly seen. One of the bodies seem to be continous with the endoplasmic reticulum (arrow). × 78.000.

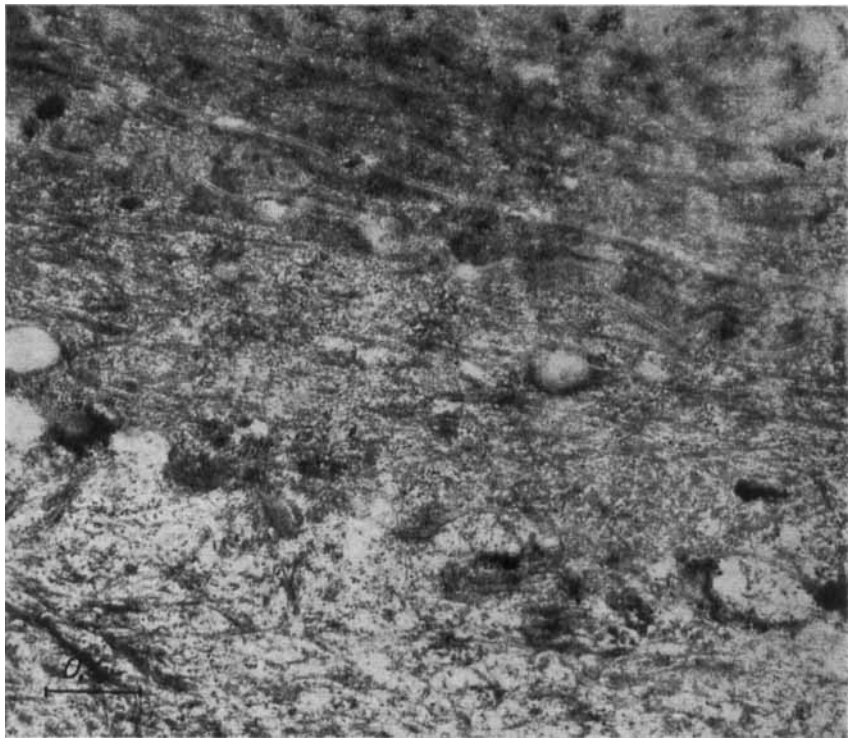

Fig. 10. Border zone stratum granulosum — stratum corneum. The intercellular spaces are narrow and rather straight. The border between the two layers is rather distinct. × 36.000.

Stratum spinosum

The spinosum cells were stellate with centrally located nuclei (Fig. 7). At the border to the stratum granulosum they were more flattened with the longest diameter parallel to the tissue surface. The round nuclei had deeper infoldings than in the basal layer. The nuclear-cytoplasmic ratio of the spinosum cells was smaller than that of the basal cells. The tonofilaments were abundant, they ran in thick bundles which crossed the cytoplasm in various directions (Fig. 8). A cytoplasmic zone around the nucleus was rather free from filaments, and here the usual organelles were found. The mitochondria were numerous throughout this zone and often situated in the wider infoldings of the nucleus (Fig. 7). In the cytoplasm granules of various density and size were observed.

The intercellular space was as wide as and often wider than that observed in the basal layer. The cell membranes were highly convoluted; cytoplasmic projections interdigitated freely between cells (Fig. 8). The desmosomes

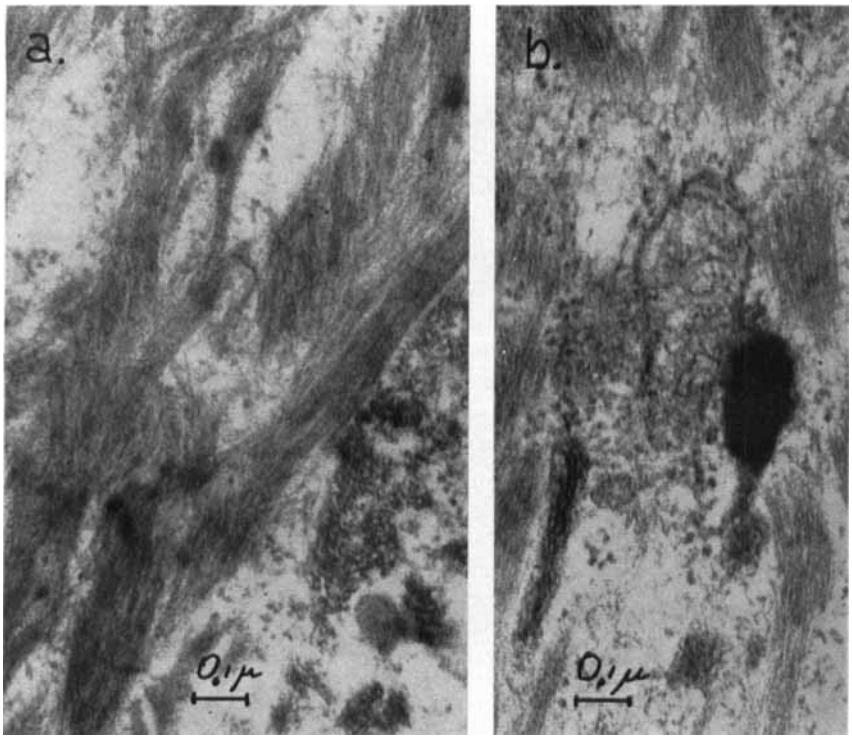

Fig. 11. From the granular layer. *a*. From the lower part of the stratum granulosum. Keratohyalin granules closely associated with the tonofilaments. × 73.000. *b*. From the upper part of the stratum granulosum. A keratohyalin granula close to a disintegrating mitochondrium. × 73.000.

seem to be more numerous than in the stratum basale. Tight junctions and intermediate junctions also occurred frequently.

Clear cells were interspersed between the epithelial cells (Fig. 9). They showed the same characteristics as described for the clear cells of the basal layer, except that none of the granules observed, could be classified with certainty as mature melanin. So-called rod-shaped bodies were found in every such cell, often they were quite numerous (Fig. 9). They may measure between 1000 and 4000 Å in length and about 300 Å in width and showed rounded ends. In osmium fixed specimens there were three dotted osmiophilic bands which gave the rods a striated appearance. Two of them lied adjacent to the inner surface of the membrane and the third was centrally located in the rod. The spacing between the striations was about 100 Å. Sometimes it appeared that some of these bodies were continuous with a vesicle or the endoplasmic reticulum.

Fig. 12. Survey picture of the stratum corneum and the border to the stratum granulosum The cells are long flat and orientated parallel to the surface. No nucleus or cytoplasmic organelles are present in the cells. × 5.500.

Stratum granulosum

The cells were flattened, those higher in the layer tending to be more flat. In the lower part of the strata some of the nuclei and organelles such as mitochondria and endoplasmatic reticulum, were rather intact, but often they began to disintigrate (Fig. 11). At the border zone to stratum corneum they usually had disappeared.

The tonofilaments were not as distinct as they were in the two lower layers, especially the basal layer. The presence of keratohyalin granules was characteristic for this layer (Fig. 11). They were electron-dense, irregularly shaped granules, which differed greatly in form and size. Usually they seemed to be closely associated with the tonofilaments. Sometimes small electron-dense granules could be observed in the cells of the upper part of the stratum granulosum.

The intercellular space was diminished compared with the stratum spinosum (Fig. 10). Except for focally expanded parts, the intercellular spaces

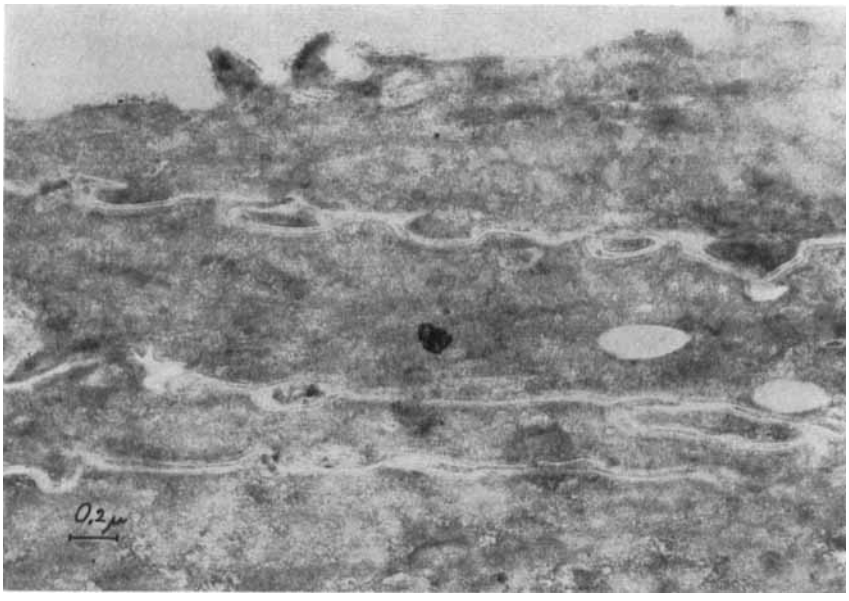

Fig. 13. From the stratum corneum. The cells consists of densely packed filaments in an osmiophilic amorphous substance. The intercellular space is narrow and rather straight. × 45.000.

seemed to consist only of desmosomes, tight junctions and intermediate junctions. These attachment devices were thus very common. At the border zone to stratum corneum the structure of the desmosomes changed and they shoved a composite structure.

Stratum corneum

The stratum corneum was usually from five to eight cells thick (Fig. 12). The border to the stratum granulosum was usually quite distinct. The cells were long, flat and orientated parallel to the surface. No nucleus or cytoplasmic organelles were seen.

Except for oval vacuoles, which seemed to be empty, the cytoplasm consisted of densely packed filaments in an osmiophilic, amorphous substance (Fig. 13). The intercellular space was very narrow and only focally widened. It followed a straighter course here than it did deeper in the epithelium. In stratum corneum the cell membrane changed in appearance, especially at the higher levels. Instead of the classical triple-layered-structure it consisted here of one single, thick, rather electron-dense layer (Fig. 14). The junctional

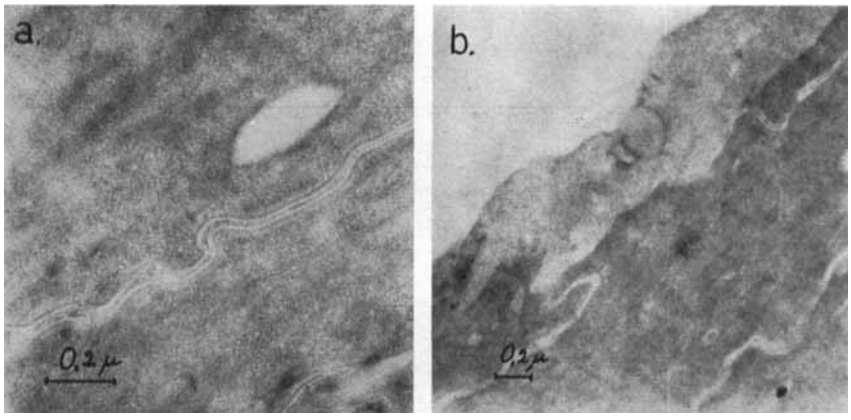

Fig. 14. From the stratum corneum. *a*. The cell membrane consists of one single, thick, rather electron dense layer. There is a modified appearance of the desmosomes. Intercellular space is narrow. × 70.000. *b*. Orifices of the intercellular space at the tissue surface. The orifices consist of modified desmosomes. Detritus on the tissue surface. × 35.000

elements could be described as modified desmosomes and tight junctions, and both types were common. The orifices of the intercellular spaces at the tissue surface were closed by modified desmosomes or tight junctions.

DISCUSSION

The intercellular attachment devices in the palatal epithelium have only been mentioned briefly here. Their appearance, differences in structure in the different layers, and significance have been reported in another paper (*Thilander & Bloom*, 1967) to which is referred.

The normal ultrastructure of the buccal gingival epithelium has been described by *Listgarten* (1964) and *Schroeder & Theilade* (1966). When comparing their results with those reported here, it is evident that one of the main differences in structure between the buccal gingival epithelium and the palatal epithelium is the outermost layer, the stratum corneum. In the buccal gingiva it is mostly parakeratotic; in every specimen here the palatal mucosa is fully keratinized. Here the stratum corneum seems to be structurally a rather homogenous layer and can not be divided into different sublayers as was described for the guinea pig epidermis (*Brody* 1959).

The palatal epithelium is as a whole rich in cytoplasmic tonofilaments. In the stratum basale they are, however, rather sparse and aggregated into thin anastomosing bundles, in which the individual filaments can be clearly discerned. In the higher layers the bundles are thicker and abundant, and the filaments show denser packing. In the bundles the individual filaments

are here more difficult to discern. According to *Odland* (1964) there has been no evidence for a significant increment in the number of tonofilaments in epidermal cells above the basal layer. This statement for the human epidermis has, however, not been generally accepted. It has further been pointed out (*Brody*, 1960) that the filaments of human epidermis showed an increase in diameter from about 50 Å in the stratum basale to about 70 Å in the stratum corneum. Measurements in the present material show a corresponding increase in diameter, the figures obtained are about 50 Å in the stratum basale and about 100 Å in the stratum granulosum. This increase in diameter affects, of course, the width of the bundles, but even taking this and the smaller nuclear-cytoplasmic ratio in the spinous layer into consideration, there seems to be a real increase in the number of filaments in the stratum granulosum and the stratum spinosum as compared to the basal layer.

During the last decade many papers have been published on the ultrastructure of the clear cells in human epidermis (*Charles & Ingram*, 1959; *Birbeck, Breathnach & Everall*, 1961; *Breathnach, Birbeck & Everall*, 1963; *Breathnach*, 1963, 1964; *Breathnach & Wyllie*, 1965; *Zelickson*, 1965) and in buccal gingiva (*Schroeder & Theilade*, 1966). The relationship between melanocytes and Langerhans cells has been discussed extensively. A basic question has been whether or not the Langerhans cell is an entity or merely a melanocyte which is being passed towards the surface. According to *Birbeck et al.* (1961) the major difference between a melanocyte and a Langerhans cell is that the latter has no melanin or premelanin granules present in the cytoplasm, but has granules of a special type, the so-called rod-shaped bodies. In recent years the relationship between the melanocyte and the Langerhans cell has been stressed. *Breatnach* (1963) stated that the Langerhans cell is a post-division stage of a mature melanocyte. In his opinion, the low level clear cell is capable of producing melanin, but the high level cell is not. In both of them there may be rod-shaped bodies, which are characteristic for the Langerhans cell. *Zelickson* (1965) had a slightly divergent opinion, as he believed the high level clear cell to be capable of producing melanin. In some recent papers *Wolff & Winkelman* (1967 a, b, c) reported some differences between Langerhans cells and melanocytes in guinea pigs with reference to the localization of nucleoside triphosphatase, dissimilar response to ultraviolet light and a variable ratio in number between these two cells. According to these authors the findings indicate that the Langerhans cell and the melanocyte represent two distinct and independent cell lines.

In the present material, where none of the specimens was taken from a pigmented area, the cytoplasm of the basal clear cells almost invariably

contains matured melanin granules. Only occasionally rodshaped bodies can be observed in the basal layer. These bodies are found in cytoplasmic projections which are devoid of melanin granules. It is not possible to decide if these projections belong to high level cells or to basal clear cells. In the high level cells, however, no granules are observed which could with certainty be classified as mature melanin. In all of these high level cells, however, there are rod-shaped bodies in the cytoplasm, and they are often numerous. In conformity with the findings of *Schroeder & Theilade* (1966) in buccal gingiva, granules resembling premelanosomes are observed in the high level cells.

As has been mentioned above, a characteristic feature of the Langerhans cell is the presence of rod-shaped bodies in the cytoplasm. It has been suggested that they are sectional profiles of disc-shaped organelles (*Birbeck et al.*, 1961), and that they may be formed by an infolding and nipping off of segments of plasma membrane, or that they may arise from collapse of vacuoles, probably Golgi vacuoles (*Breathnach*, 1964). In the present material rod-shaped bodies are found in connection with vacuoles and even close to the cell membrane. Further studies are necessary to throw more light on the formation and nature of these characteristic bodies.

SUMMARY

The material comprised biopsies from normal noninflamed palatal gingiva from 10 adults. The biopsies were taken under standardized conditions (randomized, well defined regions and healthy tissue). The epithelium was separated from the connective tissue by a 400—700 Å thick lamina densa, at the connective tissue side of which there was a zone, about 0.5 μ in width, which was sparse in fibrils. Capillaries ran close to the lamina densa.

The basal epithelial cell was columnar with a round nucleus. In the cytoplasm there were the conventional set of organelles; tonofilaments were rather sparse, and near and at the basal part of the cell membrane small vesicles occured frequently. The intercellular space was rather wide, and of attachment devices hemidesmosomes, desmosomes, tight junctions and intermediate junctions were present. The clear cells of the basal layer often contained mature melanin granules. Occasionally rod-shaped bodies were observed in cytoplasmic projections which contained no melanin granules. The corresponding cells in the spinous layer showed many rod-shaped bodies but no matured melanin. The rod-shaped bodies had a characteristic structure.

The spinous cells were stellate with a centrally located nucleus. As compared to the basal cell the nuclear-cytoplasmic ratio was here smaller, the tonofilaments and the desmosomes seemed to be more numerous. Tight junctions and intermediate junctions were present.

In the stratum granulosum the cells were flattened, the nucleus and the cytoplasmic organelles disappeared gradually and keratohyalin granules appeared. The intercellular space was narrow. Composite desmosomes, tight junctions and intermediate junctions were present.

In the stratum corneum the cells were long, flat and fully keratinized. The intercellular space was narrow and the desmosomes were modified in structure. Tight junctions were common.

RÉSUMÉ

ETUDE AU MICROSCOPE ÉLECTRONIQUE DE L'ÉPITHÉLIUM PALATIN HUMAIN NORMAL

Le matériel comprenait des biopsies de gencive palatine normale non inflammée provenant de 10 adultes. Les biopsies ont été prélevées dans des conditions normalisées (régions bien définies, choisies au hasard, et tissu sain).

L'épithélium était séparé du tissu conjonctif par une lamina densa de 400—700 Å d'épaisseur, dont le coté tourné vers le tissu conjonctif présentait une zone pauvre en fibrilles d'une largeur d'environ 0,5 μ. On constatait la présence de capillaires le long de la lamina densa.

La cellule épithéliale basale était une cellule cylindrique à noyau rond. On trouvait dans le cytoplasme l'ensemble habituel d'organites; les tonofibrilles étaient assez clairsemées, et, près de la partie basale de la membrane cellulaire, on observait fréquemment de petites vésicules. L'espace intercellulaire était assez large, et, comme éléments de cohésion, on observait des hémidesmosomes, des desmosomes, des »tight junctions» et des »intermediate junctions». Les cellules claires de la couche basale contenaient souvent des granules de mélanine à maturité. Des corps en forme de bâtonnets étaient parfois observés dans des prolongements cytoplasmiques ne contenant pas de granules de mélanine. Les cellules correspondantes de la couche épineuse présentaient de nombreux corps en forme de bâtonnets, mais pas de mélanine à maturité. Les corps en forme de bâtonnets avaient une structure caractéristique.

Les cellules de la couche épineuse avaient une forme étoilée avec un noyau central. Par comparaison avec la cellule basale, le rapport noyau/cytoplasme était ici plus petit; les tonofibrilles et les desmosomes semblaient être en

plus grand nombre. On observait des »tight junctions» et des »intermediate junctions».

Dans la couche granuleuse, les cellules étaient aplaties; le noyau et les organites cytoplasmiques disparaissaient progressivement, et des granules kératohyalins apparaissaient. L'espace intercellulaire était étroit. On observait des desmosomes complexes, des »tight junctions» et des »intemediate junctions».

Dans la couche cornée, les cellules étaient allongées, aplaties, et entièrement kératinisées. L'espace intercellulaire était étroit et la structure des desmosomes était modifiée. Les »tight junctions» étaient fréquentes.

ZUSAMMENFASSUNG

EINE ELEKTRONENMIKROSKOPISCHE UNTERSUCHUNG ÜBER DAS NORMALE PALATINALE EPITHELIUM DES MENSCHEN

Das Material bestand aus Biopsien von normaler, nicht inflammierter palatinaler Gingiva von 10 Erwachsenen. Die Biopsien wurden unter standardisierten Bedingungen gewonnen (wahllos, von wohl definierten Regionen und gesundem Gewebe). Das Epithel war von einer 400—700 Å dicken Lamina densa vom Bindegewebe getrennt, an deren Bindegewebe-Seite eine ungefär 0,5 μ weite Zone zu sehen war, die sparsam an Fibrillen war. Kapillaren sah man dicht an der Lamina densa.

Die basale Epithelzelle war säulenförmig mit einem runden Kern. In dem Zytoplasma fand man die konventionelle Anzahl an Organellen; Tonofibrillen waren recht sparsam, nahe und direkt an dem basalen Teil der Zellenmembrane sah man oft kleine Bläschen. Der Interzellularraum war recht breit. Hemidesmosomen, Desmosomen, »tight junctions» und »intermediate junctions» waren vorhanden. Die klaren Zellen der basalen Schicht enthielten oft reife Melaninkörnchen. Gelegentlich sah man stabförmige Körper in dem Zytoplasma, die keine Melaninkörnchen enthielten. Die entsprechenden Zellen der Lamina Spinoza zeigten viele stabförmige Körper aber keine reifes Melanin. Diese stabförmigen Körper hatten eine sehr charakteristische Struktur.

Die Dornzellen waren sternförmig mit einem zentral gelegenen Kern. Mit der Basalzelle verglichen war das Verhältnis zwischen Kern und Zytoplasma hier kleiner und die Tonofibrillen und die Desmosomen schienen zahlreicher. »Tight junctions» und »intermediate junctions» waren vorhanden.

In dem Stratum granulosum waren die Zellen flach, der Kern und die Organellen des Zytoplasmas verschwanden fortschreitend und keratohyaline

Körnchen traten in Erscheinung. Der Interzellularraum war eng. »Composite» Desmosomen, »tight junctions» und »intermediate junctions» waren vorhanden.

In dem Stratum Corneum waren die Zellen lang, flach und völlig keratinisiert. Der Interzellularraum war eng und die Desmosomen waren in ihrer Struktur geändert. »Tight junctions» traten häufig hervor.

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Address:
Department of Oral Surgery,
School of Dentistry,
University of Umeå,
Umeå 6, Sweden