# AN ELECTRON MICROSCOPIC STUDY OF THE HUMAN AXILLARY APOCRINE GLAND

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## INTRODUCTION

According to Kuno (1956) sweat glands were discovered by Purkinje in 1833, and described by his pupil Wendt. Almost simultaneously they were described in 1834 by Breschet and Roussel de Vouzeme.

Montagna (1956) states that it was Krause (1844) who first observed that the sweat glands in the axilla and a few other sites differed from the commoner sweat gland by being larger, while Rothman (1954), quoting an editorial in the *British Medical Journal* (1939), says that the axillary glands were first described by Horner in 1846.

In 1887 Ranvier (see Kuno, 1956) differentiated the 'holocrine' secretion of the sebaceous gland from the 'merocrine' secretion of the sweat glands, and Schiefferdecker (1922) further subdivided the mode of secretion of the merocrine glands into eccrine, and epicrine or apocrine, so naming the gland with which this paper is concerned.

Three decades later the work of Hurley & Shelley (1954) helped considerably to clarify our knowledge of the functioning of the gland.

In this paper a description will be given of the secretory and ductal parts of the gland as seen in the electron microscope.

## MATERIAL AND METHODS

Axillary skin was obtained from a 34-year female under general anaesthesia for excision of an axillary abcess. The axilla was swollen by the volume of pus, but the abcess seemed well contained and the overlying skin was quite normal in appearance.

Fixation, embedding, and sectioning was in the manner described in a previous paper, Charles & Smiddy (1957), fixation commencing about 10 min. after the first incision.

The sections were examined on carbon-filmed grids in a Metropolitan Vickers EM3 electron microscope.

## RESULTS

Pl. 1, fig. 1 shows part of a section of the secretory region of the apocrine gland. A single layer of columnar secretory cells of various lengths project into the lumen. The cells are based on myoepithelial cells whose outer wall forms the limiting membrane between the gland and the dermis.

The secretory cells contain dark secretory granules (*gr.*) and lighter mitochondria in which, on close examination, very unusually arranged cristae can be detected.

Nuclei are present in the majority of cells, but no nucleoli are sectioned. The Golgi apparatus can be observed in four of the secretory cells, especially in the one marked (*g.*), and in its vicinity a great number of tiny vesicles are seen. These vesicles, as will be shown clearly later, accumulate at the cell apices.

Canaliculi run between the upper parts of adjacent cells, as can be seen more clearly in Pl. 1, fig. 2, an oblique transverse section. This contradicts Kuno (1956, p. 46) who believes that canaliculi are absent. Cell membranes form the delicate protuberances, or papillae, projecting into the canaliculi.

On the two left-hand cells the membrane is papillate at the apex, the two next cells show a smooth apical membrane, and in the two right-hand cells the apical membrane has ruptured and a loss of vesiculate material has left an underlying clear space, the so-called hyalin cytoplasm (Montagna, 1956). The membranous ring (*t.s.*) in the lumen on the left of Plate 1, fig. 1 appears to be a transverse section through this clear region of the cytoplasm of a cell. The walls between adjacent cells are devoid of tonofibrillar prickles.

The Golgi apparatus and secretory granules are more clearly seen in Pl. 2, fig. 3. Located among the granules and close to the nucleus it appears to be giving rise to the innumerable tiny vesicles which are confined to its vicinity.

The secretory granules are of two kinds, 'smooth' (*s.g.*) and 'rough' (*r.g.*). The former can be differentiated from the mitochondria only by the absence of cristae, whereas the rough granules show a peripheral granulation into small dense particles which appear collectively as a dark margin on the granule. In other sections the granule may appear as a large, apparently hollow, oval structure with a shell of dense, various-sized droplets or granules; or consist of a lighter 'kernel' embedded in dense, finely particulate material.

The myoepithelial cells are much more strongly developed in the apocrine gland than in the eccrine. When longitudinally sectioned they are 60 $\mu$ or more in length, containing long dark fibrils embedded in a lighter inhomogeneous looking material (Pl. 1, fig. 1), which fibrils appear in transverse section as dots (Pl. 2, fig. 4). Between the cells, and covering also those parts of the myoepithelium in contact with the dermis (Pl. 3, fig. 4), there is a dark, homogeneous, material assumed to be an extensible cementing substance. Occasionally the secretory cells project downwards between the myoepithelial cells and make direct contact with the dermis (Pl. 2, fig. 5). At their base the secretory cells have a much infolded basal membrane which is seen to be double when transversely sectioned (Pl. 2, fig. 5). Between the myoepithelium and the secretory cells intercellular spaces are commonly found.

Pl. 3, fig. 6 illustrates the appearance of the wall of the duct of the apocrine gland. In this section it is about three cells thick, the outer cells, at the bottom of the figure, being next to the dermis and the inner ones line the lumen of the duct. The outer limiting membrane is covered with a fine network of fibrous material, reticulin, while the surfaces of the inner cells are papillate. Embedded in the wall is a large clearer structure assumed to be a non-medullated nerve fibre. The cells of the duct are clearly different from the secretory cells. They are comparatively rich in mitochondria, which are generally much smaller than those found in secretory cells, but secretory granules and vesicles are absent. Golgi structures have not so far been observed. A well-developed prickle system is seen which suggests that the

duct is quite robustly constructed; there is much tonofibrillar material in the cytoplasm.

The papillae are simple structures, which consist of an outer denser membrane enclosing a homogeneous inner cytoplasm; they are mere protuberances of the cell surface.

Under higher magnification the unmedullated nerve fibre appears very similar to Robertis & Ferreira's (1957) electron micrograph of an unstimulated nerve-ending in the adrenal medulla of the rabbit. There is a clear cytoplasm, bounded by the synaptic membrane, containing a number of mitochondria and many synaptic vesicles. Also present are granules showing internal structure which do not appear to be mitochondria, and a single dense granule showing no internal structure.

Pl. 4, fig. 7 shows a general view of the opening of the duct into the hair follicle. The opening is very irregular and multiple, many more smaller openings (*s.o.*) being observable if the area covered by the figure were increased. The surfaces bordering the lumen are richly papillate. Individual cells are sharply outlined by a very strongly developed prickle system, and contain much tonofibrillar material. This suggests that, although in this region they are much frayed by the channellings of the duct opening, the cells are in fact more robust than might at first be expected.

An interesting point here is that, for the first time, we see in the lumen some evidence of the products of the secretory cells. A fair amount of vesiculate material can be seen, together with what is presumably cell debris. These facts are better appreciated by looking at Pl. 4, fig. 8, which is an enlargement from the bottom right corner of Pl. 4, fig. 7. Here the vesicles are clearly seen and are obviously different from the transversely sectioned papillae. They are, indeed, generally smaller than the vesicles observed in the apices of the secretory cells, being about the same size as those in the region of the Golgi structure.

The prickle system, with intervening double cell walls, is well shown in the figure. Also to be observed are the intracellular canals (*ic.c.*) which convert the cytoplasm of cells bordering the lumen into a veritable sieve. These canals tend to disappear in cells away from the lumen; their like has been observed also in the ductal cells of the eccrine gland (Charles, unpublished).

## DISCUSSION

So far as the present structural investigation goes it seems to support what Rothman (1954) calls the 'time-honoured view' of apocrine secretion—that the gland both secretes simply through the membranes of its cells and necrobiotically by a presumed exudation of cell contents after apical breakdown of the membrane. The evidence for simple secretion is the presence of canaliculi between the secretory cells, and the protrusion of the bordering cell surfaces into delicate papillae, so often associated with secretory tissue, whose purpose is presumably to increase surface area. The membranes bordering the canaliculi are invariably intact, and, while it is difficult to understand the function of these canals if the gland secretes only by apical breakdown of the cell, it is easy to understand their function if there is, additionally, secretion through the cell walls. The more robust and numerous papillae of the non-secretory duct, especially at its opening in the hair follicle, may be concerned with altering the composition of the original secretion before its final

exudation as sweat, much as the kidney tubules control the composition of the glomerular filtrate before its passage as urine (Rothman, 1954, p. 190). The relatively large number of mitochondria found in these cells, and the innervation of the duct tend to support such a postulated function. It is most unlikely that the papillae function as cilia to sweep out the secretions because motile cilia, contrasting with the simple papillae, have a complex electron microscopic structure, see Grigg & Hodge (1949), or Fawcett & Porter (1954).

The apocrine function of gland cells is puzzling in so far as no cellular exudate or debris has been observed in the lumen of the secretory part of the gland. This fact is mentioned by Montagna (1956, p. 166), and it would doubtless be instructive to section a dilated tubule, or non-osmidrotic gland (Kuno, 1956, p. 49), both of which are said to contain abundant luminal debris.

There is certainly a loss of apical contents when the membrane breaks down, but the loss seems to consist only of a proportion of the innumerable small vesiculate structures observable in the cell cytoplasm; other granules, mitochondria, and the residuum of the vesicles draw themselves closely about the nucleus and remain in the ruptured cell, whose apical membrane withdraws inwards in response to the slight decrease of volume. The presence of these vesicles in the secretion has been observed only at the orifice of the duct (Pl. 4, fig. 7) where there also occurred a structure which may, as equally it may not, have been a mitochondrial remnant, or a secretory granule. The size of the vesicles suggests that they have become more finely dispersed during their upward passage; their presence in the sweat could well give it its milky appearance. It is possible, however, to question whether the material at the orifice has not come down, rather than up, the duct, and is of foreign origin.

The observations in this paper are confined to one lot of material, and as such lack the advantages to be gained from observing individual and developmental variations. Differences between 'broken-down' and intact cells have not been great. It is unnecessary for cells to elongate greatly before rupture because short plump cells have been observed with ruptured apices; this, together with the apparent absence of severe collapse of apocrinely secreting cells, agrees with Kuno's (1956, p. 49) contention that the variation of size in the cells is inherent, and not due to their being observed at different stages of secretory activity.

It seems quite clear that apocrine secretion by the cells is not an especially well co-ordinated process; indeed it appears rather haphazard, ruptured cells mingling with intact. Because of this any clear eccrine-type secretion from the unruptured cells would always be mixed with milky apocrine secretion, so it would normally be difficult for the apocrine gland to exude a clear sweat. The presence of canaliculi, however, supports the possibility of eccrine-type secretion, and is consistent with the transitional eccrine functioning of the apocrine during infancy (Kuno, 1956, p. 52). Holmgren (1922) and Ota (1950), cited in Montagna (1956, p. 165), postulate eccrine cells in the apocrine gland. Functionally it seems likely that their belief is correct, but structurally different cells have not been observed.

The apical breakdown of the apocrine cells appears to be a slow eroding process, rather than a dramatic one brought about by internal cell pressure. Nevertheless, a sudden contraction of the myoepithelium must surely cause such internal pressures,

and cannot be without effect on the secretion of the cell during the later stages of membrane breakdown. If we except this mechanical effect, however, apocrine secretion would appear to depend on the ageing of the cells, possibly under hormonal control (Hurley & Shelley, 1954), but relatively or completely unresponsive to sudden stimuli. The eccrine-like function may, on the other hand, be more responsive to such stimuli, and it is not inconceivable that under certain conditions an apocrine gland may function very much in the manner of an eccrine.

It is likely that the vesiculate structures which leave the cell when it ruptures are formed in the Golgi apparatus. This apparatus is commonly found in the apocrine cells, and occupies a position just above the nucleus, between it and the cell apex. As shown in Pl. 2, fig. 3 the vesicles in this region are considerably more numerous than in the rest of the cytoplasm, and of a somewhat smaller size.

Speculation on the origin of the other secretory particles is even less certain. They are of a size similar to the mitochondria, and the so-called smooth granules differ from the mitochondria only in the absence of the characteristic cristae. For the rough granules there is some indication of development stages, because they have the appearance of being derived from an originally smooth granule by granulation of the surface into small dense particles, which gradually spreads inwards to the centre. Whether in fact the smooth granule is a development stage of the rough granule, or whether both granules are completely different entities, cannot be said. The nature of the small dense particles formed during granulation is also unknown; they may be lipid and they could equally well be pigment.

It is difficult to understand why secretory granules are so rarely, if at all, found in the lumen. Difficulty is experienced also with the secretory granules in the cells of the eccrine gland (Charles, unpublished) where there is no support at all electron microscopically for Ito's postulate (cited in Kuno, 1956, p. 52) of apocrine secretion by minute protuberances of the inner cells of the secretory part of the gland. In this case there seems no way whatsoever by which the granules can escape, whereas in the apocrine gland there is a way but it does not seem to be used. Whether we should consider these granules as reserve depots of material to be broken down as required and secreted in a soluble (eccrine) or emulsified (apocrine) form, or whether the granules are by-products of cellular metabolism, is something which needs further investigation. The present position of our knowledge is most unsatisfactory, and I feel a more dynamic study of the granules will have to be forthcoming before we can make any appreciable advance.

The mitochondria show a wide variation of shape and size, and while the arrangement of cristae on some of them is relatively conventional, the arrangement on the others is odd. In these, cristae-regions project as cristae-blisters giving the mitochondrium an unusual outline. Since the secretory granules are always smooth in outline this may indicate that they do not arise by transformation of the mitochondria.

The complex infolding of the basal membrane of the secretory cell is presumably designed to increase the surface area in contact with nutrient fluids from the dermis. Intercellular spaces seen between the myoepithelial cell and the base of the secretory cell may be artefacts; they may also arise naturally, because the myoepithelium will almost certainly pucker the secretory layers during contraction. It is of interest

in this connexion that Hurley & Shelley (1954) mention the great difficulty of fixing material with the myoepithelium in the uncontracted state. By means of the intercellular spaces the contraction of the myoepithelium will circulate nutrient fluid obtained from the dermis, but as contractions occur only once in perhaps 24 hr. it is obvious that this cannot be the usual method of nourishing the secretory cells.

## SUMMARY

A description is given of the electron microscopic histology of the apocrine sweat gland. The mechanism of apocrine breakdown, and the difficulties of ascertaining the nature of the secretion, are described. It is considered that the old view that there is eccrine and apocrine secretion by the gland is correct. The papillate nature of the cell surfaces lining the lumen of the duct, together with the relatively rich mitochondrial content of the cells and the innervation of the duct, suggests that the latter exerts some control on the composition or concentration of the sweat.

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## KEY TO ABBREVIATIONS

*c.*, canaliculi; *c.d.*, cell debris; *c.r.*, clear region of cytoplasm; *d.*, dermis; *d.f.*, dark fibrils; *f.*, tonofibrils; *g.*, Golgi apparatus; *gr.*, secretory granule; *i.s.*, intercellular space; *lum.*, lumen; *mit.*, mitochondrium; *my.*, myoepithelium; *n.*, nucleus; *no.*, nucleolus; *p.*, papillae; *p.m.c.*, papillate apical membrane of secretory cell; *pr.*, prickle system; *r.*, reticulin; *r.g.*, rough secretory granule; *r.m.*, ruptured apical membrane; *s.g.*, smooth secretory granule; *s.m.c.*, non-papillate apical membrane of secretory cell; *s.o.*, smaller openings; *s.v.*, secretory vesicles; *v.*, vesiculate material.

## EXPLANATION OF PLATES

### Plate 1

Fig. 1. Part of a transverse section of the secretory tubule. The Golgi apparatus is well seen in one cell. In the right-hand cells the apical membranes have ruptured and a clear region of so-called 'hyalin cytoplasm' has formed underneath. A transverse section through a clear region of the cell apex with ruptured membrane is shown (*t.s.*). × 4500.

Fig. 2. A slightly oblique transverse section at a level near the middle of the secretory cells. The canaliculi and papillae are well shown. × 10500.

### Plate 2

Fig. 3. An enlargement to show the Golgi apparatus and secretory granules of a secretory cell. The particulate nature of the dense peripheral material of the rough granules is seen. × 24500.

Fig. 4. Showing the basal myoepithelial cells in transverse section. The dark fibrils appear as black dots. The moderately electron-dense cementing substance (*c.s.*) is almost absent at (*l.m.*), the limiting membrane between the gland and the dermis. A large intercellular space is shown between a myoepithelial cell and the base of the secretory cell. The basal membrane of the secretory cell is much folded, but its double nature cannot be seen because it is obliquely cut. × 14000.

Fig. 5. A longitudinal section of a secretory cell showing the complex infolding of its basal membrane, which forms the limiting membrane (*l.m.*). The cell is flanked by myoepithelial cells. The dense dots in this and succeeding figures are particles of gold sol about 160 A.U. diameter, used as an aid to focusing (Flewett & Tymms, 1956). × 33000.

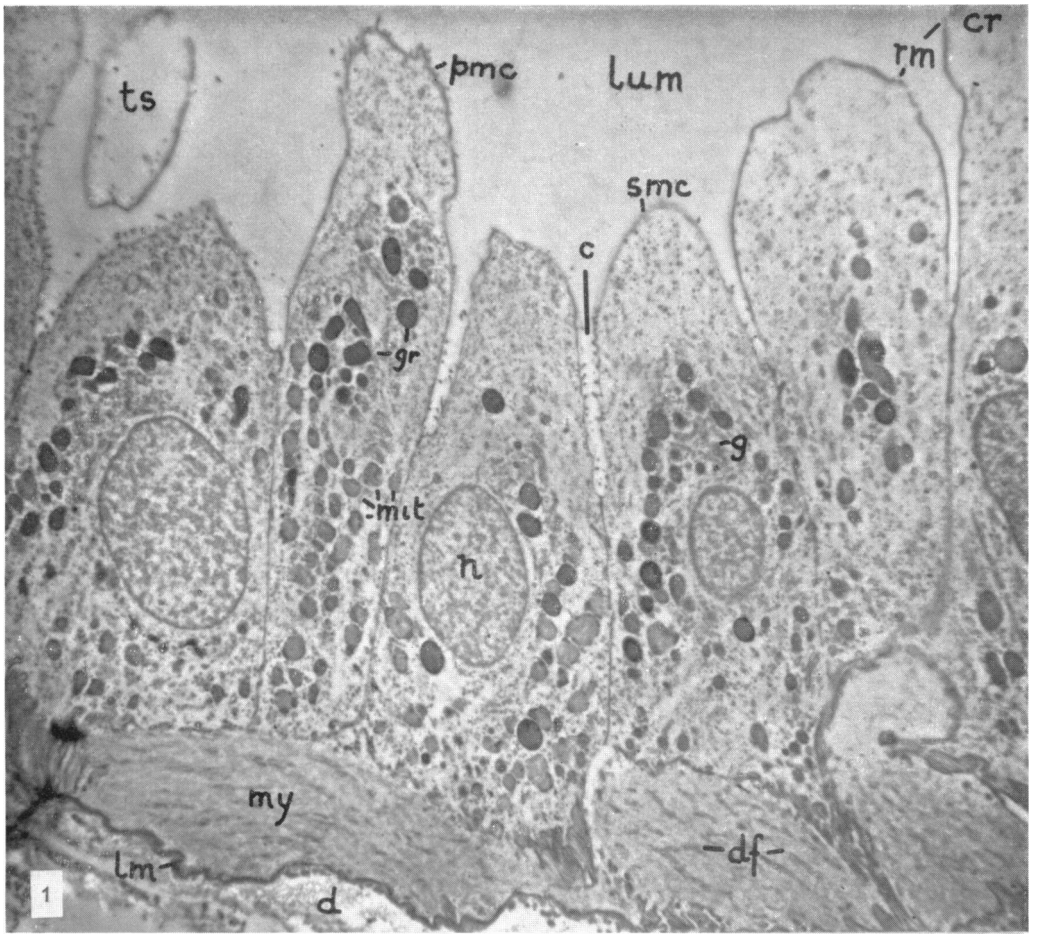
### Plate 3

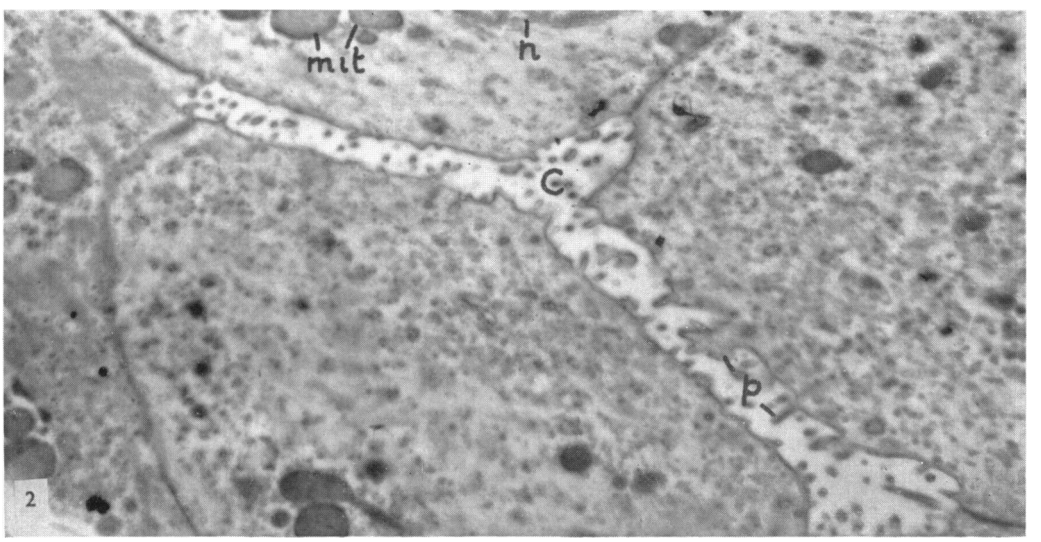
Fig. 6. A section through the duct wall. The upper cells line the lumen and are papillate, while the lower cells are in contact with the dermis. An unmedullated nerve fibre is shown (*nmn.*). In one, possibly three, cells the dense material seen attached, or near, to the nuclear membrane is perhaps sex chromatin (Moore, Graham & Barr, 1953). × 10000.

### Plate 4

Fig. 7. The opening of the apocrine duct in the hair follicle. The opening is very irregular and can only be partly shown in this figure, and there is some evidence of the secretory products of the gland. × 4500.

Fig. 8. Enlarged view of part of the region in the lower right corner of the previous figure. The vesiculate material is now more clearly seen, and is obviously different from the transversely sectioned papillae. Intracellular canals (*ic.c.*) give a sieve-like appearance to the cytoplasm of the cells immediately next to the lumen. Exceptionally numerous prickles with intervening cell walls (*c.w.*) are seen. × 15500.

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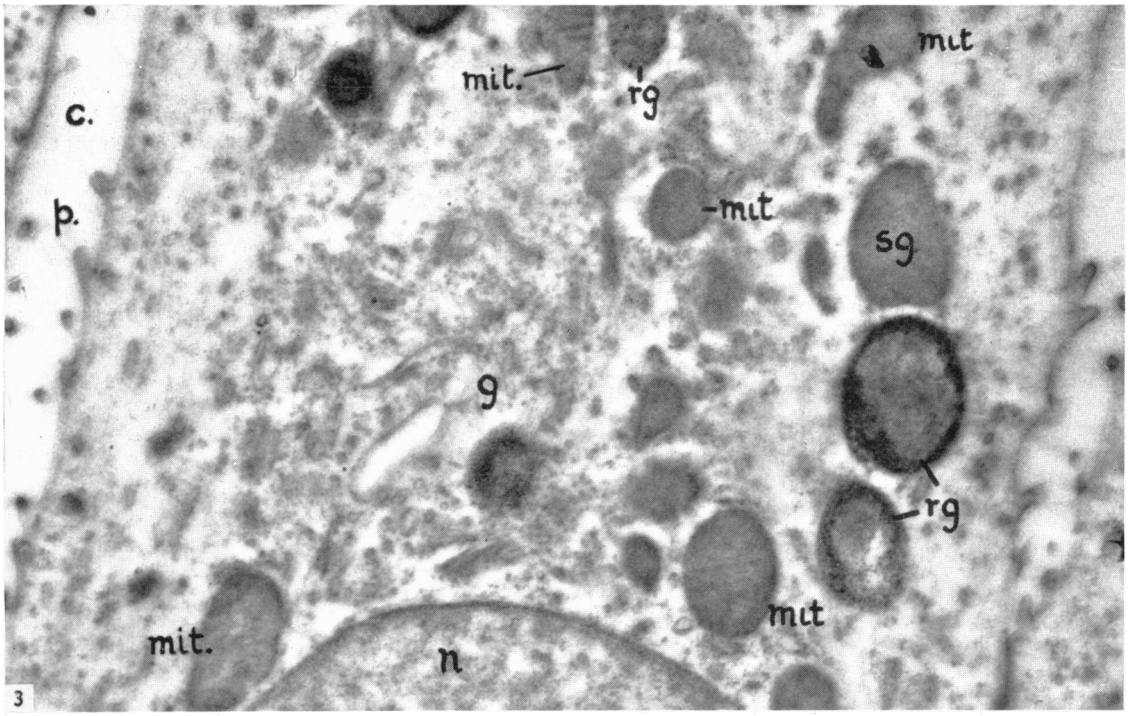


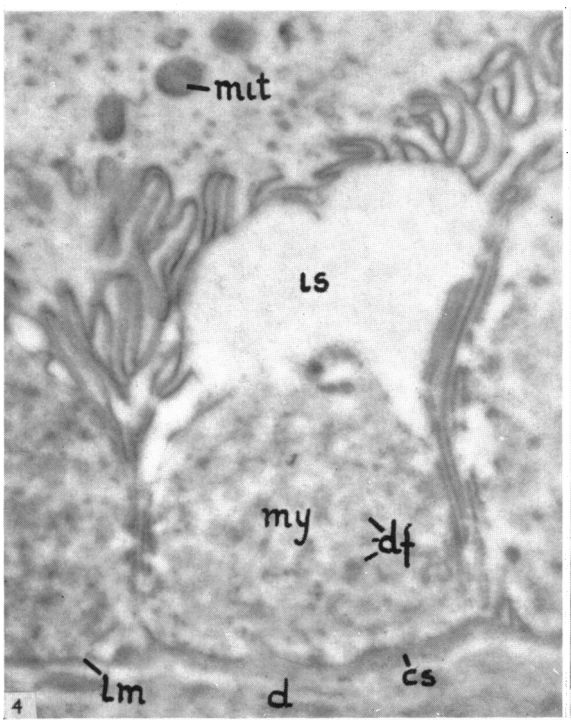


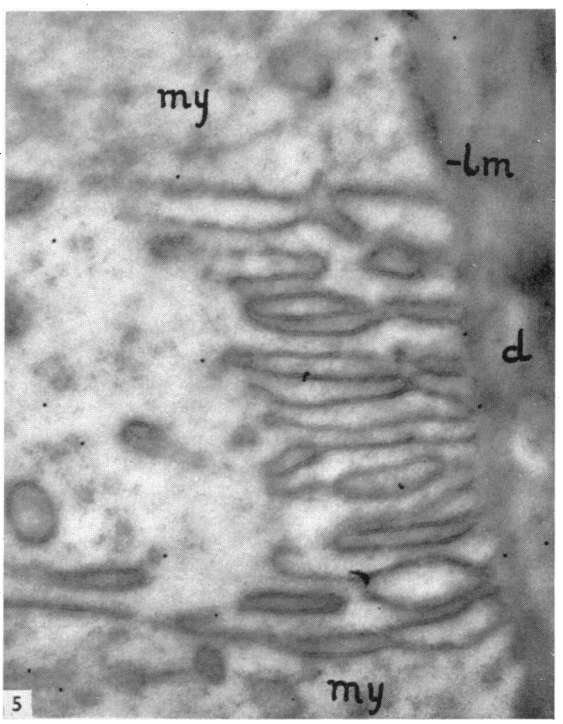


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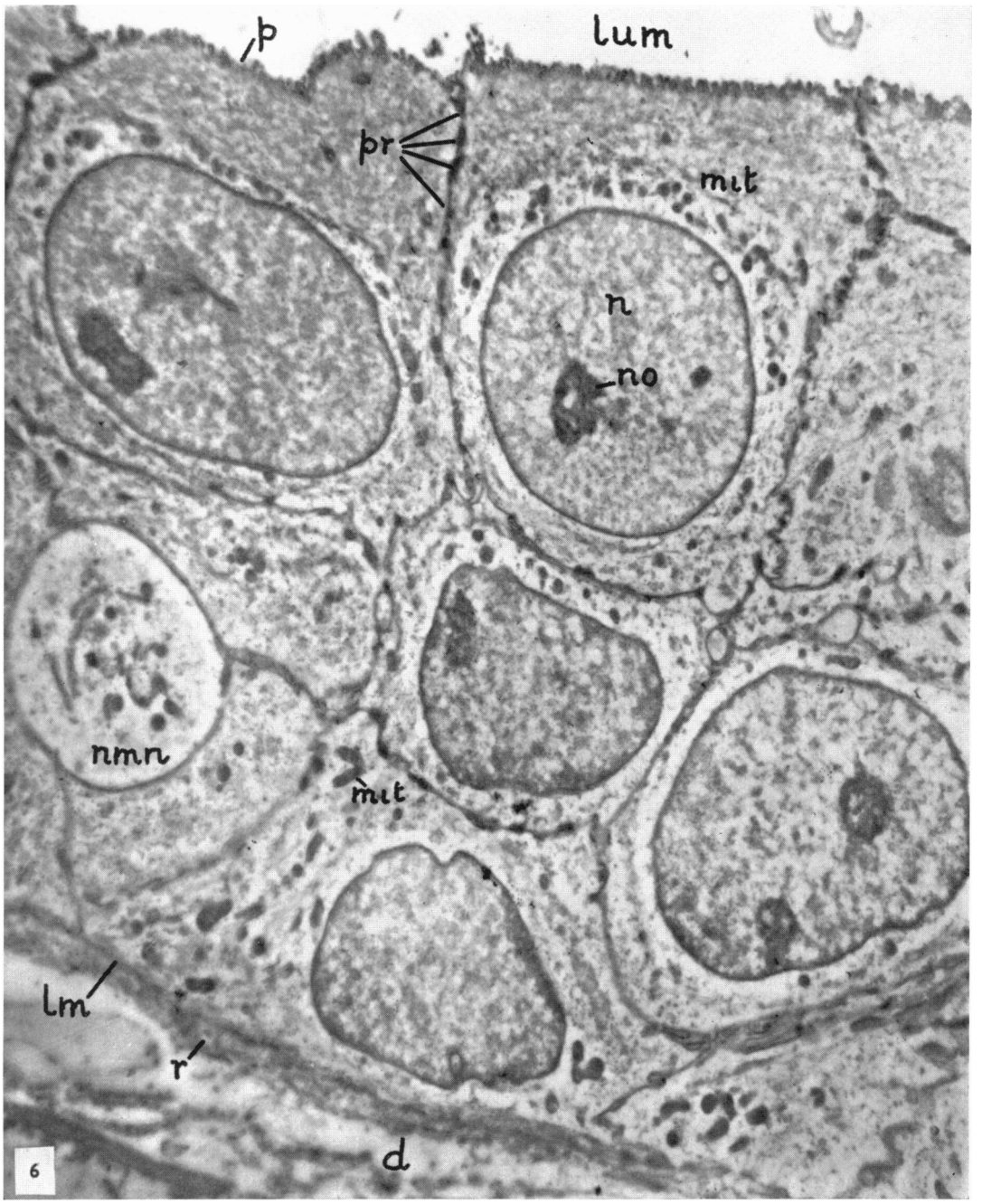
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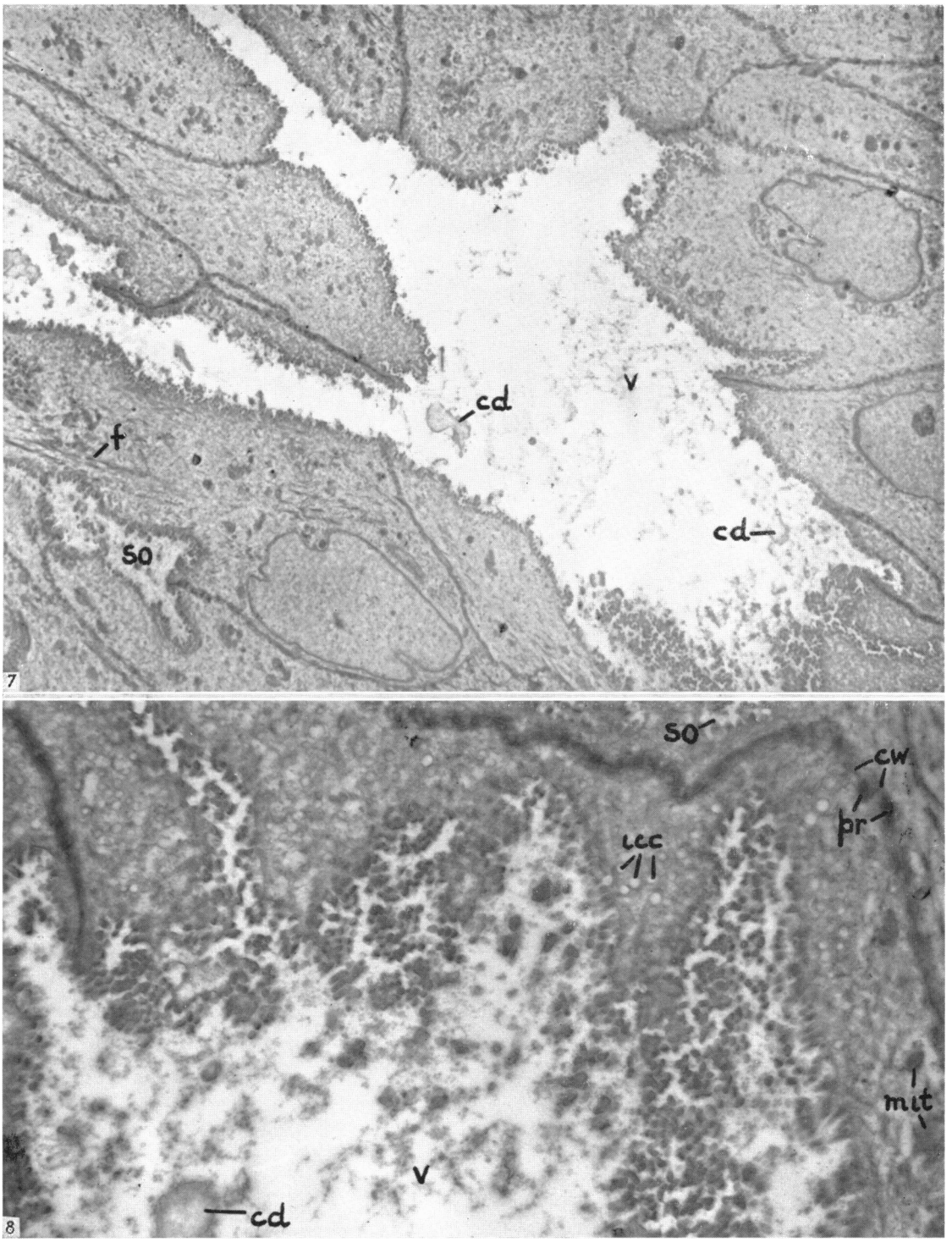


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