Arch. Soc. Amer. Oftal. Optom. (1968) - 6 - 393

DATA ON THE ULTRASTRUCTURE OF MÜLLER'S CELLS OF THE RETINA *

BY

MAGDA RADNOT, M. D. - B. LOVAS, M. D.

Budapest, Hungría

The main part of the glial tissue of the retina is formed by Müller's cells. In different extensions, they can be found in all layers of the retina, from the outer limiting membrane to the inner one. On the base of light microscopic investigations it had been assumed that both limiting membranes are composed of these cells. From the followings it can be seen that there is essentially no outer limiting membrane and that the inner limiting membrane is not formed of Müller's cells. On the basis of *Yamada, Sjöestrand, Missotten, Fine* and *Zimmermann, Inomata's* investigations as well as those of *Radnót* and *Lovas,* the importance of Müller's cells is far greater than could be assumed according to histological pictures.

The present investigations were carried out on rabbit's, rhesus' and human eyes. The material was embedded into Araldit, following fixation with glutaraldehyde and osmium; section was carried out on the Porter-Blum-ultramicrotome; micrographes were made with a Hitachi HU-10 electron microscope at 75 kv.

The first picture originates of a human retina, so that the cells of the external nuclear layer, the nucleus of the photoreceptors, its perikaryons as well as the inner segments are seen. The intercellular space of the photoreceptors is filled by Müller's cells, well discernible in the form of dark lines in this preparation fixed in osmium. On the upper part of the picture, in accordance to the inner segments of the photereptors densities are observed at the same height in the photoreceptors as well as in Müller's cells. These densities, arranged on the same level, in accordance to which vivid staining can be observed in the light microscopic preparations, seem to form the outer limiting membrane. As

*** First Eye Clinic and Laboratory of Electron Microscopic University Medical School Budapest.**

seen, here the photoreceptors are closely connected to each other. Microvilli are protruding from the Müller's cells between the inner segments. This microvilliform structure can well be observed on Fig. 2, where they display a longer running. On the bottom of the said figure, part of the cell-nucleus of the photoreceptors is seen, whereas in the inner segments several organits as ribosomas, endoplasmic reticulum and mitochondria are visible.

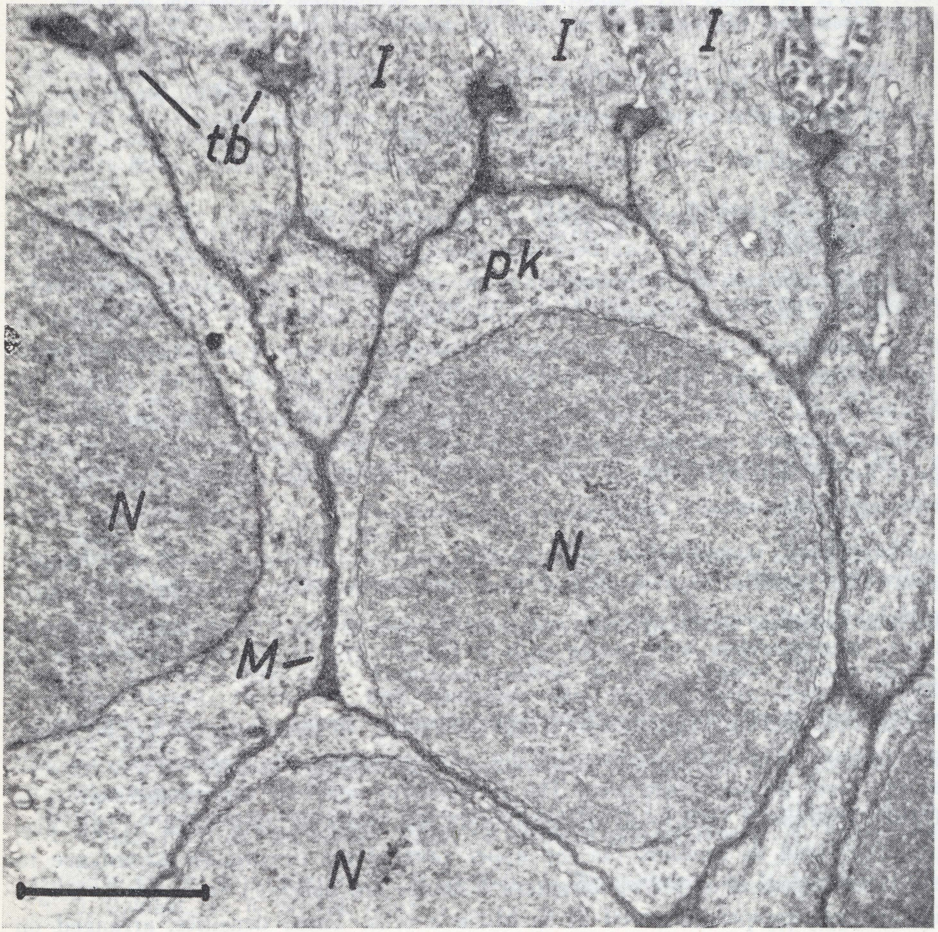

Fig. 1

Human retina. Emb. Araldit. 33.000 X.

I = inner segment, tb = terminal-bar, pk = perikaryon, N = nucleus of the photoreceptors, M = intercellular layer of the Müller's cells.

The centrosome of Müller's cells is observed in the form of diplosoma underneath the above described densities; as seen on Fig. 3, the cross section of the tubules of 9 x 3, is well distinguishable; underneath.

Müller's cells can also be found between the synapses of the photoreceptors. Fig. 4 illustrates a peduncle and several spherules of a human retina. In one of the rod synapses a crystalliform inclusion is seen. This will be described in detail elsewhere /*Lovas* and *Radnót; Radnót, Lovas* and *Trux*/. Between the

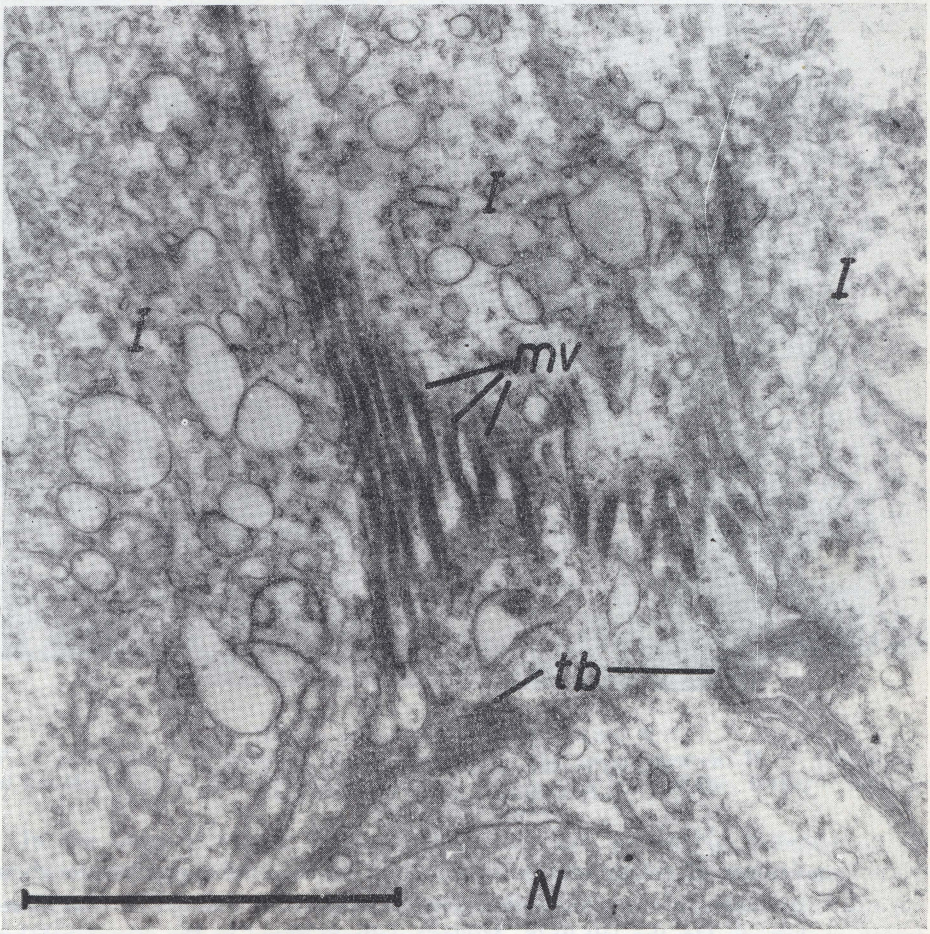

Fig. 2

Human retina. Emb. Araldit. 68.000 X.
I = inner segment, N = nucleus of the photoreceptors, mv = microvilli, tb = terminal bar.

seen, here the photoreceptors are closely connected to each other. Microvilli are protruding from the Müller's cells between the inner segments. This microvilliform structure can well be observed on Fig. 2, where they display a longer running. On the bottom of the said figure, part of the cell-nucleus of the photoreceptors is seen, whereas in the inner segments several organits as ribosomas, endoplasmic reticulum and mitochondria are visible.

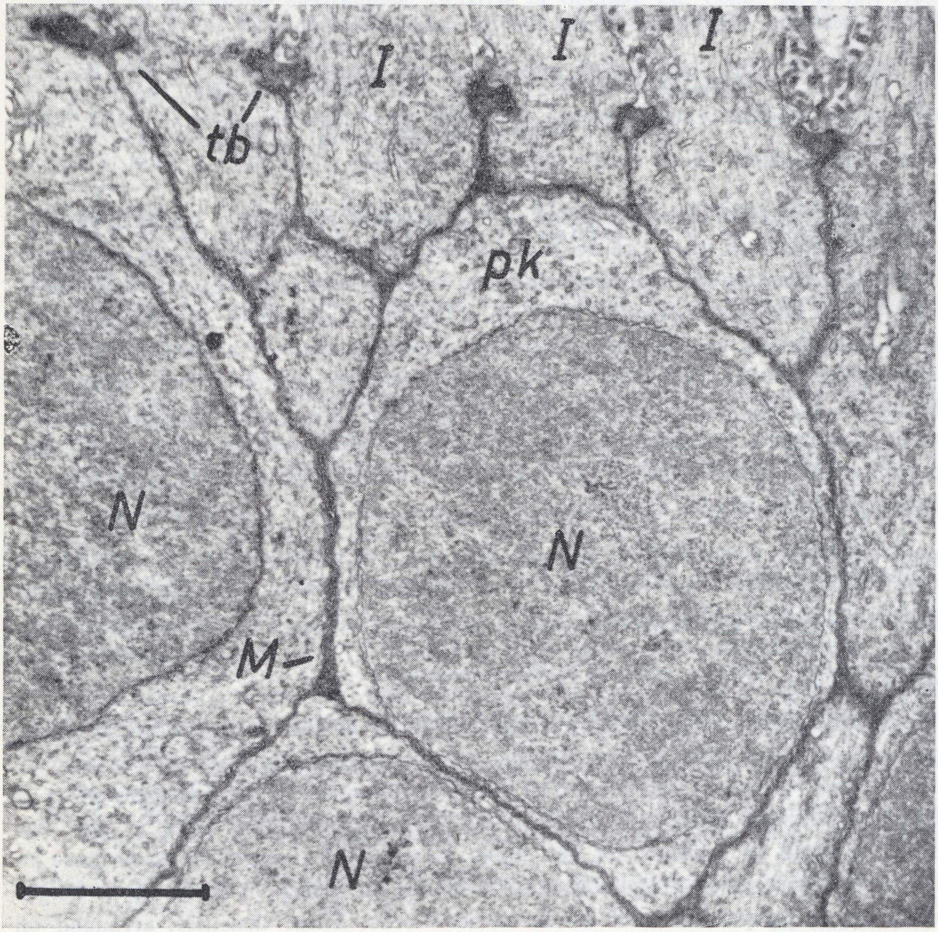

Fig. 1
Human retina. Emb. Araldit. 33.000 X.
I = inner segment, tb = terminal-bar, pk = perikaryon, N = nucleus of the photoreceptors, M = intercellular layer of the Müller's cells.

The centrosome of Müller's cells is observed in the form of diplosoma underneath the above described densities; as seen on Fig. 3, the cross section of the tubules of 9 x 3, is well distinguishable; underneath.

Müller's cells can also be found between the synapses of the photoreceptors. Fig. 4 illustrates a peduncle and several spherules of a human retina. In one of the rod synapses a crystalliform inclusion is seen. This will be described in detail elsewhere /*Lovas* and *Radnót; Radnót, Lovas* and *Trux*/. Between the

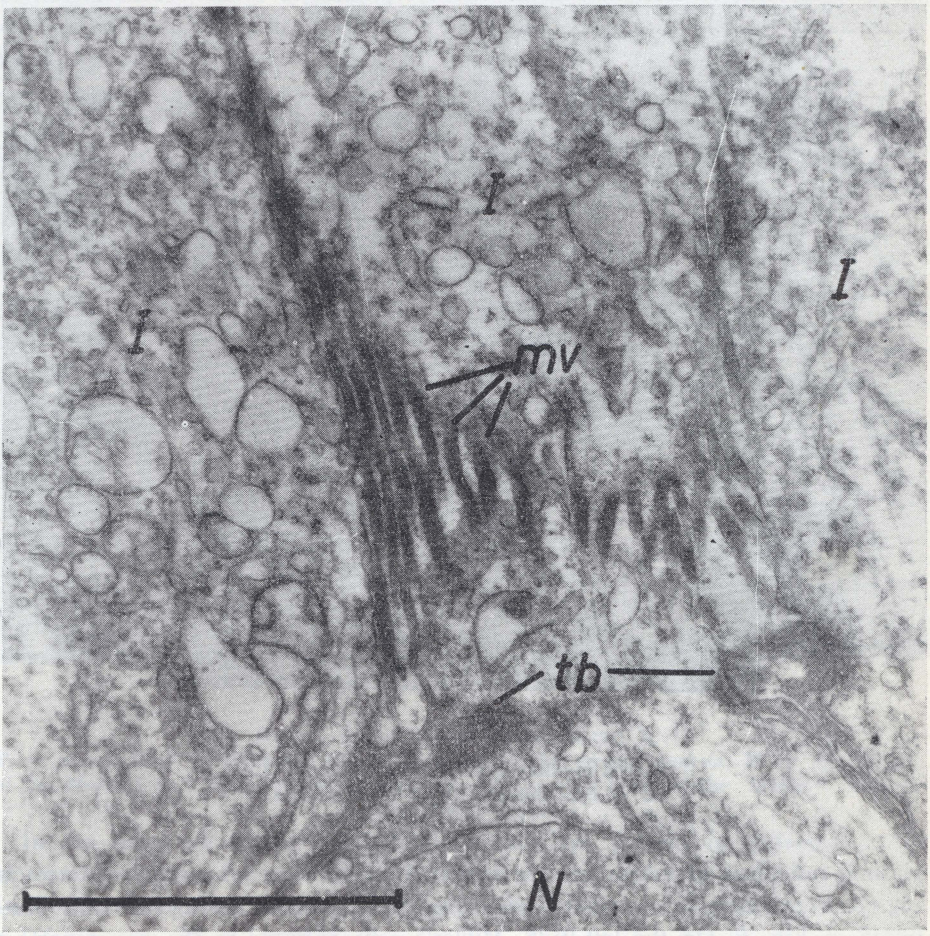

Fig. 2

Human retina. Emb. Araldit. 68.000 X.
I = inner segment, N = nucleus of the photoreceptors, mv = microvilli, tb = terminal bar.

rod and cone synapses Müller's cells are situated. In the magnified micrograph in intercellular space, four cytomembranes can be observed. The synaptic end of the cone, the peduncle, is filled with synaptic vesicles and the dendrites of the second neuron are penetrating in it in the form of several triads. Above the triads, the synaptic lamellae are well discernible.

The nucleus of Müller's cells is found in the inner nuclear layer. They are easily recognizable being mostly polygonal and also darker than the nuclei of the rest of cells, as seen in Fig. 5. The cytoplasme of Müller's cells is full of endoplasmic reticulum, of smooth surface and only a smaller quantity of endo-

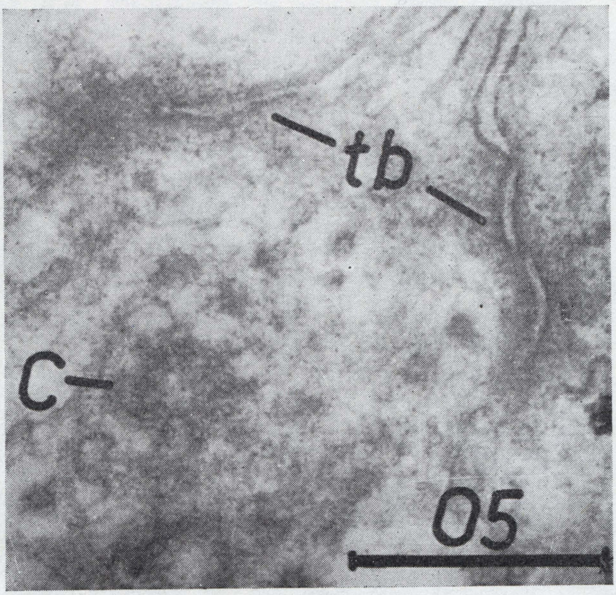

Fig. 3

Rhesus monkey retina. Aradit. 112.000 X.
C = cytocentrum, tb = terminal bar.

plasmic reticulum of rough surface is found in it, as can be seen scattered in Fig. 5. Frequently, this ergastoplasme displays a parallel arrangement, as illustrated in Fig. 6. On the left side, Müller's cells is seen, in the upper part, a weakly developed Golgi apparatus, on the bottom, the reticulum of rough surface. On the right and upper side, the nuclear parts og bipolar cells are present.

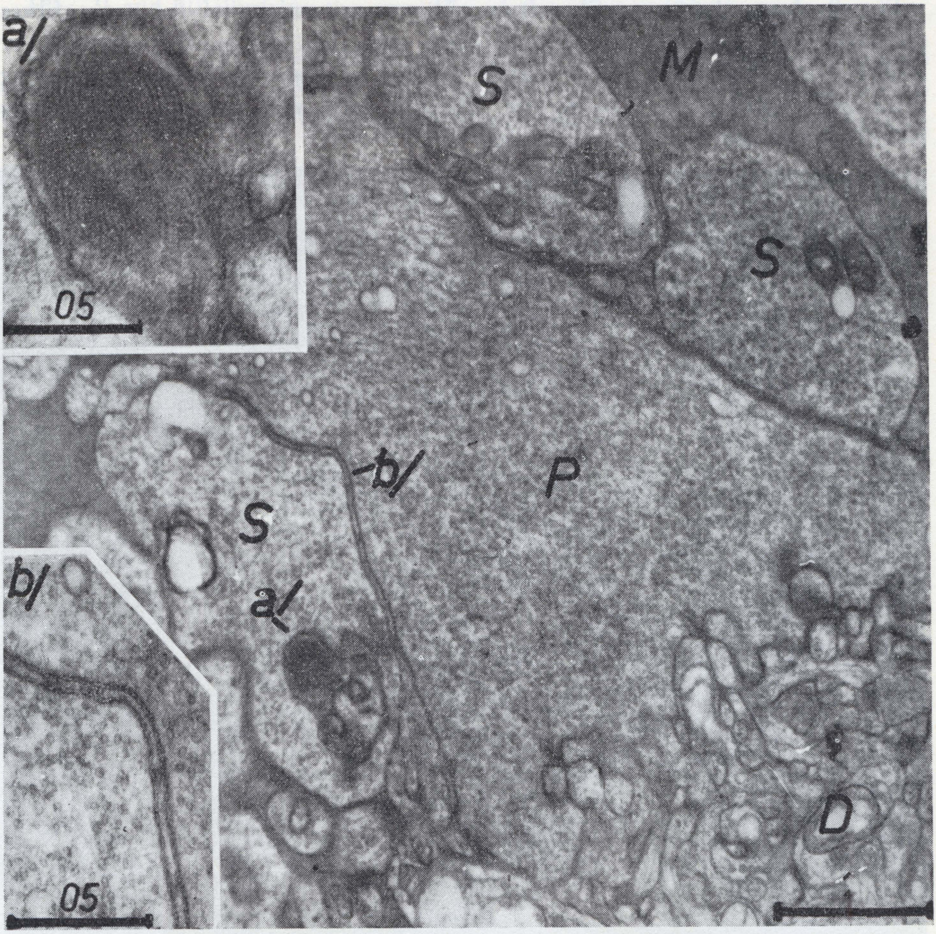

Fig. 4

Human retina. Emb. Araldit. 28.000 X.
P = peduncle, S = spherule, D = dendrites of the second neuron, M = cytoplasma of the Müller's cell, a/=crystallike inclusion, b/2 = thin layer of the Müller's cells in intercellular space.

In the inner plexiform layer, Müller's cells are present in different extensions according to the species. Its extension in the rabbit is much larger than in the rhesus monkey or in man. The ganglion cells are generally also separated from each other by Müller's cells. Fig. 7 illustrates the ganglion cells of the rabbit, with several organits in it: ribosomes, Golgi apparatus, endoplasmic reticulum, etc. On the two sides it surrounded by Müller's cells displaying a smooth endoplasmic reticulum and glycogen granules.

Fig. 8 shows the nerve fibre layer. The cross sections of the nerve fibres are seen. They touch each other at some sites, but are mostly separated by Müller's cells. The nerve fibres contain tubules in even distribution and among them mitochondria are also to see. Müller's cells show smooth endoplasmic reticulum and many glycogen granules.

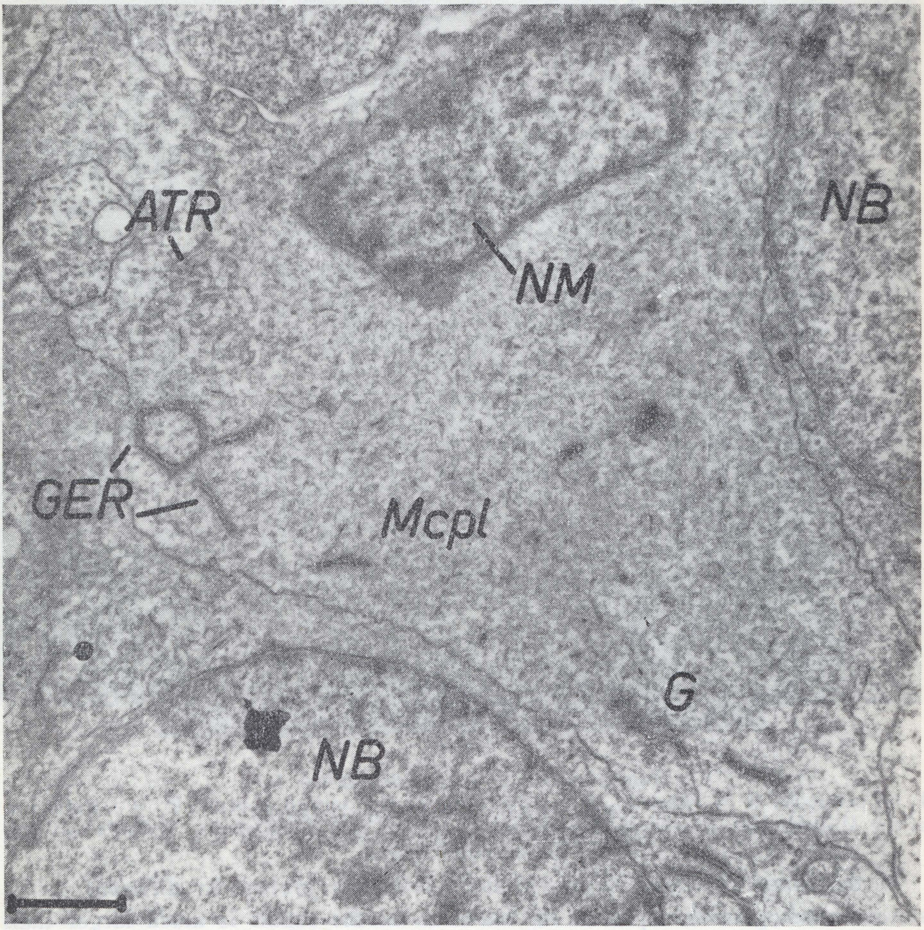

Fig. 5

Rabbit retina. Emb. Araldit. 20.400 X.
NM = nucleus of the Müller's cells, NB = nucleus of the bipolar cells, Mcpl = cytoplasma of the Müller's cells, G = Golgi apparatus, ATR = agranular tubular reticulum, GER = granular endoplasmic reticulum.

Figs. 9 and 10 illustrate the structure of the inner limiting membrane.

On Fig. 9 the column-like ending of Müller's cells is seen with many smooth endoplasmic reticulum. Its cell membrane of undulated running terminates on the surface of the inner limiting membrane, best seen on Fig. 10, originating

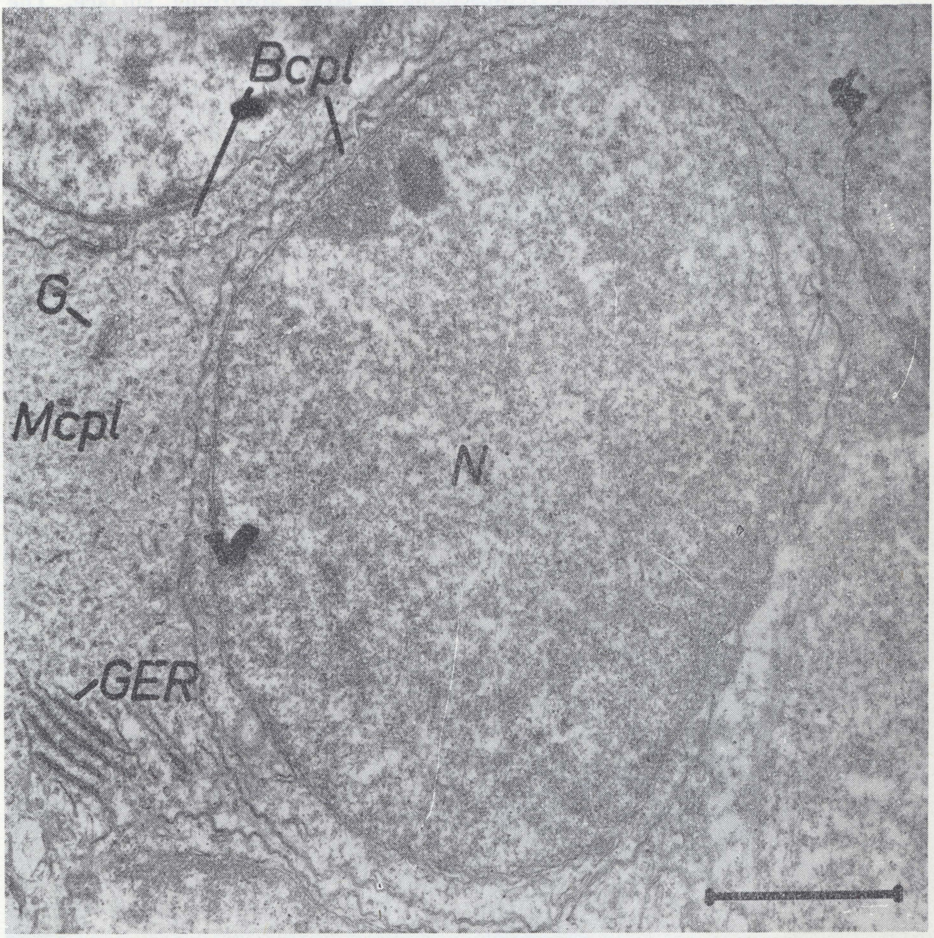

Fig. 6

Rabbit retina. Emb. Araldit. 35.000 X.

N = nucleus of the bipolar cells, G = Golgi apparatus, GER = granular endoplasmic reticulum, Mcpl = cytoplasma of the Müller's cells, Bcpl = cytoplasma of the bipolar cells.

of a human retina fixed in osmium. The inner limiting membrane is of vitrous character and of finer structure in which Müller's cells are so-to-say anchored.

Müller's cells terminate with an extensive villiform system within the inner segments of the photoreceptors, representing a large absorbing surface. The centrioles of Müller's cells is located beneath the densities forming the so-called

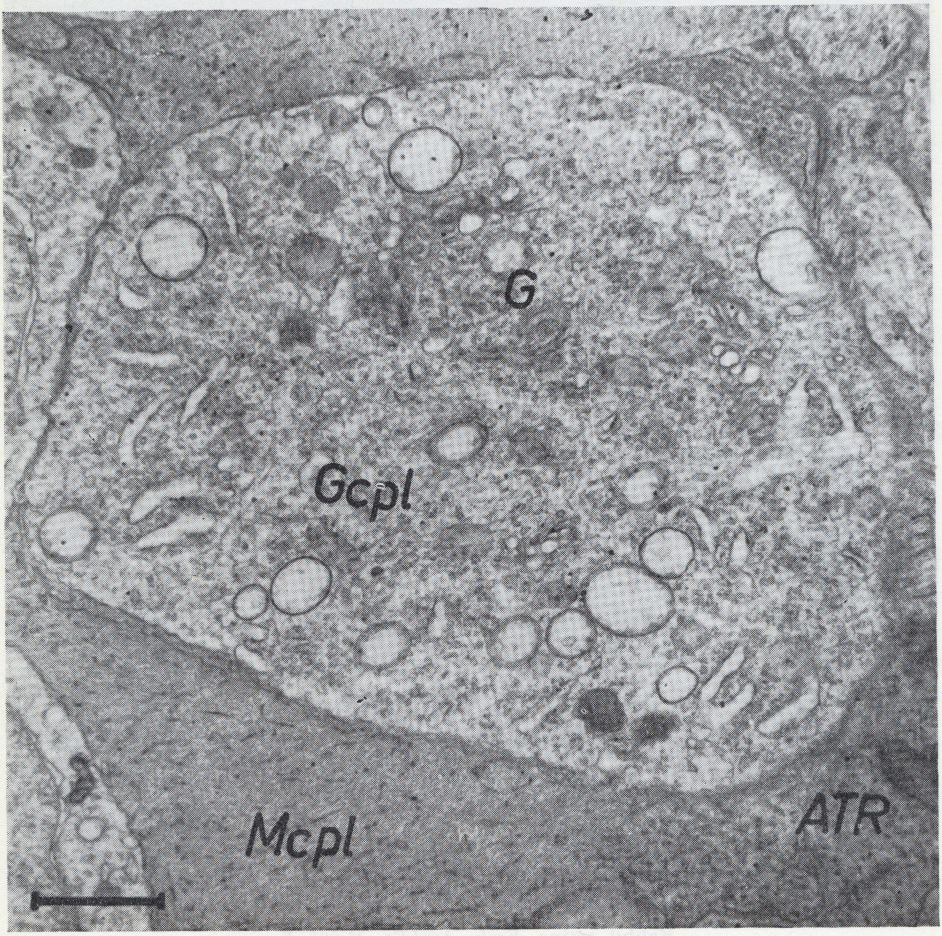

Fig. 7

Rabbit retina. Araldit. 24.000 X.
Gcpl = cytoplasm of the ganglion cells, G = Golgi apparatus, ATR = agranular tubular reticulum, Mcpl = cytoplasm of the Müller's cells.

outer limiting membrane. At this same site are present the mitochondria of these cells. The entire cytoplasm is full of endoplasmic reticulum of smooth surface lending these cells a sponge-like structure. The weakly developed Golgi apparatus is located in the inner nuclear layer and the endoplasmic reticulum

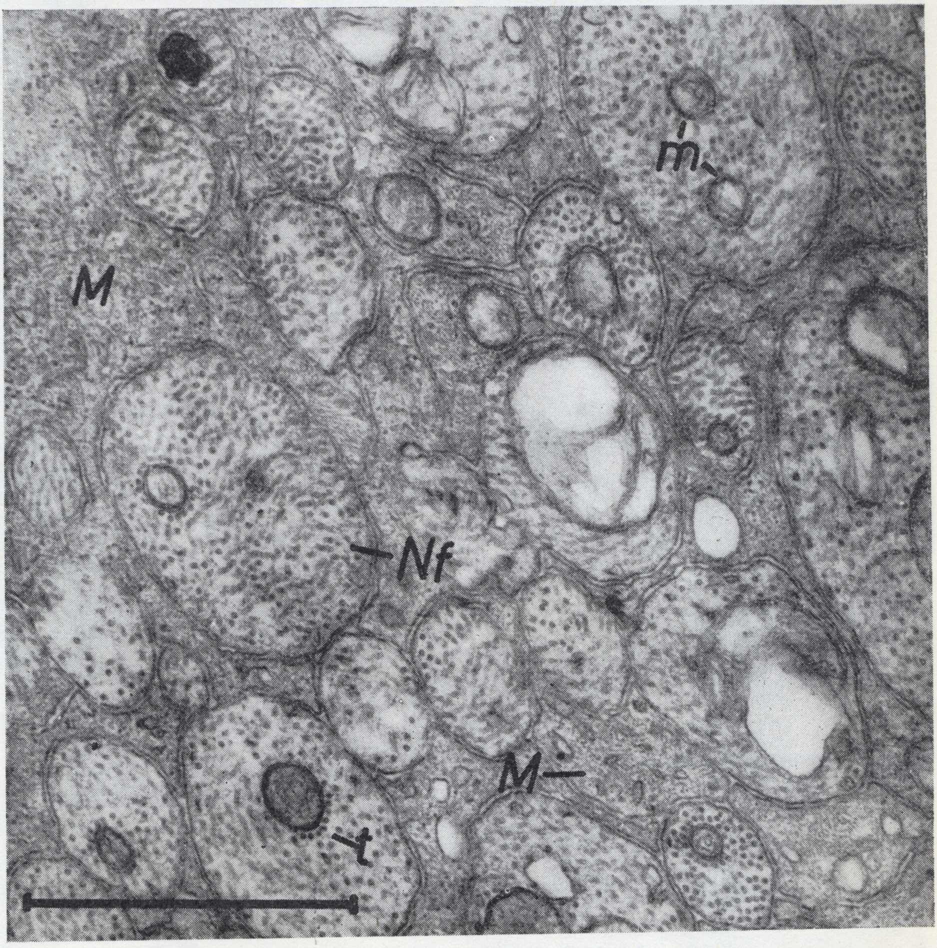

Fig. 8

Rhesus monkey retina. Emb. Araldit. 59.000 X.
Nf = nerve fiber, M = Müller's cell, t = tubules, m = mitochondria.

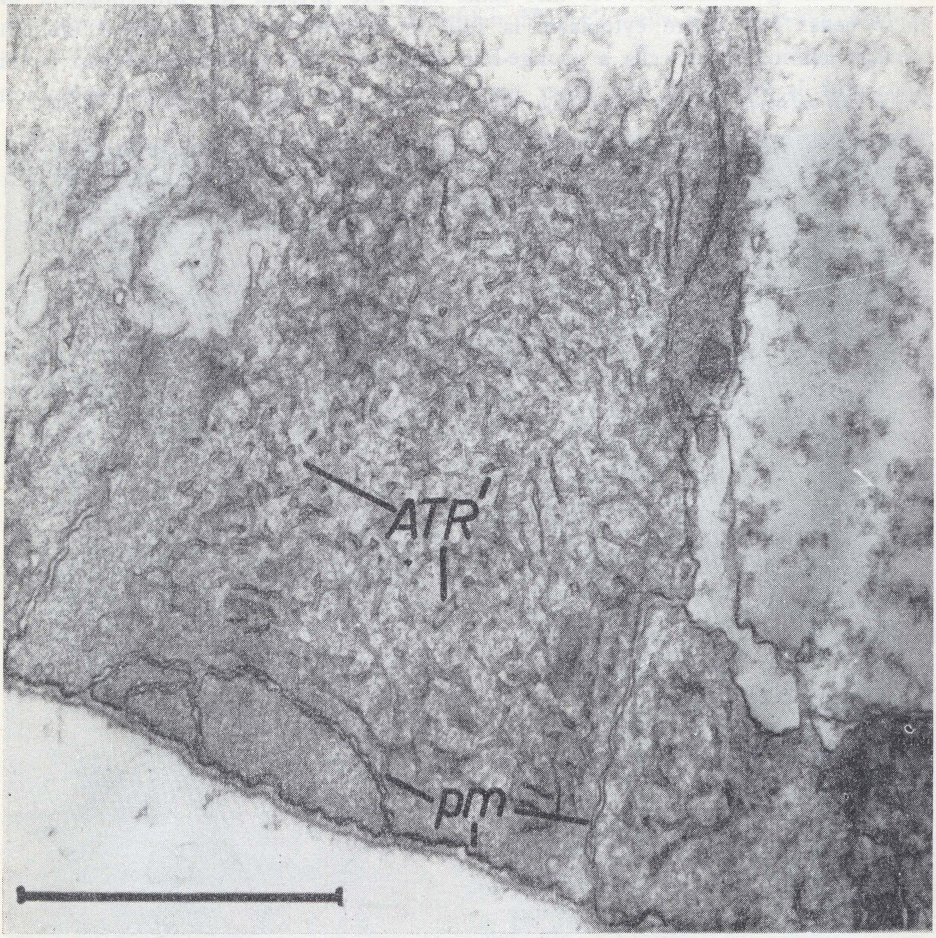

Fig. 9

Rabbit retina. Emb. Araldit. 58.000 X.
ATR = agranular tubular reticulum, pm = plasma membran.

of rough surface forms ducts in small number. The number of ribosomas is also small. Müller's cells, as seen in the above figures, take part to different degrees in the formation of every layer of the retina. They divide the different nervous elements from each other. Due to their extension, they form essentially the largest part of the retinal mass. In can be read in every text book that they represent the main supporting element of the retina. Electron microscopy, however, reveals that they have other most important functions, too. This is especially conspicuous in the case of pathological cases. The fact that Müller's cells play a role in the supply of the first neuron is already obvious under physiological conditions; after all, there are no vessels present in the area of the first neuron. It is, however, assumed that they have a role also in the supply of the two other neurons, Müller's cells being present everywhere around the vessels. Several worers have already called attention to great quantities of glycogen in Müller's cells and enzymatic activity was also demonstrated.

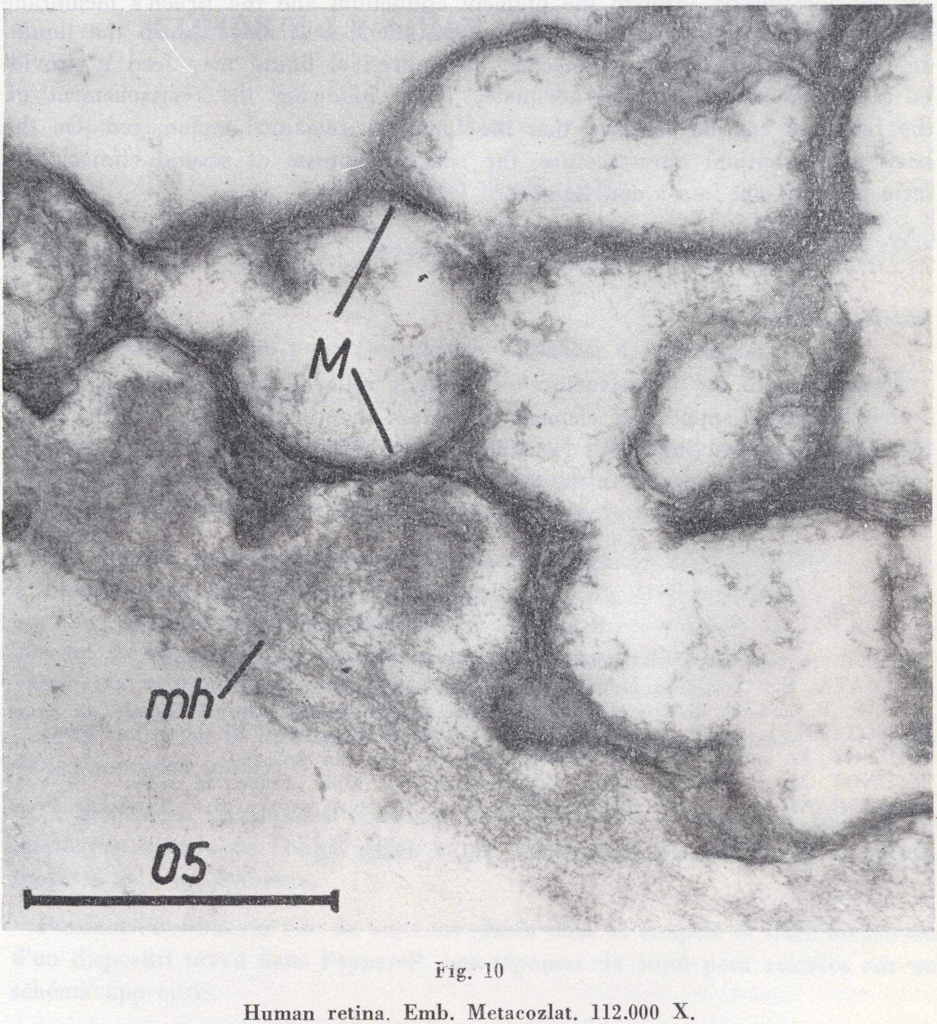

Fig. 10

Human retina. Emb. Metacozlat. 112.000 X.
M = Müller's cell, mh = membrana hyaloidea.

There exist several diseases in which the retina detaches itself for some longer period and following subsidence of the disease, i.e. after the retina attaches itself back to the base, the retinal functions become restored. This phenomenon could only with difficulties be explained on the base of light microscopic investigations. Electron microscopy gave, however, a satisfactory interpretation.

The substance feeding the first neuron gets into the subretinal space from the choriocapillary, through the pigment epithelium and the Bruch's membrane and from here the villiform structure of Müller's cells may absorb the liquid. In case the retina becomes detached the subretinal liquid may feed it provided its composition remains adequate. Thus, following the reattachement of the retina, it can be assumed that the functions remained undamaged. On the basis of the retinal ultrastructure, the pathomechanism of several clinical patterns are thus put into a new light.

Summary.

Description of the ultrastructure of Müller's cells of the retina. Müller's cell is not simply a supporting element but, from the point of view of the nerve element, has a most important function. Besides supplying the first neuron, Müller's cells may play a role in the supplying the two other neurons.

REFERENCES

FINE, B. S., and L. E. ZIMMERMANN: Invest. Opht. 1. 304-326, 1962.
INOMATA, H.: Acta Soc. Opht. Jap. 69, 2133-2143, 1965.
LOVAS, B. and M. RADNOT: Morphológiai és Igazságügyi Orvosi Szemle, in press.
MISSOTTEN, L.: Bull. Soc. Opht. Belg., 136, 3, 1964.
RADNOT, M. and B. LOVAS: Graefes Arch. f. Opht., in press.
RADNOT, M., B. LOVAS and E. TRUX: Bull. Soc. Opht. Franç., in press.
SJOESTRAND, F.: in G. K. SMELSER: The Structure of the Eye. Academic Press, New York, 1961.
YAMADA, E.: XIX. Conc. Opht. Delhi, Vol. I, 1962.