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The Trabecular Meshwork of a Non-Glaucomatous Eye With the Exfoliation Syndrome

Electronmicroscopic Study

Olaf Benedikt and Paul Roll
Univ.-Eye Clinic of Graz (Head: Prof. Dr. H. Hofmann), Graz, Austria

Summary. The trabecular meshwork of a non-glaucomatous eye with the exfoliation syndrome was investigated. The exfoliation material was found mainly in massive deposits in the subendothelial region of the outer and inner wall of Schlemm's canal, in the cribriform area and the uveal meshwork. The other alterations of the trabeculum corneosclerale corresponded to the age of the patient. The concept that the accumulation of exfoliation material is an important pathogenetic factor in the development of glaucoma was not confirmed by this study.

Key words: Exfoliation syndrome – Non-glaucomatous eye – Trabecular meshwork – Ultrastructure.

Introduction

The most important clinical feature of so-called pseudoexfoliation of the lens, which is characterized by the widespread appearence of a degenerative fibrillar substance in the anterior region of the eye and is by no means confined to the lens, is the eventual development of an open angle glaucoma. This relationship was recognized by the discoverers of the condition (Lindberg, 1917; Vogt, 1925). From data in the literature the percentage of the incidence of glaucoma in pseudoexfoliation varies from 40 to 97% (Fellner and Benedikt, 1973).

In spite of many clinical and some histological investigations the exact relation between the two conditions is not yet clear. Some observers (Vogt, 1932; Giffort, 1957; Ringvold and Vegge, 1971) consider that the raised tension is due to obstruction of the trabecular meshwork with exfoliation material, others (Malling, 1923; Sunde, 1956; Leydhecker, 1973) suppose that it is more probable that the same degenerative process which causes the pseudoexfoliation, is itself responsible for the development of glaucoma.

Send offprint requests to: Doz. Dr. Olaf Benedikt, University Eye Clinic, Auenbruggerplatz 4, A-8036 Graz, Austria

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Electron microscopic investigation of non-glaucomatous eyes with pseudoexfoliation might be useful in clearing up this problem. To date only one paper (Ringvold and Vegge, 1971) concerning this subject has been published, and we therefore add our own case report.

Materials and Methods

In this study we investigated the trabecular tissue of an 82 year old female patient whose left eye was enucleated because she suffered from a malignant melanoma of the choroid. Before enucleation a typical trabeculectomy was done (Benedikt, 1975).

Preoperative examination had demonstrated the existence of the so-called exfoliation syndrome of both eyes. The optic discs showed a physiologically symmetrical cupping with a cup/disc ratio of 0,3. There were no field defects. The intraocular pressure of both eyes varied between 10 and 14 mm/Hg. The value for outflow facility measured tonographically was 0,17 in the right eye and 0,16 in the left eye.

Fixation of the specimen with 4% glutaraldehyde was done immediately after trabeculectomy. After postfixation with 1% osmium tetroxide and dehydration through graded alcohol the tissue was embedded in Epon 812. Ultrathin sections were cut with a Reichert's Ultramikrotom OmU_2 and were double stained with uranyl acetate and lead citrate. Examination was performed with a Zeiss electron microscope EM 9S-2.

Electronmicroscopic Results

Investigation of the specimen obtained by trabeculectomy showed the following characteristic alterations.

Schlemm's canal appeared normal in all sections and was lined by a continuous endothelium on both sides (Fig. 1). The endothelium of the inner wall was marked by an undulating structure and the endothelial cells contained well developed nuclei, a moderate amount of mitochondria, golgi apparatus, rough surfaced endoplasmatic reticulum, ribonucleic acid granules, glycogen, multivesicular bodies and many pinocytotic vesicles. Another important finding on the inner wall endothelium was the presence of numerous giant vacuoles. We observed them in any part of the cell, either free in the cytoplasm or in connection with the nucleus (Figs. 1, 2). These giant vacuoles, which were generally electron clear, had a variable diameter from 3 μ to 10 μ. They were often bound by a smooth unit membrane. Several of these structures were superimposed, some of them possessed basal as well as apical openings and formed communications between the intercellular spaces of the trabecular meshwork on the one side and Schlemm's canal on the other. In addition to empty giant vacuoles we found a few containing a large amount of characteristic fibrillar material (Fig. 2). This material (exfoliation material) consisted of rough surfaced fibrils which were straight or slightly bent and had often split ends (Fig. 3). Their length reached up to 1 μ and their diameter was about 35 nm. These fibrils appeared in irregular aggregates and disordered bundles and were often intermingled with a finely fibrillar component. Cross-sections showed a tubular character (Fig. 3, arrow).

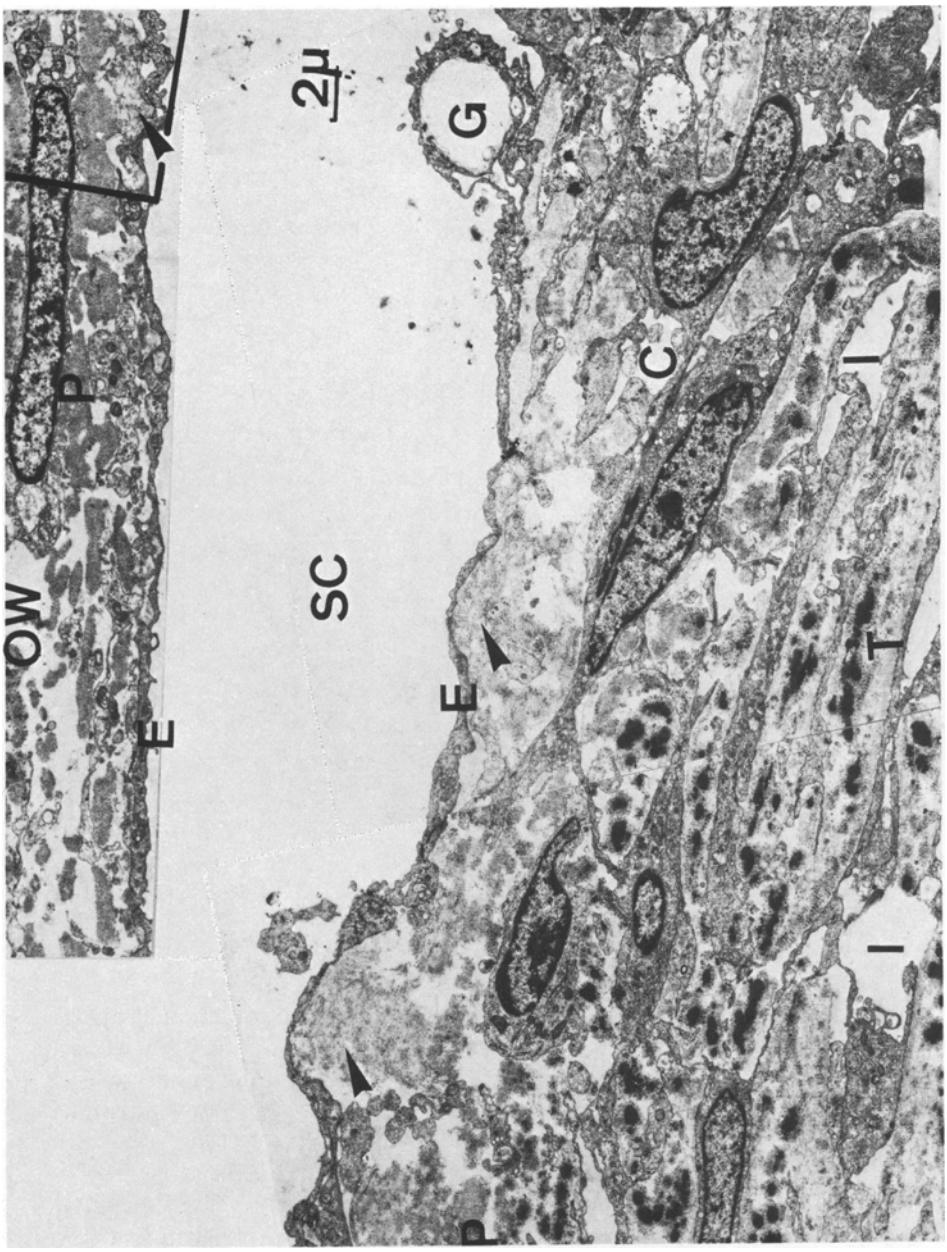

Fig. 1. Partial micrograph of Schlemm's canal (*SC*), cribriform region (*C*), and the outer wall of Schlemm's canal (*OW*). Note the subendothelial deposits of exfoliation material in the inner and outer wall (arrows). *P* – osmiophilic homogeneous plaques, *G* – giant vacuoles within the endothelium of the inner wall, *T* – trabecular beam, *I* – intertrabecular space. ×3,600

Most of these massive fibrillar accumulations of exfoliation material not bound by giant vacuoles were adjacent to the inner wall endothelium of Schlemm's canal and formed protrusions into the lumen. In this region the endothelium was extremly thin, but we found some with normal thickness in spite of very massive fibrillar deposits. These fibrils appeared either alone or

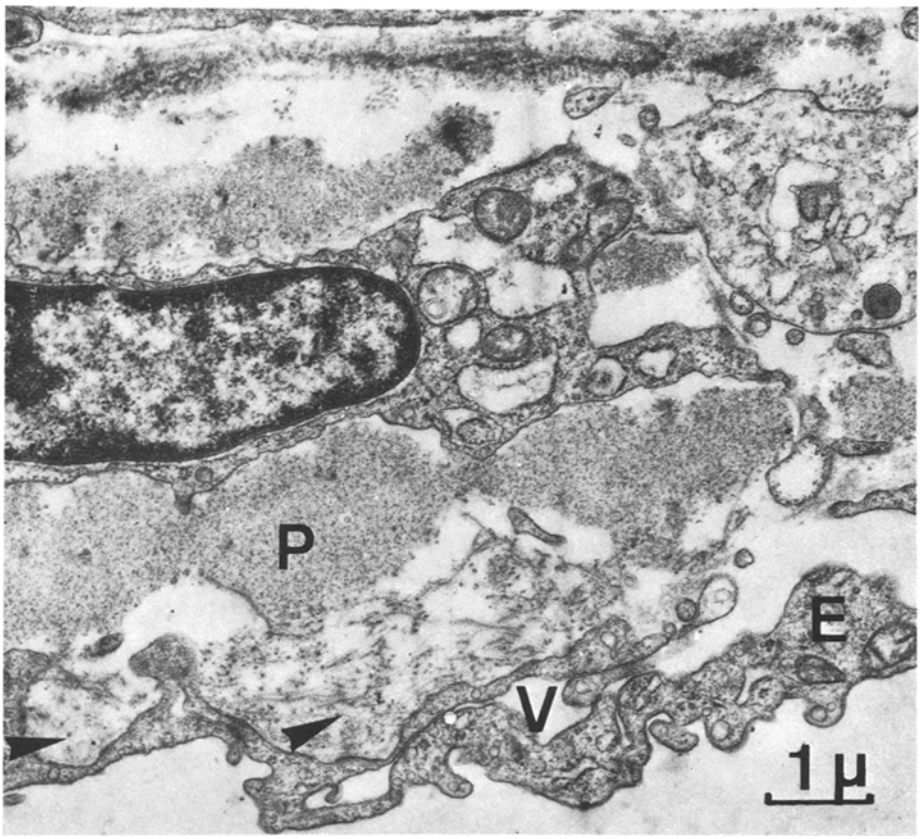

Fig. 1a. Part of the outer wall of Fig. 1. Subendothelial accumulations of exfoliation material (*arrows*) which are in close contact with the homogeneous plaques (*P*). *V* – vacuolar structures in the outer wall endothelium (*E*). × 14,400

in conjunction with other extracellular elements in the subendothelial region, chiefly homogeneous osmiophilic plaques. These plaques were concentrated in the subendothelial and the adjacent cribriform area. In the outer wall of Schlemm's canal we observed a moderate amount of exfoliation material which was concentrated near the outer wall endothelium (Fig. 1a) but was also observed between the cellular layers of this region. These fibrils were often intermingled with normal extracellular elements. The cellular layers of the cribriform region were loosely packed with extracellular components such as homogeneous osmiophilic plaques in different formations (i.e. partly periodic, nodular structures which were embedded in an osmiophilic ground substance), further elastin-like structures with a central increase in density, basal membrane-like material and a fine fibrillar component just inside the inner wall endothelium.

The intercellular spaces of the cribriform area were mainly well developed and were only sometimes obstructed by cell debris and extracellular material (Fig. 1). In addition the cells of this region contained a moderate amount of

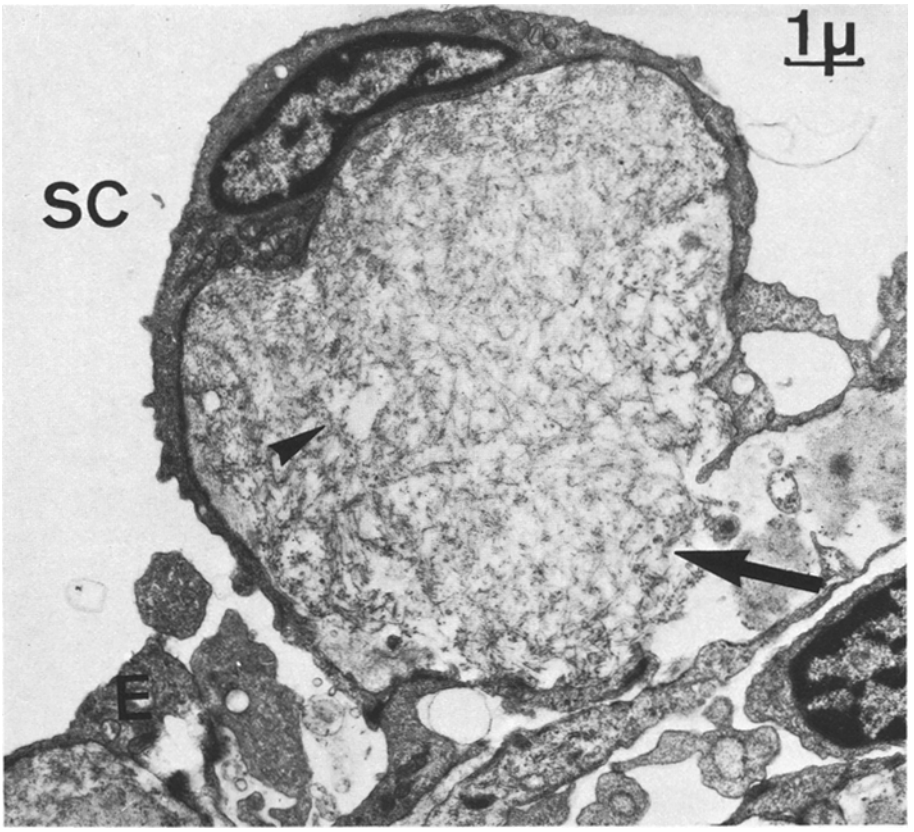

Fig. 2. Giant vacuole, into which a great amount of exfoliation material is embedded. Note the basal opening of the vacuole (*arrow*). *E* – inner wall endothelium, *SC* – canal of Schlemm. × 10,500

mitochodria, rough surfaced endoplasmatic reticulum and vesicular elements, and often had long interlacing processes.

The trabecular beams of the trabeculum corneosclerale and trabeculum uveale were partly normal and partly and variably degenerated. The most marked changes appeared to be sclerosis and thickening. This thickening was related to the subendothelial basement membrane of the lamellae that sometimes showed a multilayered configuration and contained abundent banded material (curly collagen) with a periodicity of 90–100 nm. In beams with normal thickness we found a moderate content of curly collagen and a slight loosening of the collagen fibrils in the central part of the trabeculae (Fig. 4).

Between most of the trabecular beams well developed intertrabecular spaces were present (Fig. 4). They were only sporadically obstructed by extracellular tissue fragments and single cell organelles of disrupted endothelial cells. In this region we found no deposits of exfoliation material; those could only be found in the subendothelial area of Schlemm's canal and in the trabeculum

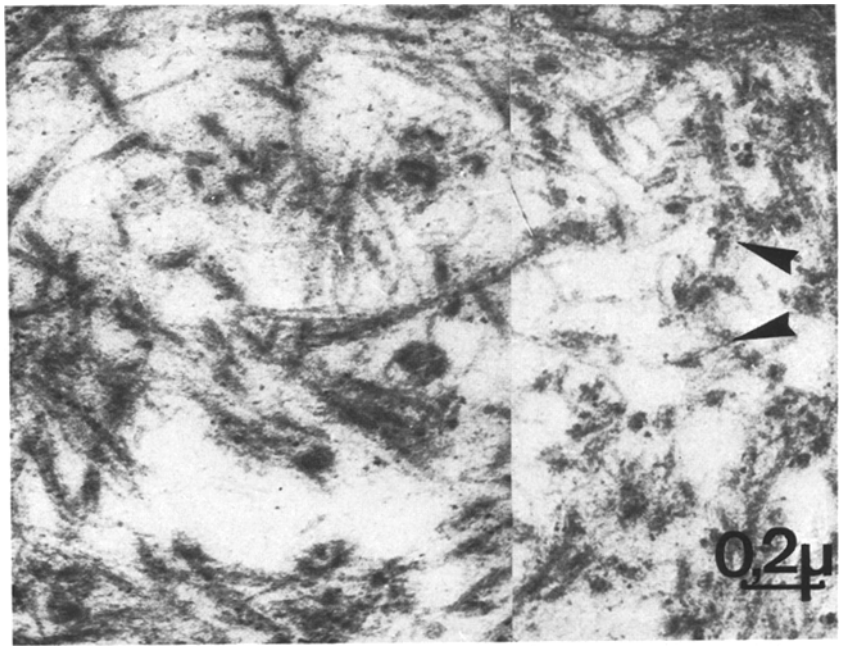

Fig. 3. Note the straight or slightly bent exfoliation fibrils with their split ends. Cross-sections show a tubular character (*arrow*). ×5,700

uveale. There it was often adjacent to the uveal trabecular sheets and sometimes connected with the basement membrane of the sheets if the trabecular endothelium was absent. In most cases trabecular endothelial cells appeared normal while some others showed clarification of the cytoplasm, vacuolar degeneration (Fig. 4) or were completely disrupted leaving behind only cell debris and organelles in the intertrabecular spaces.

Discussion

Electron microscopic investigation of a specimen obtained by trabeculectomy from an eye with so-called pseudoexfoliation without clinical signs of glaucoma, shows that the typical fibrillar material described by Blackstad et al. (1960), Bertelsen et al. (1964), Ashton et al. (1965), Ringvold (1970), Benedikt et al. (1973) is present to a considerable degree within the trabecular meshwork and adjacent to the endothelium of Schlemm's canal. These findings correlate well with electron microscopic studies done in numerous eyes suffering from glaucoma capsulare (Ringvold and Vegge, 1971; Rohen, 1973; Harnisch, 1977; own investigations not yet published). It seems, therefore, that the exfoliation material can be found in the trabecular meshwork in every case of pseudoexfoliation, whether glaucoma exists or not.

The theory that the elevation of the intraocular tension is caused by the obstruction of the aqueous pathways by the exfoliation fibrils presupposes a

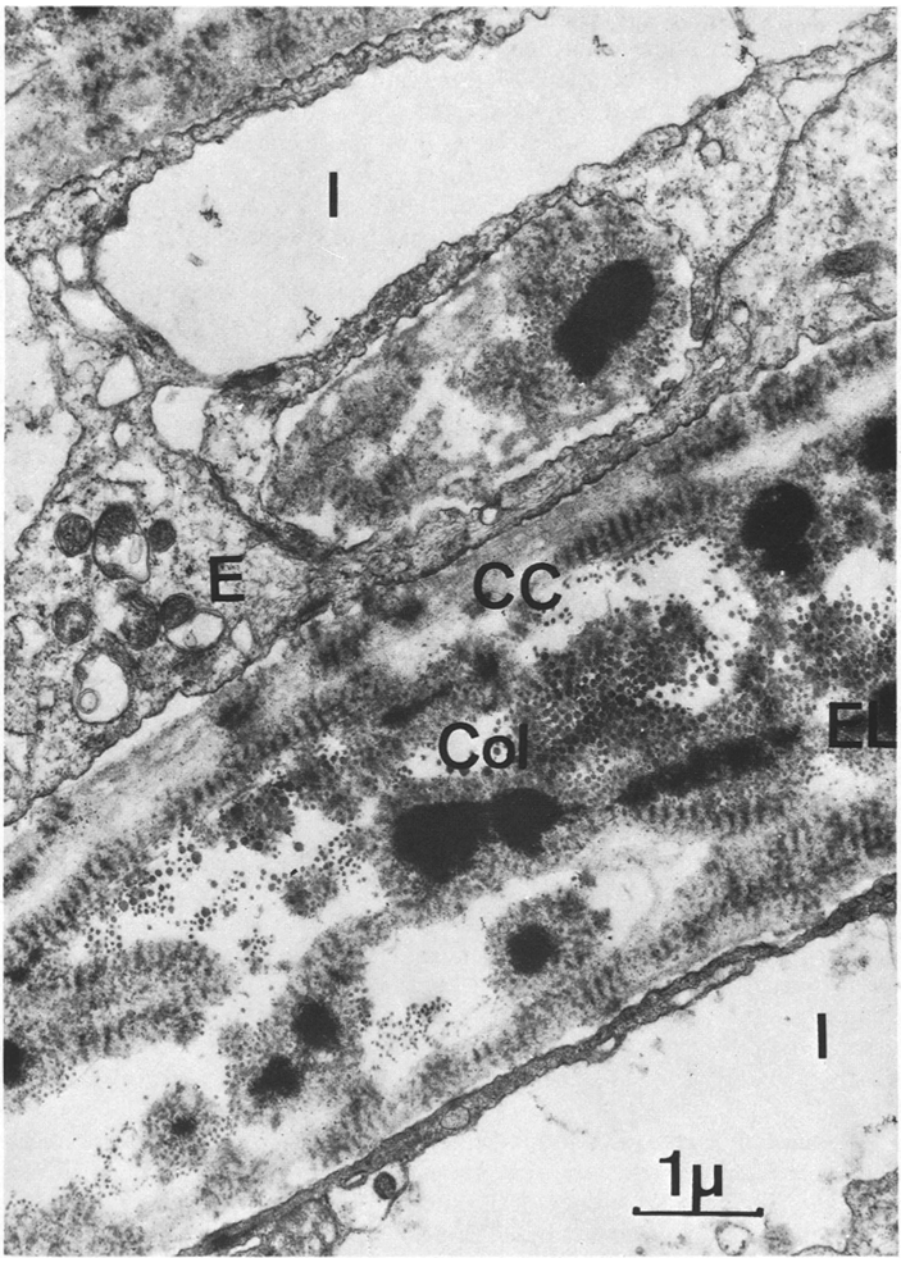

Fig. 4. Trabecular beam of the trabeculum corneosclerale which shows disrupted collagen fibrils (*Col*) in the central part and embedded curly-collagen (*CC*) in its so-called basement membrane. Between the single trabecular beams there are well developed intertrabecular spaces (*I*). *E* – endothelial cell, *EL*– elastin-like material. ×15,000

difference in the amount of exfoliation material within the trabecular meshwork in eyes with and without glaucoma. This relationship has been established by Ringvold and Vegge (1971) who investigated a non-glaucomatous and two glaucomatous eyes with pseudoexfoliation. In the eye without glaucoma the authors found exfoliation material only in the two or three innermost intertrabecular spaces, i.e. closest to the anterior chamber, whereas the material in the two eyes with glaucoma was present both in the intertrabecular spaces and inside the trabeculae, in the juxtacanalicular tissue and adjacent to the inner and outer wall of Schlemm's canal.

This clear relationship was not be confirmed by us. Our case of exfoliation syndrome *without* glaucoma showed the typical exfoliation material to a variable degree mainly lying close to the endothelial lining of Schlemm's canal, in the cribriform region and in the uveal meshwork. The investigation of 20 eyes of exfoliation syndrome *with* glaucoma also revealed, in each case, the occurrence of exfoliation material in variable amounts in all regions of the trabeculum. The amount present showed no correlation with the severity of the glaucoma. Thus other structural alterations are likely to be causative in the impairment of outflow in cases of glaucoma capsulare. These changes are, according to our unpublished studies somewhat similar to those found in eyes with glaucoma simplex (Rohen und Witmer, 1972; Tripathi, 1972, 1977) and consist of the diminuation or absence of the giant vacuoles of the *inner wall* of Schlemm's canal, increase of fibrous and amorphous elements, a build-up of basement membrane-like material and dense osmiophilic plaques, an increase of curly collagen, an accumulation of vesicular structures and degenerated cell organelles in the *subendothelial region*, sclerosis and thickening and compaction of the *trabecular lamellae* and a narrowing or collapse of *Schlemm's canal.*

Some changes are not typical and can also be found in other types of glaucoma and normotensive senile eyes (Tripathi, 1972, 1977; Rohen and Lütjen-Drecoll, 1971; Rohen et al., 1973). In contrast to all eyes with glaucoma capsulare investigated to date, our case is characterized by a large number of giant vacuoles of the inner wall endothelium and numerous free pathways in the cribriform region and in the trabecular meshwork which maintain the passage of aqueous humor. The occasionally increased accumulations of curly collagen in the trabecular meshwork and of extracellular components in the cribriform area are probably senile alterations and due to the advanced age of the patient (Tripathi, 1977).

Another important question is whether the exfoliation material is produced in situ or brought in by the aqueous humor. The presence of exfoliation material in the outer wall of Schlemm's canal supports the "in situ" theory, though it seems possible that some material is also brought by aqueous humor and caught in the uveal trabecular sheets. The alterations of the cells, which include degenerative changes as well as dilatation of rough surfaced endoplasmatic reticulum, are not specific and contribute nothing to the solution of this problem.

Concerning the pathogenesis of the glaucoma capsulare, it is very likely that there is no causative relationship between the build-up of the exfoliation material and the development of the glaucoma, but that a common etiologic factor can bring out both the typical signs of the pseudoexfoliation and the

atypical changes of the trabecular meshwork leading to the impairment of the aqueous outflow. The glaucoma should therefore be regarded as primary in type.

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