Pathology of the glaucomas

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It is hoped that this review of pathological mechanisms in glaucoma will provide a basis for discussion by pointing out matters of which we are still ignorant and by challenging some of the currently accepted concepts. It is convenient to divide considerations of pathology into two parts:

- (1) The cause of the pressure elevation.
- (2) The ocular damage resulting from raised intraocular pressure.

Cause of elevated intraocular pressure

PRIMARY OPEN-ANGLE GLAUCOMA

In the normal eye, the main resistance to aqueous outflow is in the outermost region of the trabecular meshwork, which is adjacent to and forms the inner wall of Schlemm's canal. In primary open-angle glaucoma, there is increased resistance to outflow, and we assume that the abnormal additional resistance is in the same location. Examinations of pathological anatomy show scarring and sclerosis in the trabecular meshwork, but the specimens are usually taken from advanced cases and it has not been decided to what degree trabecular changes may be due to damage secondary to long-standing elevated intraocular pressure rather than the primary defect. Electron microscopy, which Dr. Tripathi will cover in detail, shows fewer vacuoles in the endothelium of Schlemm's canal in patients with glaucoma. Again, it is not clear whether the fewer vacuoles account for diminished outflow facility or whether they merely reflect alterations in flow dynamics because of resistance elsewhere in the outflow pathway. For example, chemical changes in the juxtacanalicular connective tissue could result in impaired fluid flow with no apparent morphological alteration, but the altered flow pattern might be reflected in the endothelium. Some evidence seems to show occlusion of collector channels in cases of established glaucoma, but it is again a problem to decide if this is the primary event or if collapse of channels is induced mechanically by elevated intraocular pressure acting on resistance in the trabecular region.

Pseudoexfoliative glaucoma and pigmentary glaucoma seem to be related to primary open-angle glaucoma. What is not at all clear is whether the pseudoexfoliative and pigmentary materials contribute to the outflow obstruction or whether the material is simply trapped in the meshwork which has poor outflow facility to begin with.

PRIMARY ANGLE-CLOSURE GLAUCOMA

Narrow angles are an inherited configuration of the anterior segment that leaves an eye

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susceptible to angle closure. The lens is far forward. This results in extensive contact between lens and iris, which produces a "pupillary block" to the flow of aqueous into the anterior chamber. Aqueous humour produced posteriorly pushes the peripheral iris forward to embarrass further or close the angle, which is abnormally quite narrow to begin with. Narrowing of the angle, and hence likelihood of angle closure, is enhanced by progressive growth of the lens. Extreme swelling of the lens with advanced cataract formation can narrow and close angles that were initially quite wide.

There are certain other factors that may play a role in individual cases. In some patients thickening of the uveal tract by vascular congestion or oedema may contribute to the narrowing and closure of the angle. Misdirection and entrapment of aqueous humour posteriorly in the vitreous cavity may also result in a tendency to forward displacement of the lens, and this may lead to angle closure even when pupillary block is relieved by an iridectomy. We accept this as the probable mechanism in cases of malignant glaucoma, or in some cases of shallow chamber with angle closure in aphakia that is not relieved by iridectomy, but only occasionally is this given consideration as a possible initiating mechanism in unoperated cases of angle closure. In cases of "plateau iris", the peripheral iris is anteriorly placed and the angle is susceptible to closure, even if pupillary block is surgically relieved. Our clinical inability to predict with certainty which angles will close reflects our incomplete understanding of all the mechanisms involved in angle closure.

If the angle is closed and therapeutically re-opened in time, the trabecular meshwork may remain undamaged by the event (reversible angle closure). However, closure may leave portions of the meshwork damaged if the re-opening of the angle is delayed, and prolonged closure may leave the iris permanently adherent to the meshwork (synechiae). Clinical experience suggests that the time necessary for damage or synechiae to develop is not the same for all eyes, and is shorter with increasing amounts of accompanying inflammation. Most eyes with angle closure that come for histopathological examination have uncontrollable glaucoma by virtue of extensive permanent synechiae.

PRIMARY CONGENITAL GLAUCOMA

In tissue sections, there is an anterior insertion of the iris onto the meshwork. Scleral spur is poorly developed, and ciliary muscle passes by it to achieve direct insertion into trabecular sheets. Schlemm's canal is sometimes absent but this is undoubtedly a secondary change due to long-standing glaucoma that was present in eyes that came to enucleation and pathological examination.

The histological abnormalities suggest incomplete development of the angle. For example, in normal development, scleral spur intercepts the previously present connections of ciliary muscle to trabecular sheets. Also, iris insertion recedes in the course of development until it reaches the appropriate place on the ciliary body (Smelser and Ozanics, 1971). By gonioscopy, it is difficult to distinguish congenital glaucoma from the normal infant angle, both of which are quite different from the adult angle. Normal infant angles undergo continued development to become like adult angles, but angles in eyes with congenital glaucoma apparently do not.

Often, at the time of surgery for congenital glaucoma, the surgeon has the vivid impression that there is a thin transparent membrane on the inner surface of the trabecular meshwork that is disrupted by the goniotomy knife. A logical conclusion is that such a thin non-perforated membrane might be the cause of trabecular obstruction. This

membrane has been elusive in tissue sections, especially because most specimens are from cases of long duration after multiple surgical manipulations so that primary changes are difficult to separate from secondary changes. When it is not seen, advocates suggest that the hypothetical membrane could have been destroyed by surgical manipulations or in tissue preparation. On the other hand, when the "membrane" is seen, sceptics point out that it has the appearance of a sclerotic sheet that could have formed secondarily.

About 3 years ago, Drs. E. A. Maumenee and W. T. Green sent me tissue from a 10-month-old child with infantile glaucoma to examine by scanning electron microscopy. The trabecular region consisted of a compressed tissue with rough inner surface, but no apparent openings. Schlemm's canal was apparently absent. An imperforate sheet of material was stripped from the inner trabecular surface of one piece of tissue (Fig. 1), but it was not possible to say whether this was a sheet formed by secondary fusion of innermost trabecular sheaths or was the elusive membrane that was the initial cause of pressure elevation.

FIG. 1 Scanning electron micrograph of angle structures in a 10-month-old child with glaucoma. A membrane that has been torn off the trabecular meshwork (T.M.) is still attached to the root of the iris. $\times 180$

Since that time, I have obtained satisfactory specimens for light and transmission electron microscopy from three eyes of two patients undergoing trabecular surgery for congenital glaucoma. Dr. David Worthen examined tissue from the same specimens by scanning electron microscopy. These specimens differed from the first specimen in that they were from fresh cases in infants between 3 and 6 months old. Both were unequivocal cases of glaucoma. In one case in which I was the surgeon, I could see quite well an apparent transparent membrane on the trabecular surface arising from the iris root and inserting into Schwalbe's line. In the other case, the surgeon spontaneously reported having seen the same thing. This "membrane" could also be seen on dissection of the specimens under the dissecting microscope, but it turned out that in sections and on scanning electron microscopy (Fig. 2) this "membrane" was the uveal meshwork whose openings could not be appreciated at the magnification of operating and dissecting microscopes. No imperforate membrane was identified, and the meshwork had openings of normal appearance.

FIG. 2 Pair of scanning electron micrographs of the same specimen from two angles. The angle structures from a 3-month old child with glaucoma are shown. The uveal meshwork (UV. M.) looked like a membrane at surgery and during examination under the dissecting microscope. Included in the field are Schlemm's canal (SCH), ciliary body (C.B.), corneo-scleral meshwork (C.S.), and the root of the iris. $\times 270$

GLAUCOMA ASSOCIATED WITH CONGENITAL ANOMALIES OR PERINATAL OCULAR DISEASE

Not all cases of infantile glaucoma are cases of primary glaucoma. Some are related to inherited or congenital diseases that affect the eye or are secondary to other types of perinatal ocular disease. Conversely, not all congenital anomalies result in buphthalmos, but some result in glaucoma of later onset. The mechanisms for the development of glaucoma are varied, and in most cases there has been little adequate histopathological examination and a poor understanding of the mechanisms involved.

In some conditions, glaucoma occurs in the presence of an open but congenitally abnormal angle. In cases of Axenfeld's and Reiger's anomaly, the abnormality is prominently represented by iris strands in the angle, although the abnormalities resulting in obstruction are not elucidated. In buphthalmos associated with neurofibromatosis, the Sturge-Weber syndrome, or congenital rubella (Fig. 3, overleaf), the angle may resemble clinically and histopathologically the angle of primary congenital glaucoma. Indeed, in many reports in the literature which describe the histopathology of primary congenital glaucoma, the eyes became available for examination after the patient had died of a congenital heart defect. It is quite possible that many of these were cases of congenital rubella which were unrecognized at that time. The mechanism for glaucoma can be different in some specific cases, such as direct involvement of the angle with a fibroma.

In some cases the glaucoma is related to angle closure from pupillary block. This occurs because of a subluxated lens in some cases of Marfan's syndrome, the Ehlers-Danlos syndrome, or homocystinuria. Small spherical lenses, such as those which occur in Marfan's syndrome or Marchesani's syndrome, cause a pupillary block that is aggravated by constriction of the pupil. This is relieved by iridectomy or dilation of the pupil. In

FIG. 3 *Congenital glaucoma in a 6-day-old girl who died of heart failure, presumably due to intrauterine rubella. The angle is similar to that of primary congenital glaucoma, with the iris inserted into the trabecular meshwork in front of Schlemm's canal. $\times 60$*

persistent hyperplastic primary vitreous (PHPV), the lens is pushed forward by the cyclitic membrane, and a similar phenomenon can occur in retrolental fibroplasia. Angle closure that is essentially similar to primary angle closure may occur in cases of microcornea.

There are cases of glaucoma associated with Marfan's syndrome or spherophakia (Marchesani's syndrome) in which there is no angle closure, and there is assumed to be an associated microscopic angle anomaly to account for the glaucoma.

Cases of buphthalmos with aniridia may be assumed to have an angle anomaly associated with the aniridia, and indeed in some cases there seem to be remnants of mesodermal tissue on gonioscopy. Many cases that do not have glaucoma early in life develop glaucoma later when the iris remnant begins to impinge upon the trabecular meshwork and form synechiae.

ANTERIOR SEGMENT INFLAMMATION

During the acute inflammation, most cases of iridocyclitis are accompanied by a low intraocular pressure by virtue of altered formation of aqueous humour. In some cases, there is elevation of intraocular pressure due to obstruction of aqueous outflow that overcomes the pressure-lowering effect of diminished aqueous production. Histopathology shows inflammatory cells in the trabecular spaces, and these would seem to account for the obstruction, but there may also be an element of trabecular thickening (oedema) and increased aqueous viscosity during acute inflammation.

Even though we think the obstruction is quite reasonably explained by the inflammatory debris, we remain ignorant of the cause of the inflammation, and satisfactory treatment is often difficult to achieve. Particularly obscure is the nature of the glaucomatocyclitic crisis of Posner and Schlossmann and of treatment-resistant glaucoma associated with relatively mild anterior chamber reaction.

When acute inflammation subsides, evidence of previous inflammation may remain. This evidence includes adhesions of the posterior surface of the iris to the anterior surface of the lens or vitreous (posterior synechiae). (In evaluating tissue sections, one must recognize that fixatives cause iris and lens to become adherent if they are in contact with one another during fixation. Such adhesions can be mistaken for synechiae, but true synechiae are composed of fibrous scar tissue causing adherence of the two structures). Posterior synechiae may form not only after spontaneous iridocyclitis, but also after inflammation accompanying trauma or surgery.

If the posterior adhesions are extensive enough to obstruct the flow of aqueous humour into the anterior chamber through the pupil (and through an iridectomy if one is present), the peripheral iris will be lifted forward (*iris bombé*). The angle may close even in eyes with previously quite wide angles and permanent iridocorneal adhesions (peripheral anterior synechiae) would be expected to form rapidly if the eye is acutely inflamed.

Peripheral anterior synechiae can also form in the absence of pupillary block. In some instances this appears to arise from narrowing of the angle associated with oedema of the ciliary body and peripheral iris accompanying the inflammation. In other instances, keratic precipitates may form a pillar across the angle recess, and these may be organized to form a fibrous tissue adherence. These synechiae are generally localized and rarely extensive enough to produce glaucoma.

In some cases of chronic glaucoma that remains after acute inflammation has subsided, there are no peripheral synechiae. Tissue sections from such cases show scarring of the trabecular meshwork, and presumably inflammatory debris caught within the meshwork during the acute inflammation caused localized scarring. In some instances (*e.g.* trachoma), it is thought that inflammation may cause scarring of the collector channels and cause glaucoma by this mechanism.

BLUNT TRAUMA

Eyes with permanent glaucoma after blunt trauma show scarring of the trabecular meshwork. The healed trabecular region may show sclerosis and closing of Schlemm's canal. Sometimes proliferation of corneal endothelium over the region produces an extended Descemet's membrane. Most eyes that come to enucleation with trauma-induced glaucoma also show extensive peripheral anterior synechiae that formed as the disrupted uveal and trabecular tissue healed together by scarring.

Often blunt trauma sufficient to damage the trabecular region also causes choroidal rupture, dislocation or rupture of the lens, hyphaema, or recession of the angle. It is important to recognize that these injuries merely accompany trabecular damage and usually do not themselves play a direct role in raising the intraocular pressure. Traumatically dislocated lenses usually have no relation to accompanying glaucoma, but sometimes the new location of the lens causes pupillary block and angle closure. This may also occur with subluxation of the lens. Extreme pupillary block occurs if the lens is dislocated into the anterior chamber with the iris pressed against the posterior surface of the lens.

PENETRATING INJURY AND SURGERY

Perhaps the most common cause of permanent glaucoma after a penetrating injury, including surgery, is peripheral anterior synechiae that formed either when there was a collapse of the anterior chamber or when the iris was incarcerated into the perforating corneo-scleral wound. Other intraocular structures besides the iris can, of course, impinge upon the meshwork, or the outflow channels can suffer direct injury.

Rarely an open corneal or corneo-scleral perforation provides the tract for corneal or conjunctival epithelium to grow into the eye. The epithelium grows to cover the inner surfaces of the eye, and when the angle structures are covered an intractable glaucoma results unless the original perforation remains open to provide egress for aqueous humour.

In cases in which an iron foreign body is retained by the eye, there may be late development of glaucoma related to ocular siderosis. Special stains demonstrate iron in the trabecular meshwork and there are also sclerotic changes.

TUMOURS (MELANOMA, LEIOMYOMA, DIKTYOMA, XANTHOGRANULOMA, ACUTE LEUKAEMIC INFILTRATES, ETC.)

Tumours can extend into the trabecular meshwork and physically obstruct the outflow channels. Tumours in the posterior segment (melanoma and retinoblastoma) may shed cells into the eye that are carried by the aqueous humour into the meshwork, where they lodge and obstruct outflow. In some cases of choroidal melanoma, there has been lysis of the pigment and macrophages filled with the lysed pigment are trapped in the trabecular meshwork, exactly as occurs in phakolytic or haemolytic glaucoma. This has been termed "melanomalytic glaucoma". In some cases there may also be closure of the angle related to posterior synechiae that cause "iris *bombé*", forward displacement of iris and lens by a massive posterior tumour, or rubeosis iridis (Yanoff, 1970).

ALPHA CHYMOTRYPSIN

Intraocular pressure often becomes raised transiently after cataract extraction in which alpha chymotrypsin is used. Monkeys similarly develop glaucoma after alpha chymotrypsin is injected into the posterior chamber. The pressure elevation results from zonular fragments that become caught in the meshwork and obstruct the aqueous outflow (Fig. 4). This mechanism has been deduced from careful experimentation (Chee and Hamasaki, 1971) and the fragments have been visualized by electron microscopy (Anderson, 1971).

FIG. 4 Scanning electron micrograph, showing zonular fragments (z) in trabecular meshwork of an owl monkey with alpha-chymotrypsin glaucoma. $\times 900$

RUBEOSIS OF THE IRIS

This neovascularization of the iris occurs in eyes afflicted with a variety of conditions, most of them characterized by intraocular haemorrhages. These include diabetes mellitus, Eales's disease, retinal vasculitis, choroidal melanoma, and central retinal vein or artery occlusion.

Clinically, it is recognized that intraocular pressure rises when a fibrovascular membrane grows up from the angle recess to cover the trabecular meshwork. The fibrovascular membrane also forms on the entire anterior iris surface. It covers only the anterior

surface, and does not extend posteriorly through the pupil where the iris surface is covered by epithelium. Nor does the membrane extend beyond the trabecular meshwork onto the posterior corneal surface unless there is corneal perforation or other corneal disease.

Rapidly thereafter, the fibrous membrane contracts, pulling iris around the rim of the pupillary opening (ectropion uveae) and pulling peripheral iris up to Schwalbe's line (peripheral anterior synechiae). Eyes that come to enucleation because of rubeosis are in this advanced stage of the disease (Fig. 5).

FIG. 5 *Neovascular glaucoma in a 22-year-old man who had been diabetic since age 6. Inset shows fibrovascular membrane on anterior iris surface at higher magnification. Storage of glycogen in iris pigment epithelium gives vacuolated appearance in diabetics. $\times 50$ Inset $\times 130$*

That the fibrovascular membrane should obstruct outflow is easily understood. The mystery is what induces the fibrovascular proliferation, and the pressing question is how to treat cases of rubeosis.

ESSENTIAL IRIS ATROPHY

In this mysterious unilateral disease, full-thickness holes develop in the iris stroma and epithelium. Glaucoma results when the trabecular meshwork is occluded by anterior synechiae that form in the periphery. Histopathology (Fig. 6) shows the iris pigment epithelium to be healthy in areas where the stroma is still intact, and clinical descriptions have reported transillumination defect in areas that still have stroma remaining. This suggests that the primary atrophic process is in the stroma, and that the pigment epithelium becomes defective only after the overlying stroma is destroyed. The peripheral synechiae have an appearance that suggests retraction of iris tissue away from the hole into the angle (Fig. 6). Again, as in the other secondary glaucoma, we see the mechanics of the obstruction, but we do not know the cause and we are unhappy with our current efforts at treatment.

FIG. 6 Essential iris atrophy of 3 years' duration in a 48-year-old woman. Focal stromal atrophy is apparent, and the stroma appears to be retracted into the angle. Uncontrollable glaucoma resulted from obstruction of access to the trabecular meshwork (TRAB). $\times 22.5$

PHAKOLYTIC AND HAEMOLYTIC GLAUCOMAS

Phakolytic glaucoma occurs in eyes with advanced cataracts that are undergoing lysis. Macrophages engorge themselves with the lysed material as it is released from the lens. These engorged cells become lodged in the trabecular meshwork, and are the apparent cause of obstruction. The clinical picture is that of a severe elevation of intraocular pressure, cells in the anterior chamber, and secondary cataract. This can be misdiagnosed as iritis with secondary glaucoma and cataract.

Haemolytic glaucoma occurs in eyes with long-standing vitreous haemorrhages. After the red cells undergo lysis, macrophages take up the lysed material and become lodged in the trabecular meshwork, as in phakolytic glaucoma.

Effects of raised intraocular pressure

OPTIC NERVE

In tissue sections cupping of the disc from chronic glaucoma is represented by loss of nerve fibres and glial cells from the optic nerve head (compare Figs 7 and 8). In most cases eyes are removed only when there is total cupping and in tissue sections there are no tissue elements remaining. Usually, there is also a backward displacement of the perforated collagenous sheets that form the framework of the lamina cribrosa. The orbital portion of the optic nerve shows ordinary columnar optic atrophy.

The pathogenic mechanisms of cupping have not been conclusively demonstrated. Intraocular blood flow is affected by elevations in intraocular pressure, particularly in the region of the optic nerve head, and especially in cases of extreme elevation of the intraocular pressure. This would suggest that interference with blood flow is a mechanism by which elevated intraocular pressure exerts its damaging influence upon the optic disc, and there is clinical evidence that strongly supports this idea. However, the evidence is not conclusive, and other mechanisms may play a role in disc cupping. These presumably will come up for discussion as the symposium proceeds.

In acute glaucomas, the nerve fibres and the disc show hydropic swelling, presumably the result of ischaemia. If high intraocular pressure is maintained, swelling continues for several days and all the histopathological features of papilloedema are manifest. Ultimately, the nerve fibres and glia disappear from the disc, resulting in the typical

FIG. 7 *Normal optic disc of a 17-year-old girl who died of Pseudomonas pneumonia.* $\times 37.5$

FIG. 8 *Glaucomatous cupping of disc in an eye enucleated because of painful bullous keratopathy. The collagenous sheets of the lamina cribrosa are not bowed backward more than in the normal eye (Fig. 7), and cupping is accounted for by loss of nerve fibres and glial cells. Peripapillary retina is thinner by virtue of disappearance of nerve fibre layer and ganglion cell layer.* $\times 22.5$

picture of glaucomatous cupping. The orbital portion of the optic nerve may show "cavernous optic atrophy", in which the spaces between the septa previously occupied by nerve fibres are now distended with acid mucopolysaccharide. There is no inflammatory reaction to this material, and presumably it represents concentrated vitreous which has been forced through the necrotic disc tissue into the optic nerve by the raised intraocular pressure (Lampert, Vogel, and Zimmerman, 1968). The nerve fibres become atrophied and, where there are no cavernous spaces, the histological picture is that of columnar optic atrophy.

RETINA

The chief histological feature in advanced glaucoma is the absence of the ganglion cells and nerve fibre layer. The glial elements in the inner retinal layers remain and sometimes appear hypertrophied. The radial peripapillary capillaries, which supply the nerve layer, are atrophied, and it has been suggested that the glaucomatous damage to nerve fibres results from the effect of increased intraocular pressure upon these vessels (Kornzweig, Eliasoph, and Feldstein, 1968). However, these radial peripapillary capillaries also atrophy when the nerve fibre layer disappears in cases of descending optic atrophy (Cogan, personal communication), and this demonstrates that loss of peripapillary capillaries can be secondary to nerve fibre loss.

UVEAL TRACT

In advanced cases of glaucoma the choroid may show some thinning and atrophy with vascular sclerosis. Changes are particularly marked in the peripapillary region, and in this area, the retinal pigment epithelium may also be affected. This corresponds to the peripapillary glaucomatous halo found on ophthalmoscopic examination.

The ciliary body and iris likewise show some degree of fibrosis and hyalinization in advanced cases. There may be slight uveal ectropion in the region of the pupil. In cases where there has been acute extreme elevation of intracapsular pressure, there may be segments of iris that have undergone ischaemic necrosis with complete disappearance of the stromal cells, and the remaining tissue may be pale-staining and contain residual pigment.

CORNEA AND SCLERA

If pressure elevation is marked, there is initially simple corneal oedema with thickening of the stroma and formation of epithelial vacuoles. If the oedema is long-standing, a degenerative pannus develops in which connective tissue is laid down between Bowman's membrane and the epithelium. The sclera is relatively unchanged except in very advanced cases of glaucoma, in which there may be ectasia, usually in the region overlying the ciliary body or at the limbus.

In infantile glaucoma, both the cornea and sclera are stretched so that the eye becomes enlarged. Because of the stretching the cornea may show breaks in Descemet's membrane.

LENS

Cataracts are frequently seen in the eyes of patients with advanced glaucoma. It is often difficult to decide whether the cataract is due to the age of the patient, or is secondary to nutritional difficulty of the anterior segment because of elevated intraocular pressure, to medical treatment for glaucoma, or to surgical treatment of glaucoma. One specific type of lens opacity, *Glaukomflecken*, appears at the anterior lens surface in cases of acute glaucoma. In tissue sections (Fig. 9), the opacities seem to be areas of anterior epithelial necrosis. After the acute attack, opacities recede inward from the surface as the lens continues to grow and deposits new lens fibres.

FIG. 9 *Anterior lens surface from an eye that suffered acute glaucoma*

Light photomicrographs were taken of tissue sections in the collection of Dr. David G. Cogan, Boston, Massachusetts except for Figure 9, which was obtained from the Armed Forces Institute of Pathology, Washington, D.C., through the courtesy of Dr. Lorenz Zimmerman.

COMMENTARY

ROLE OF THE VITREOUS IN THE CAUSATION OF CAVERNOUS ATROPHY

Cause of cavernous atrophy of the optic nerve

It appears that the primary cause of cavernous degeneration is infarction of the circulation in the optic nerve. Changes then occur which are analogous to the lacunar infarcts which Pierre Marie described in the basal ganglia. In chronic glaucoma this process goes back in the optic nerve. Histologically there is no reaction with microglia or macrophages. If the pressure is high, as in angle-closure glaucoma, an ischaemic infarct occurs in which there is a proliferation of glial cells and macrophages and scarring with degeneration of the nerve fibres. Later, when the nerve fibres have degenerated, small openings remain in the lamina cribrosa through which larger molecules can be forced backwards under high pressure. It is thought that this is how the vitreous comes to be forced into the optic nerve so that the septa previously occupied by nerve fibres become distended with acid mucopolysaccharide. The supporting connective tissue does not undergo degeneration as it is able to withstand a very much higher intraocular pressure.

On the experimental evidence available to him, Mr. S. S. Hayreh (see p. 184) felt that the vitreous was unlikely to pass through the lamina cribrosa, as he had never been able to find any trace of colloidal iron in the optic disc or nerve after it had been injected into the vitreous, however high the pressure was raised.

Aqueous outflow pathway in normal and glaucomatous eyes

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The discovery by Schlemm (1830–31) of a circular canal in the angular region of the human eye has led to extensive investigations being carried out to establish its structure and function in relation to the drainage of the aqueous humour. There is little doubt at present as to the free flow of the aqueous through the intercommunicating spaces of the trabecular meshwork. However, the question whether or not the endothelial lining of Schlemm's canal constitutes a structural barrier to the aqueous outflow has been debated for well over a century. We remain especially indebted to Professor Norman Ashton, who clarified the anatomical relations of Schlemm's canal and associated structures by elegant injection models and painstaking studies of their microstructure (Ashton, 1952, 1960; Ashton, Brini, and Smith, 1956).

Over the past decade, the application of electron microscopy has brought renewed interest in correlating the structure and function of the exit pathway of the aqueous. This report is mainly concerned with the presentation of my personal observations on the fine structure of the trabecular apparatus in relation to aqueous outflow in normotensive eyes of primates and lower mammals and with special reference to the pathological alterations in the angular region of some cases of primary glaucoma.