

Chapter 7

Glaucoma

“Glaucoma” is a generic term for a common group of ocular diseases which, if untreated, can result in an irreversible loss of visual function. An inappropriate intraocular pressure linked to damage to the neuronal tissue in the optic nerve head is common to all forms of glaucoma.

Classification

Glaucoma can be divided into five main subgroups:

- 1 Congenital.
- 2 Primary open.
- 3 Primary closed.
- 4 Secondary open.
- 5 Secondary closed.

Normal drainage anatomy

Aqueous humour is produced in the ciliary processes by active transport and diffusion. The aqueous leaves the posterior chamber, passes through the pupil into the anterior chamber, and finally drains via the trabecular meshwork (Figures 7.1, 7.2). Drainage is by two mechanisms: conventional drainage through the trabecular meshwork (90%) and unconventional drainage via the uveoscleral outflow (10%).

Knowledge of the normal chamber angle is crucial to an understanding of many pathological processes in the spectrum of glaucoma (Figure 7.3). The iris root is usually at 45 degrees to the inner surface of the trabecular meshwork. A line can be drawn from the posterior end of Schlemm's canal, through the scleral spur, to the periphery of the chamber angle. This is a useful landmark in identifying the normal location of the iris root and appreciating abnormal relationships, for example early angle closure

and angle recession. The meridional fibres of the ciliary muscle insert into the scleral spur and the oblique layers insert into the uveal layer of the trabecular meshwork.

The outer part of the trabecular meshwork lies within the scleral sulcus (Figure 7.4) and the inner part fuses with the anterior face of the ciliary body. The trabecular meshwork is formed by collagenous beams and plates lined by endothelial cells. In conventional morphology, the trabecular meshwork is divided into three layers. The two innermost layers are the uveal and corneoscleral. The outermost layer is formed by the endothelial cells loosely arranged within mucopolysaccharides and collagen (Figures 7.4, 7.5). The outermost layer is variously termed juxtacanalicular (USA) or cribriform (Europe).

Several functions are ascribed to the trabecular meshwork. The juxtacanalicular layer provides resistance to maintain intraocular pressure and prevents reflux of blood from Schlemm's canal. The endothelial cells lining the trabeculae within the meshwork have a capacity for phagocytosis. This function is necessary due to the breakdown of the tissues of the anterior segment during life (for example the breakdown of tissues in the iris stroma and iris pigment epithelium).

Abnormalities in the outflow system lead to reduced outflow facility and increased intraocular pressure.

Pathological examination of a glaucomatous eye

A cupped disc is a pathological hallmark of longstanding glaucoma. Enucleation, whilst never carried out for uncomplicated primary open angle glaucoma, is sometimes performed in the secondary forms of aqueous outflow obstruction, i.e. tumours, vascular disease, uveitis, and trauma.

Figure 7.1 A section through the anterior segment of a normal eye demonstrating the anatomical features. The yellow colour of the lens is due to gluteraldehyde fixation.

Figure 7.2 A diagram to illustrate the routes of aqueous movement through the posterior chamber into the anterior chamber. Aqueous leaves the trabecular meshwork through the canal of Schlemm and collector channels drain into the episcleral veins. An alternative drainage pathway is into the supraciliary space (uveoscleral outflow).

Figure 7.3 In a paraffin section, the structures surrounding the chamber angle are easily identified. The trabecular meshwork is located on the inner surface of Schlemm's canal. The ciliary muscle fibres insert into the scleral spur and into the uveal layer of the meshwork. The dilator pupillae is seen as a thin red line above the pigmented epithelium of the iris. The chamber angle should reach as far as the imaginary line drawn from the posterior limit of the canal of Schlemm through the scleral spur and ending at the iris root.

Figure 7.4 The morphological distinction between the various layers in the trabecular meshwork is more easily demonstrated diagrammatically. Traction by

the ciliary muscle on the scleral spur and the uveal meshwork opens the tissue and facilitates outflow: this is the action of pilocarpine when used to treat open angle glaucoma. The lining endothelium of Schlemm's canal transports aqueous by the formation of giant vacuoles and transcellular channels. The inset shows: (1) the resting stage, (2) an invagination from the inner surface, (3) the transcellular channel, and (4) recovery after the pressure in the canal is equal to that in the juxtacanalicular layer. The scleral sulcus represents a groove on the inner peripheral surface of the cornea and contains the outer part of the trabecular meshwork and Schlemm's canal.

Figure 7.5 In a thin plastic section (1 μm) stained with toluidine blue it is possible to see the difference between the uveal layer which fuses with ciliary muscle and the corneoscleral layer which bridges the space between the scleral spur and cornea. The juxtacanalicular layer is inconspicuous. The endothelium which lines Schlemm's canal contains empty spaces (giant vacuoles). The thick line extending from the tip of the scleral spur to the peripheral cornea separates the uveal and the corneoscleral layers.

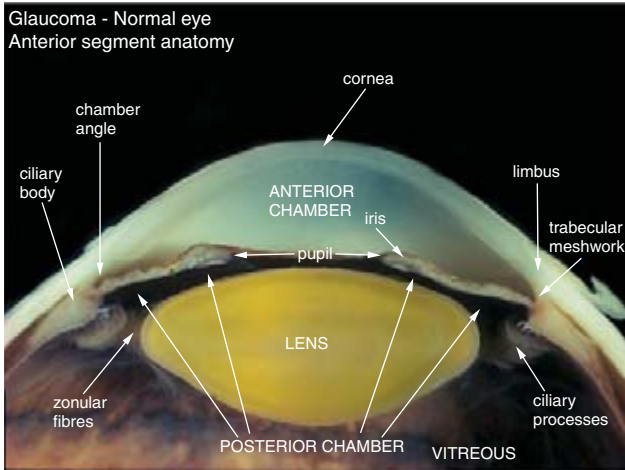


Figure 7.1

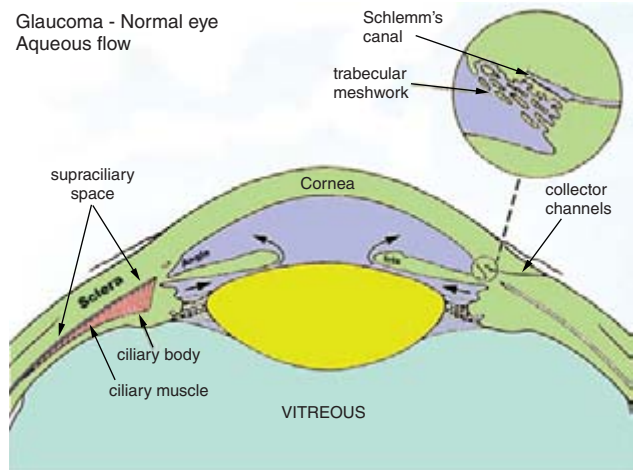


Figure 7.2

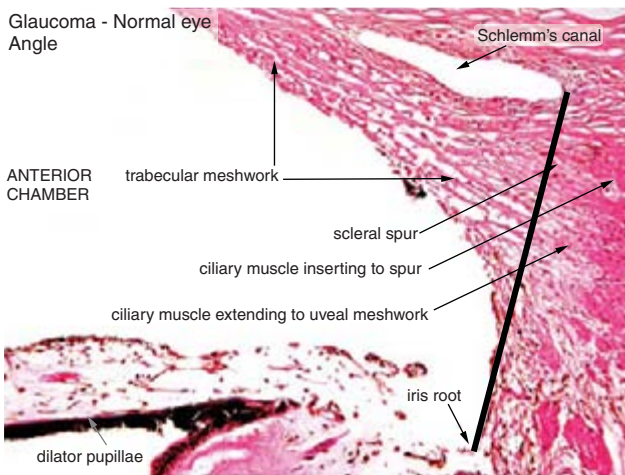


Figure 7.3

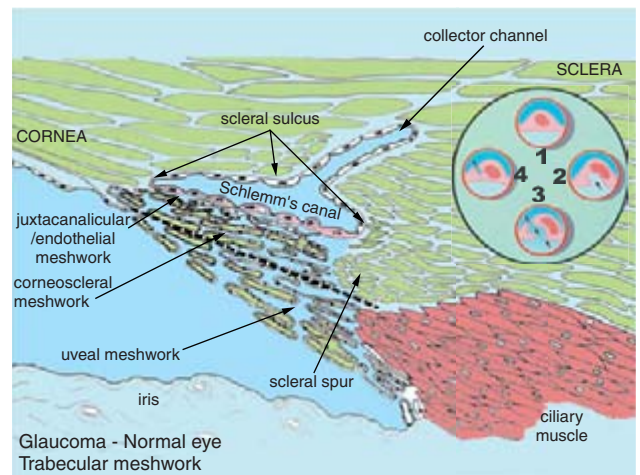


Figure 7.4

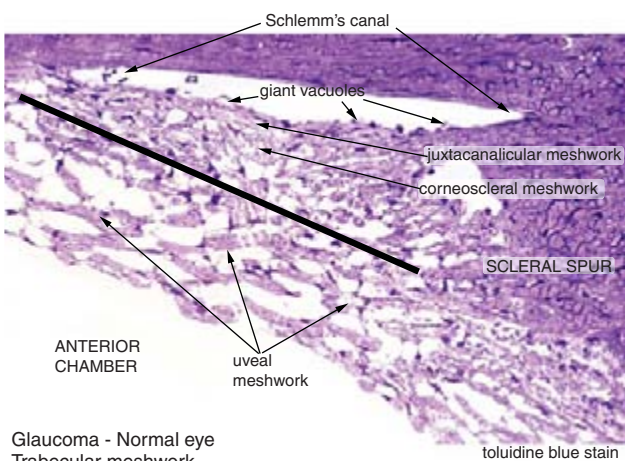


Figure 7.5

Congenital/infantile/juvenile

Congenital glaucoma is defined as a glaucoma that arises in children before the age of 2. The incidence is 1 in 10 000, although there are considerable variations amongst different racial groups. The raised intraocular pressure is due to an increased outflow resistance of an abnormally developed trabecular meshwork.

Clinical presentation

Involvement is usually bilateral with a triad of symptoms:

- 1 Photophobia.
- 2 Epiphora.
- 3 Blepharospasm.

As a result of the raised intraocular pressure, enlargement of the eye (buphthalmos) may occur up to the age of 3, at which stage in life the scleral collagen is more elastic.

Other features include corneal oedema/haze, Haab's striae, and amblyopia.

Gonioscopic examination often shows the iris insertion positioned more anteriorly when compared to a normal infant angle, but appearances can be very variable. A thin membrane initially described by Barkan may be observed straddling the angle. Existence of Barkan's membrane is controversial and histopathological descriptions are scarce.

Pathogenesis

Congenital glaucoma is a result of abnormal development of the trabecular meshwork. However, there is some development and maturation of the trabecular meshwork following birth and this may explain unilateral and arrested cases.

Genetics

There is a difference among races (possibly higher in black races) in the incidence of congenital glaucoma. About 10% of all cases have a strong hereditary component with variable penetrance. Both autosomal dominant and recessive types have been reported.

Possible modes of treatment

Treatment is usually surgical with the most common procedures being goniotomy and trabeculotomy.

Macroscopic and microscopic

Successful treatment of, and the low incidence of, this disease has resulted in a paucity of pathological material and it is only possible to provide a brief outline of the suggested abnormalities:

- 1 A membrane (Barkan's) lining the inner surface of the uveal layer (Figure 7.6).
- 2 Hypercellularity of the trabecular meshwork, i.e. a failure of resorption of primitive embryonic tissue located in the chamber angle in early embryonic life (Figure 7.7).

- 3 Abnormal insertion of the ciliary muscle into the trabecular meshwork occurs due to the absence of an intervening scleral spur (Figure 7.7).

Pathological evidence of treatment

Specimens from enucleated globes with a past history of treated congenital glaucoma often reveal pathology which is so complicated that the primary pathology is obscured.

Primary open angle

Primary open angle glaucoma (POAG) is a chronic, usually bilateral but asymmetric disease that affects 1–2% of the population over the age 40 years. If untreated, it may lead to severe visual loss and blindness.

Clinical presentation

The onset is insidious and the patient is unaware of areas of visual deficit until the disease has progressed to a late stage.

Many clinical and investigative factors are involved in the diagnosis of POAG and are constantly evolving. Traditionally the following criteria are diagnostic: raised intraocular pressure, thinning of the neuroretinal rim (optic disc cupping), and evidence of progression of characteristic visual field loss (enlarged blind spot and arcuate scotoma).

Pathogenesis

The disease is multifactorial and remains poorly understood. An imbalance between intraocular pressure and vascular perfusion of the optic nerve head will lead to sectorial atrophy. Similarly, mechanical pressure on the axons at the neuroretinal rim may interfere with axoplasmic flow and result in retrograde neuronal degeneration.

Genetics

Family history is a risk factor, although the specific genetic abnormality has not been identified in disease affecting elderly individuals.

Topical steroid treatment, in some individuals, will lead to increased intraocular pressure (steroid responders). Individuals with POAG are more likely to be steroid responders and steroid challenges were used in the past to assist in the diagnosis of POAG.

Initially, a gene on chromosome 1 (the trabecular meshwork induced glucocorticosteroid response or *TIGR* gene) was found in juvenile open angle glaucoma and later in 10% of adults with POAG. This gene is also known as the myocillin (*MYOC*) gene. Subsequently, other genes have been implicated but, as yet, the precise molecular genetics of POAG are poorly understood and multiple genes are probably involved.

Possible modes of treatment

This is beyond the scope of this text; in brief, standard glaucoma treatment involves lowering the intraocular pressure. Basic principles:

- 1 **Medical treatment:** includes topical preparations which reduce aqueous production and others that increase aqueous outflow. The latest generation (prostaglandin analogues) increase uveoscleral outflow.
- 2 **Surgical treatment:** various forms of trabeculectomy with or without antiscarring therapy.
- 3 **Laser treatment:** includes laser trabeculoplasty or cyclophotocoagulation for end-stage cases.

Microscopic

Unfortunately, the morphological study of trabeculectomy specimens has not provided definitive diagnostic features. Using a variety of sophisticated techniques, the appearance

of the outflow system in trabeculectomy specimens showed no significant difference from that of age-matched normal tissue.

Primary angle closure

A form of glaucoma in which there is obstruction to outflow of aqueous by iridotrabecular contact. Factors involved in this condition include:

- 1 **Race:** especially Eskimos and East Asians.
- 2 **Gender:** more common in women.
- 3 **Age:** middle age.
- 4 **Refractive error:** hypermetropes having smaller globes.
- 5 **Family history:** positive.
- 6 **Predisposed anatomy:** eyes with narrow angles or plateau iris (Figure 7.8).

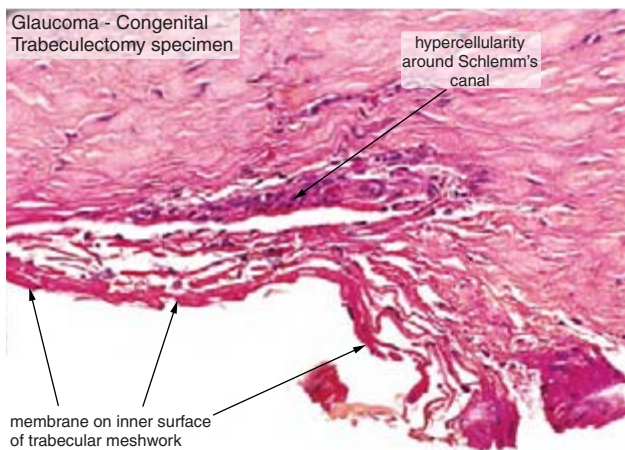


Figure 7.6

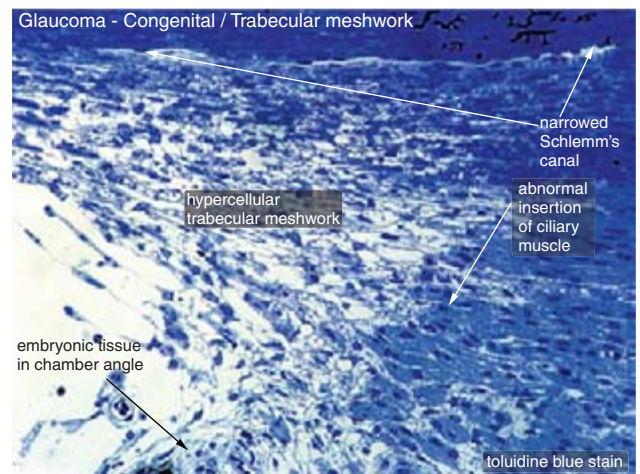


Figure 7.7

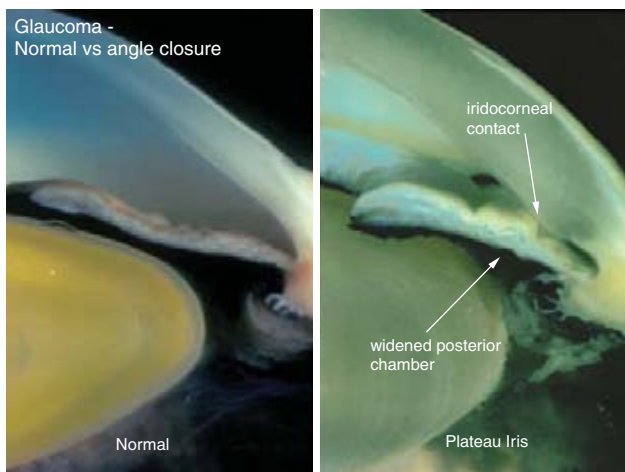


Figure 7.8

Figure 7.6 A trabeculectomy was performed in the treatment of a case of congenital glaucoma. A membrane was identified on the inner surface of the meshwork – this may possibly correspond to the Barkan's membrane, which is sometimes claimed to be observed on gonioscopy.

Figure 7.7 In congenital glaucoma, there is excessive cellular tissue within the trabecular meshwork. Schlemm's canal is narrowed. The ciliary muscle is displaced into the posterior part of the trabecular meshwork. Incomplete resolution of embryonic tissue in the chamber angle appears to be the cause of increased outflow resistance. (Thin plastic section – toluidine blue.)

Figure 7.8 It is extremely rare for a globe to be enucleated for primary closed angle glaucoma, but this chance finding of a plateau iris illustrates the pathogenesis of one type of angle closure (right). A normal angle is included for comparison (left).

Pathogenesis and clinical presentation

The anterior displacement of the peripheral iris is due to several factors:

- 1 Relative pupil block interrupts aqueous flow from the posterior to anterior chamber. Enlargement of lens with age contributes to the partial pupil block.
- 2 The pressure behind the peripheral iris rises, causes iris bombé and the angle progressively closes. Several clinical presentations are possible:
 - 1 *Acute*: a complete iridotrabecular block with rapid loss of vision, ocular pain with nausea, and vomiting. Clinically, there is conjunctival congestion, hazy cornea, raised intraocular pressure (>50 mmHg), anterior chamber flare and cells, and a fixed pupil. Gonioscopy will reveal a peripheral iridocorneal contact.
 - 2 *Intermittent*: periodic iridotrabecular block depending on iris movement. The signs and symptoms during an angle closure attack are similar to those described in acute angle closure glaucoma.
 - 3 *Creeping angle closure*: steadily progressive iridotrabecular contact (progression from 12 to 6 o'clock). The intraocular pressure rise is gradual without acute symptoms.
 - 4 *Chronic*: the end-stage result of creeping closure in which the iridotrabecular contact is complete and permanent (peripheral anterior synechiae). The final intraocular pressure may be very high with an absence of acute symptoms and the field loss and optic disc appearance are similar to POAG.

In most parts of the world, acute and subacute cases represent the commonest forms of angle closure. However, in regions such as India, chronic angle closure is very common without any history of acute attacks.

Genetics

There is a familial as well as a racial tendency, but the molecular genetics have not been identified.

Possible modes of treatment

Treatment is dependent on the stage of disease.

- 1 *Medical*: initially to control intraocular pressure prior to definitive treatment and also in chronic cases.
- 2 *Laser iridotomy*: perforation to equalise pressure differentials between the anterior and posterior chambers. The presence of fibrinolysins in the aqueous prevents fibrin deposition so that scar tissue does not form in the iris defect (see below).
- 3 *Surgical*: lens extraction, iridectomy, goniosynechiolysis, and trabeculectomy.

Pathology

In an untreated globe, a large lens will be evident. The anterior chamber is shallow and the angles closed (Figure 7.9).

The large lens blocks the pupil and initially part of the angle is closed off (Figure 7.10). As the intraocular pressure rises, the remainder of the peripheral iris becomes adherent to the trabecular meshwork (Figure 7.11).

There may be evidence of a laser peripheral iridotomy (Figure 7.12) or surgical iridectomy.

Secondary open

Exfoliation syndrome (ES)

Other names: pseudoexfoliation syndrome (PEX/PXF).

A systemic disorder which is manifest clinically as deposits on the anterior surface of the lens and glaucoma. Deposition is frequently asymmetrical and density increases with the patient's age. The title pseudoexfoliation syndrome was adopted initially to distinguish this condition from true exfoliation (splitting of the anterior lens capsule) which occurs when the lens is exposed to excessive infrared light.

Clinical presentation

Exfoliation syndrome is usually an incidental finding on the lens surface on routine examination – dilatation of the pupil shows a bull's eye pattern of central white deposits surrounded by a clear zone with coarser deposits in the periphery extending to the zonules.

Iris transillumination defects may be evident in the peripupillary region.

There may be an association with primary open angle glaucoma – the surface of the lens should be examined in all types of glaucoma. ES may be associated, less commonly, with angle closure as the deposits weaken the zonules and forward movement of the lens may occur causing pupil block.

Gonioscopy may show heavy pigmentation in the trabecular meshwork.

Pathogenesis

Previously this was considered a primary ocular disease due to release of material from the anterior surface of the lens, hence the term "pseudoexfoliation". In the past two decades it has been shown that material with the same immunohistochemical and ultrastructural characteristics can be found in extraocular tissues (for example orbit, eyelid, lung, kidney, heart, liver, and gallbladder) of affected individuals. Hence, the disorder is systemic with focal deposition in other connective tissues. The ocular pathology is due to precipitation from the aqueous as the substance circulates through the anterior segment.

Genetics

Certain races have a higher incidence (for example Scandinavians).

Possible modes of treatment

Treatment is required only if glaucoma is present and with similar principles to those described in POAG. Intraocular pressures tend to be higher and glaucoma progression is frequently more rapid than with POAG. Laser trabeculectomy is reported to have a greater effect on lowering intraocular pressure, although the response is temporary.

Cataract surgery is associated with more complications due to poor pupil dilatation and a higher incidence of zonular dehiscence.

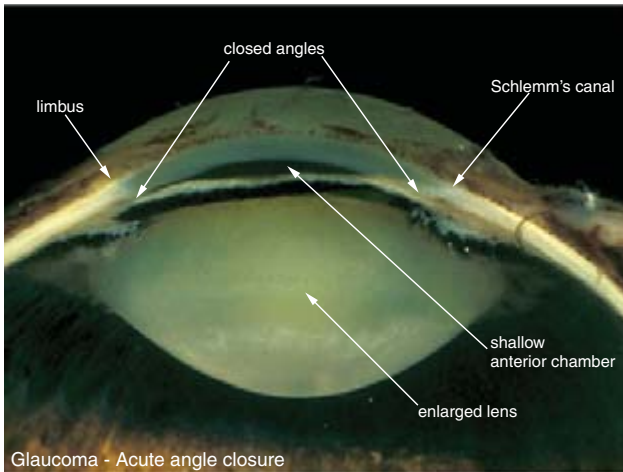


Figure 7.9

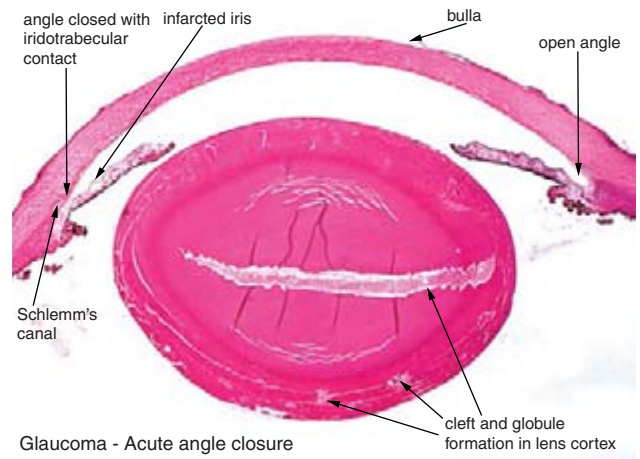
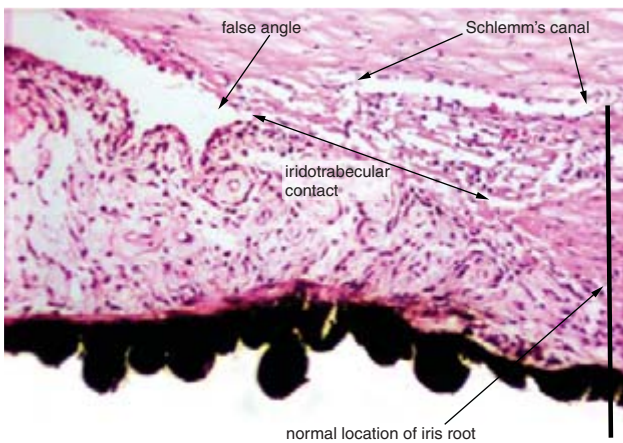
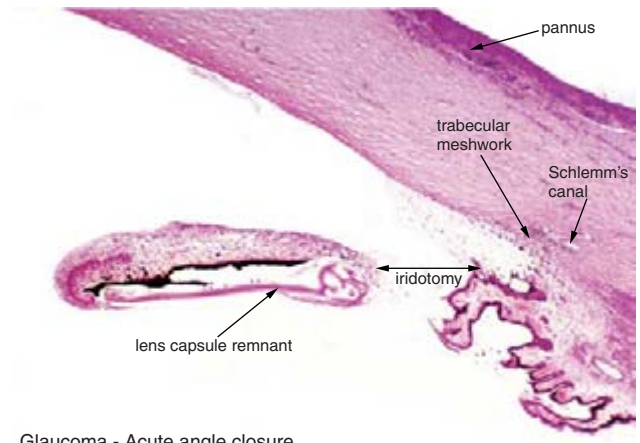


Figure 7.10



Glaucoma - Acute angle closure

Figure 7.11



Glaucoma - Acute angle closure
YAG laser iridotomy

Figure 7.12

Figure 7.9 This enucleated globe is used to illustrate an enlarged lens with pupil block and angle closure. The cornea is opaque secondary to corneal oedema and the surface is irregular due to bulla formation. NB: Enucleation is not the current treatment for acute angle closure in our institution – this is an archival case!

Figure 7.10 A low-power micrograph of the anterior segment in angle closure glaucoma demonstrates the effects of an enlarged lens and pupil block which has closed off one angle. The lens substance contains clefts and globules which are forming in the cortex and the nucleus. The result of corneal oedema is the separation of the epithelium with bulla formation. An acute rise in intraocular pressure leads to infarction of the iris stroma and the dilator pupillae – hence the irregular pupil seen clinically.

Figure 7.11 A false angle is formed when the iris stroma comes in contact with the trabecular meshwork in the case of early angle closure. The abnormal iris displacement is evident when this figure is compared with Figure 7.3. When the same line is drawn from the posterior limit of Schlemm's canal through the scleral spur, it is evident that the true angle is completely occluded.

Figure 7.12 A patient developed acute raised intraocular pressure from angle closure glaucoma which did not improve with YAG laser iridotomy. Extracapsular lens extraction was carried out which was later complicated by postaphakic corneal decompensation (bullous keratopathy). Unfortunately, the patient reported late in the development of the disease and had irreversible loss of vision: an enucleation was performed for comfort.

Macroscopic

In an enucleated globe, exfoliation substance appears as fluffy white material on the surfaces of the zonular fibres (Figures 7.13, 7.14).

For a globe to be enucleated, it is likely that the disease will be manifest as longstanding glaucoma and its associated complications (for example trabeculectomy, central retinal vein occlusion, or complicated cataract surgery).

Microscopic

In an H&E preparation, the irregular clumps of exfoliation substance have a pink amorphous appearance (Figure 7.15). Staining with PAS is not strong but is positive (Figure 7.15, inset).

In the iris, the site of deposition is on both surfaces and within the walls of blood vessels (Figure 7.16). The pigmented epithelium has a characteristic “saw-toothed” appearance, although in the peripupillary region it is often atrophic. It is thought that this atrophy is secondary to contact abrasion with the exfoliative material on the lens surface (Figure 7.17).

In the trabecular meshwork, the material is located on the inner surface of the uveal layer, in the outer part of the corneoscleral layer and is concentrated in the juxtacanalicular layer (Figure 7.18). Pigment deposition is seen in the trabecular meshwork; the melanin granules are liberated by rubbing of iris pigmented epithelium on the irregular anterior lens surface.

Immunohistochemistry

Immunohistochemistry and immunolabelling have identified a remarkable number of constituents mainly of basement membrane type (for example laminin, fibrillin, elastin, amyloid-P component, fibronectin, and vitronectin).

Special investigations/stains

The ultrastructural appearance of exfoliation substance is characteristic and consists of fine fibrillogranular material.

Pigment dispersion syndrome (PDS)/pigmentary glaucoma (PG)

In some individuals, there is a predisposition to dispersion of iris pigment from the iris pigmented epithelium (pigment dispersion syndrome – PDS). This typically occurs in 30 year olds and the quantity of pigment released decreases with age. Phagocytosis of melanosomes by the trabecular endothelial cells may lead to obstruction of aqueous outflow and glaucoma (pigmentary glaucoma – PG) in approximately one third of cases and usually within 15 years of presentation.

Clinical presentation

Gender In PDS, the male to female ratio is equal whereas in PG, the male to female ratio is 3 : 1.

Pigment dispersion syndrome The following signs are found:

- 1 Krukenberg spindle – deposits of melanin pigmentation in a vortex pattern on the posterior surface of the cornea reflecting aqueous circulation.
- 2 Iris transillumination defects – radially arranged in the midperipheral region. The iris is described as posterior bowing with a deep anterior chamber.
- 3 Darkly staining trabecular meshwork – from melanin deposition.

Pigmentary glaucoma The signs in PG are similar to PDS but, in addition, these signs include a raised intraocular pressure and glaucomatous nerve damage.

Figure 7.13 Exfoliation substance can be identified in the anterior segment of an enucleated globe (for choroidal melanoma) by the presence of white fluffy material within the zonular fibres and on the anterior surface of the lens. There is a pericentral circular clear zone on the lens surface due to abrasion by the iris. Note the patchy pigmentation of the trabecular meshwork.

Figure 7.14 Previous extracapsular cataract surgery was attempted in this eye with the complication of zonular dialysis, which necessitated intracapsular cataract surgery, and the eye was left aphakic. It is possible to identify exfoliation substance on the posterior surface of the iris. The iris pigment epithelium is deficient in the peripupillary region, most probably secondary to previous contact abrasion with the exfoliation substance on the anterior surface of the lens. A peripheral iridectomy suggests the presence of a previous trabeculectomy.

Figure 7.15 Exfoliation substance appears as pink amorphous material on the surface of the ciliary processes and zonular fibres. Clumps of the material are

present on the anterior surface of the iris. On the posterior surface, the material causes “saw-toothed” distortions of the peripheral iris pigment epithelium (H&E). The inset (PAS stain) shows the linear deposits of exfoliation substance on a zonular fibre.

Figure 7.16 In addition to deposition on the anterior and posterior surfaces of the iris, exfoliation substance can be identified in the walls of the small iris vessels. Contact with the anterior lens surface and the exfoliation substance results in the disruption of continuity of the pigmented epithelium, which otherwise has a “saw-toothed” appearance.

Figure 7.17 The deposits of exfoliation substance on the anterior surface of the lens adopt a “tree-like” configuration. The material stains weakly with the PAS stain and contains melanin pigment derived from the iris pigment epithelium.

Figure 7.18 Aqueous outflow is impeded by deposits of exfoliation substance on the inner surface of the meshwork and in the region of Schlemm’s canal. The canal of Schlemm is replaced by fibrovascular tissue.

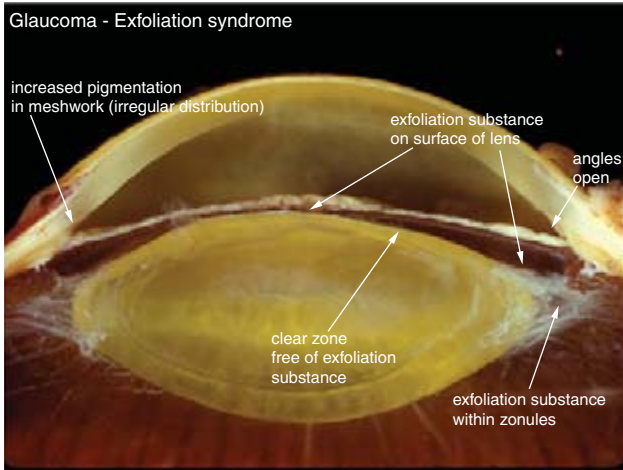


Figure 7.13

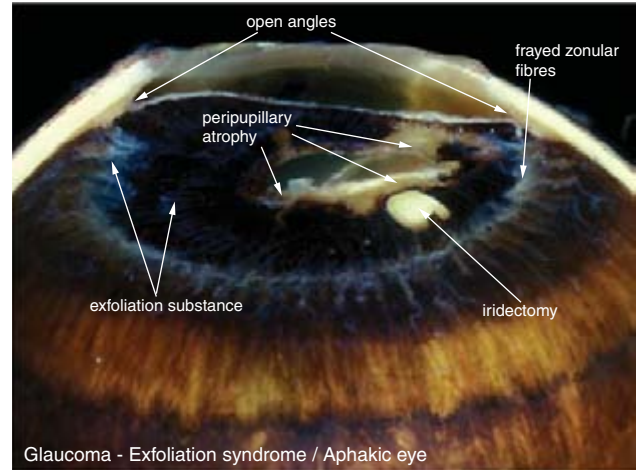


Figure 7.14

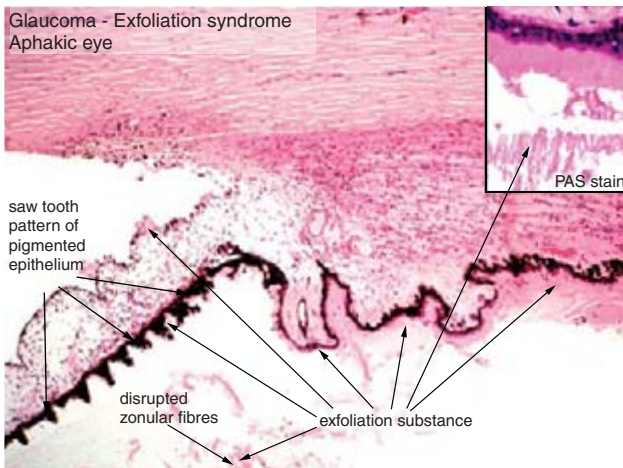


Figure 7.15

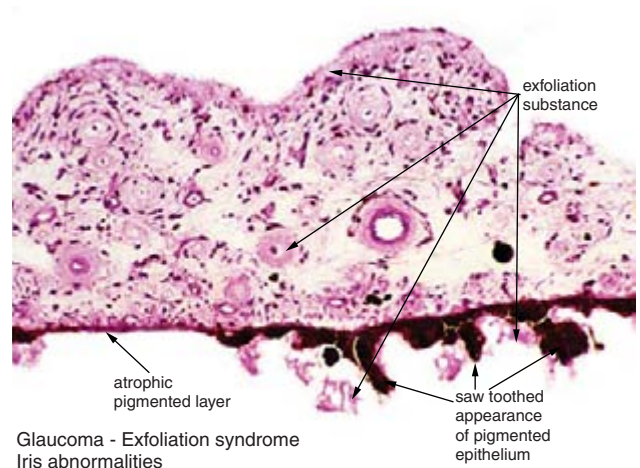


Figure 7.16

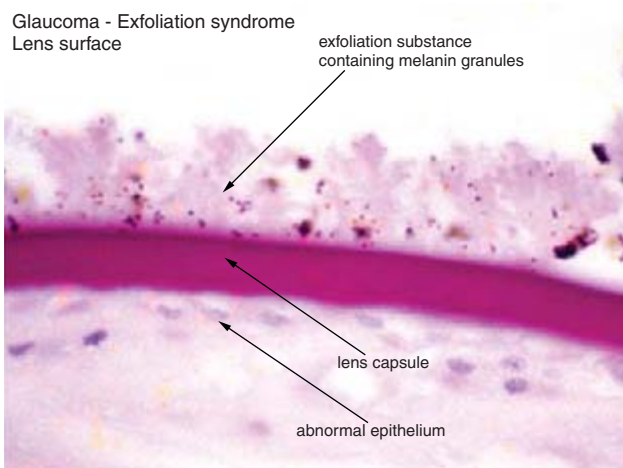


Figure 7.17

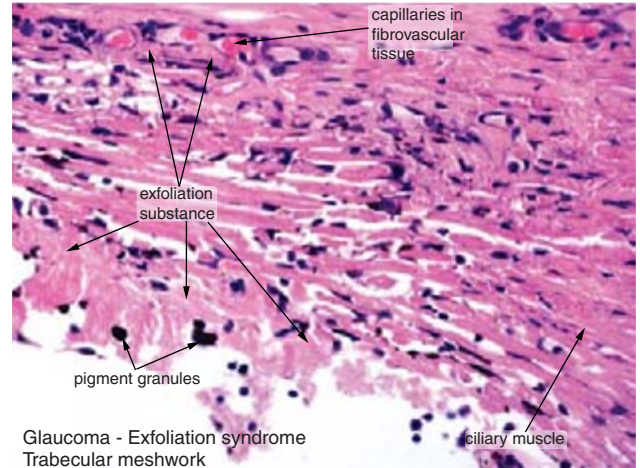


Figure 7.18

Pathogenesis

The mechanical theory suggests that in individuals with pigment dispersion there is a posterior bowing of the iris resulting in a zonule-iris rub. Reverse pupil block occurs in these eyes and may be responsible for this posterior bowing. Aqueous is pumped into the anterior chamber, the pupil acts as a one-way valve and this creates the posterior movement of the peripheral iris.

Genetics

Primarily a Caucasian condition.

Possible modes of treatment

Treatment is similar to POAG if the intraocular pressure is raised. As in ES, intraocular pressure may respond temporarily to laser trabeculoplasty. Some authors propose peripheral iridotomy as a treatment for pigment dispersion syndrome to reverse the posterior bowing of the iris.

Macroscopic and microscopic

The disease is most commonly studied in trabeculectomies.

Melanin pigment granules are phagocytosed by trabecular endothelial cells, which become swollen and eventually disintegrate (Figure 7.19).

Lens-related glaucoma

Degenerative lens disease or lens abnormalities can result in several forms of glaucoma:

- 1 A hypermature swollen cataract may lead to pupil block and secondary unilateral angle closure glaucoma (phacomorphic glaucoma). The pathology is similar to that described for primary angle closure glaucoma.
- 2 Liquefaction of the lens cortex may lead to the release of particulate material into the anterior chamber which blocks the trabecular meshwork (lens particle glaucoma). As an alternative, a macrophagic response to liquefied

lens matter fills the anterior chamber with swollen mononuclear cells which obstruct the outflow system (phacolytic glaucoma).

This section will describe phacolytic glaucoma.

Clinical presentation

A patient with a hypermature cataract is at risk of glaucoma secondary to the release of liquefied cortical material through an intact or ruptured lens capsule. The rise in pressure is acute and the deep anterior chamber contains floating white particles that may coalesce to form a pseudohypopyon.

Possible modes of treatment

After stabilisation of the intraocular pressure, surgical removal of the cataract and an anterior chamber washout is required.

Macroscopic

Although rare in developed countries, some neglected cases provide the opportunity to study phacolytic glaucoma. The sclerotic nucleus, within a capsular bag, which may or may not contain liquefied cortical material, can be identified easily (Figures 7.20, 7.21).

Microscopic

Macrophages containing lens matter can be found in an aqueous tap in phacolytic glaucoma (Figure 7.22). The original liquefied cortex may not be apparent in an H&E section (Figure 7.23). The macrophages accumulate on the anterior surface of the iris and in the inner layer of the trabecular meshwork blocking the intertrabecular spaces (Figures 7.24–7.26).

The macrophages label with appropriate markers (for example CD68).

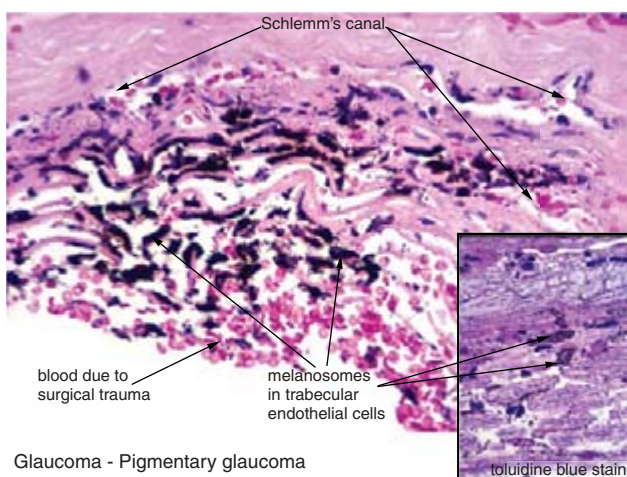


Figure 7.19

Figure 7.19 Melanin pigment granules are phagocytosed by trabecular endothelial cells and intracytoplasmic accumulation, if excessive, reduces the facility of outflow and a trabeculectomy may be required. The surgical procedure causes distortion of the trabeculae and may be complicated by haemorrhage, as in this case. The inset is taken from a plastic embedded semi-thin section to show detail of the melanosomes within the endothelial cells.

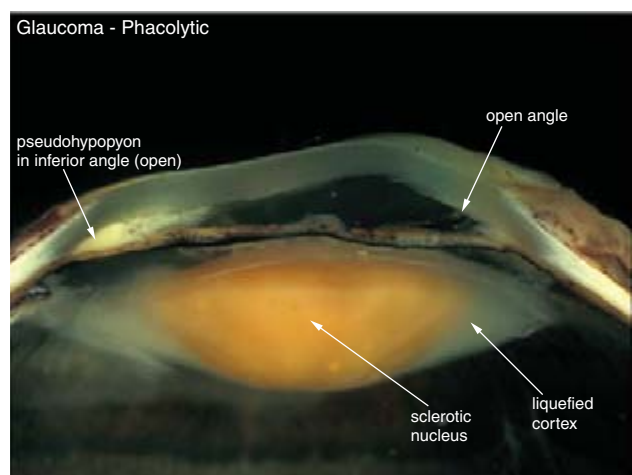


Figure 7.20

Figure 7.20 One form of lens degeneration is manifest as a persistent sclerotic nucleus within a liquefied cortex. The proteinaceous material, in liquid form, has leaked through the capsule and was in sufficient quantity to accumulate in the anterior chamber inferiorly to form a pseudohypopyon.

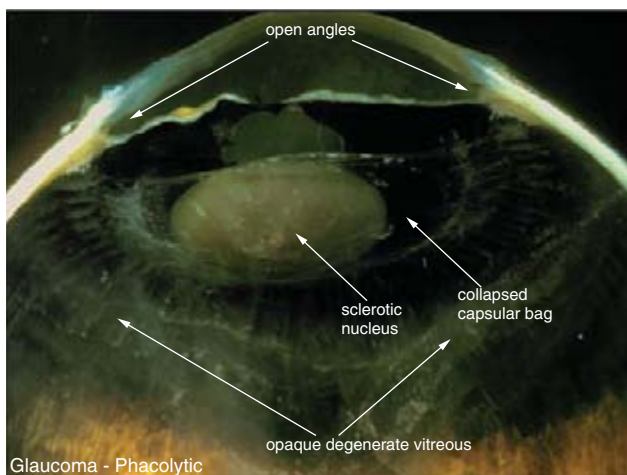


Figure 7.21

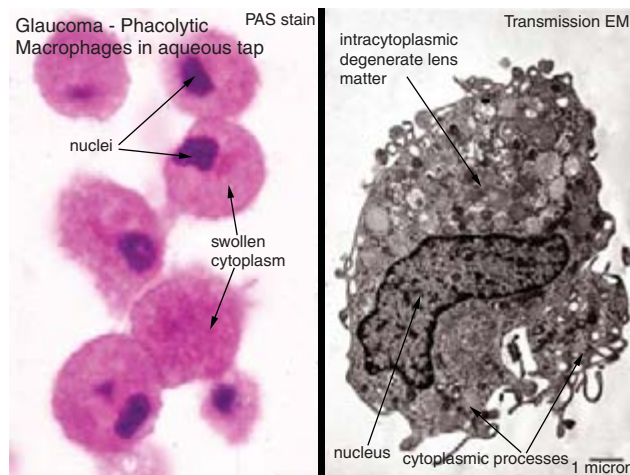


Figure 7.22

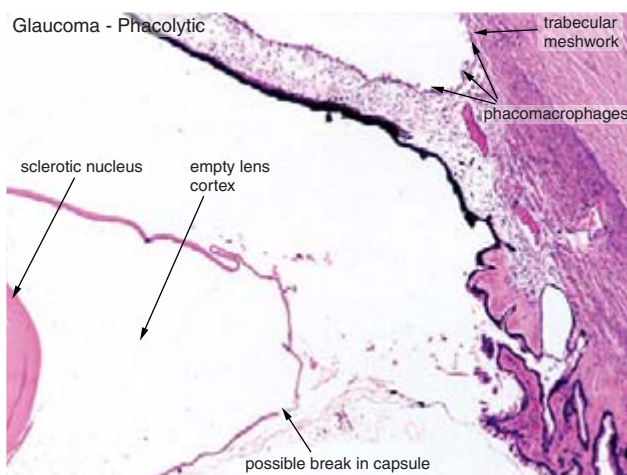


Figure 7.23

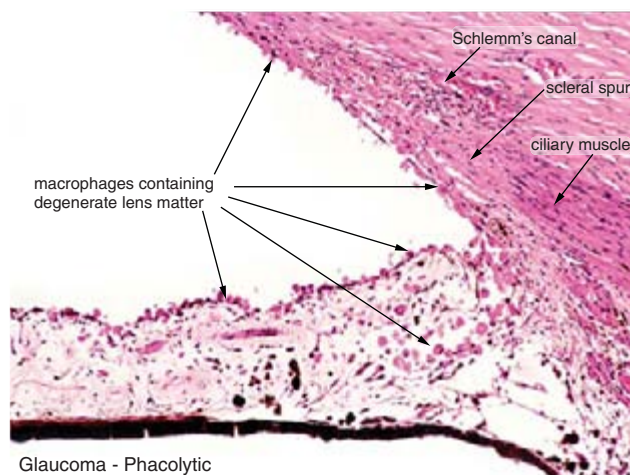


Figure 7.24



Figure 7.25

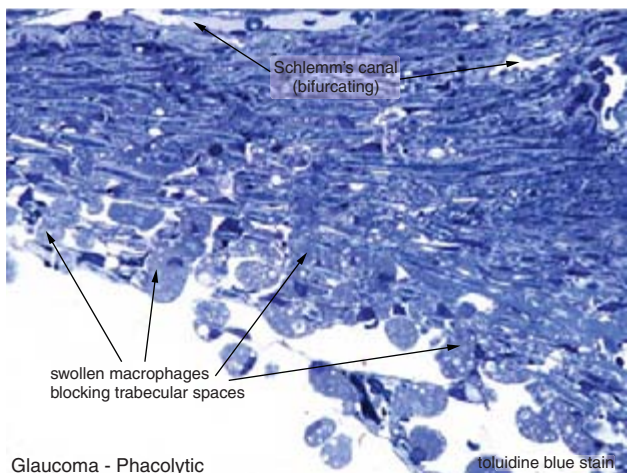
Figure 7.21 In this example of phacolytic glaucoma, a sclerotic nucleus lies within a collapsed capsular bag following the escape of liquefied cortical lens matter. The liquefied material presumably has escaped into the anterior chamber and passed through the outflow system.

Figure 7.22 In phacolytic glaucoma, an aqueous tap will identify swollen macrophages containing degenerate lens matter staining pink with the PAS stain (left). At the ultrastructural level (right), the granular vesicular structures within the cytoplasm are identical in appearance to the cytoplasmic and cell membrane fragments seen in disintegrating lens fibres in a cataract.

Figure 7.23 A low power view of the anterior segment of a case of phacolytic glaucoma reveals collapse of the capsule around a persistent sclerotic nucleus. Phacomacrophages are identified with difficulty at this level of magnification.

Figure 7.24 Pink staining, round macrophages are present in the iris stroma on the anterior surface of the iris and the inner surface of the trabecular meshwork where they are inconspicuous.

Figure 7.25 Scanning electron microscopy shows the true extent of phacomacrophage accumulation in the chamber angle in phacolytic glaucoma. It is difficult to identify the intertrabecular spaces as the cells are plugging every available opening.



Glaucoma - Phacolytic

Figure 7.26

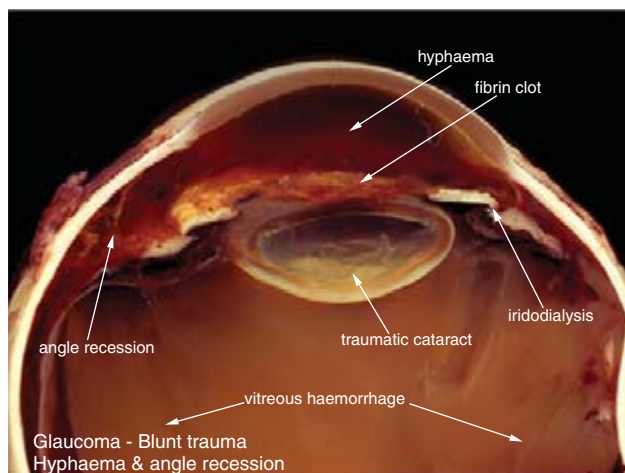
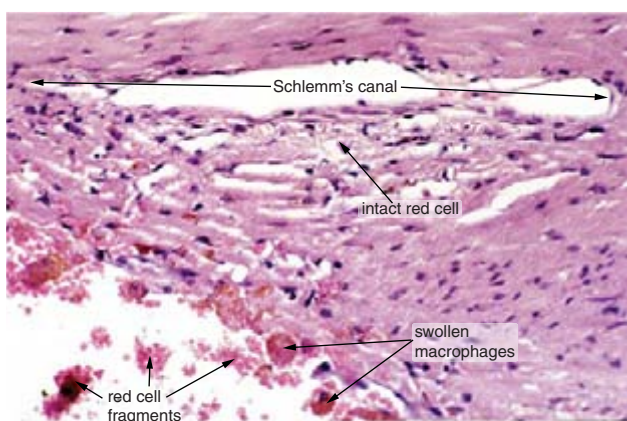


Figure 7.27



Glaucoma - Blunt trauma
Hyphaema

Figure 7.28

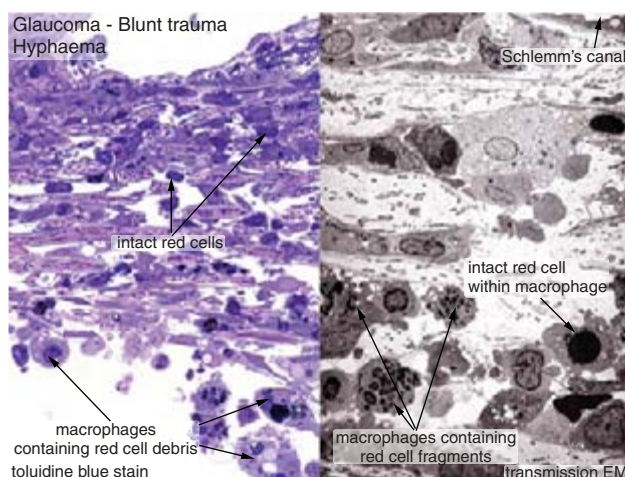


Figure 7.29

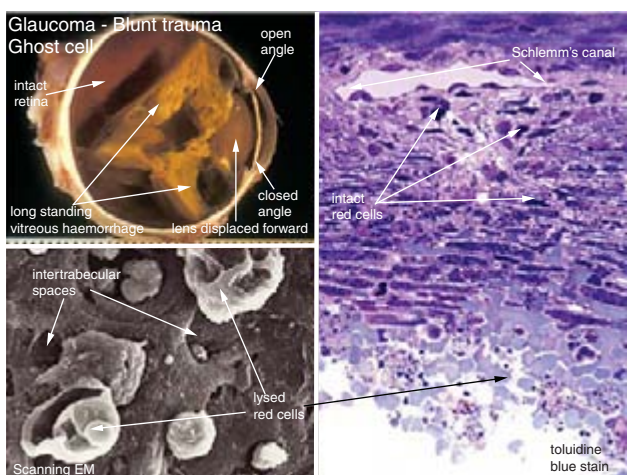


Figure 7.30

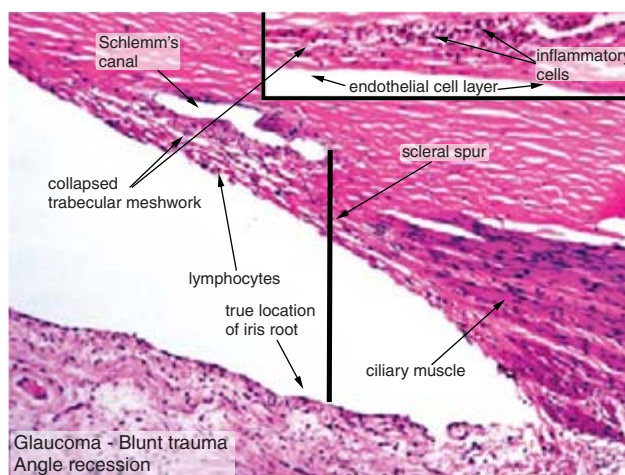


Figure 7.31

Post-traumatic glaucoma

Blunt and penetrating trauma can produce a variety of injuries that lead to acute or chronic glaucoma, but the following are the most common:

- 1 Bleeding (hyphaema) can result from a tear in the peripheral iris (iridodialysis) or separation of the ciliary body from sclera (cyclodialysis).
- 2 A tear into the anterior face of the ciliary body leads to separation and retraction of the ciliary muscle and leaves a large recess (angle recession). Figure 7.27 illustrates both 1 and 2.
- 3 An epithelial downgrowth via a corneal or limbal wound can form a membrane on the inner surface of the trabecular meshwork.

Angle recession and epithelial downgrowth are secondary glaucomas which are difficult to treat.

Hyphaema

Exposure of the trabecular meshwork to blood products in excess leads to obstruction of aqueous outflow. The acute effects are mechanical and occur because macrophages and lysed red cells are unable to penetrate the intertrabecular spaces (Figures 7.28, 7.29). The trabecular endothelial cells phagocytose the red cell residues and the resultant accumulation of iron from haem breakdown (siderosis) is toxic. The endothelial cells degenerate and eventually fibrous replacement contributes to outflow obstruction.

Ghost cell glaucoma

If the anterior vitreous face remains intact, a vitreous haemorrhage is incarcerated and red cells are lysed progressively for many weeks. A spontaneous or traumatic rupture of the vitreous face releases lysed red cells into the anterior chamber and these rigid swollen (ghost) cells are unable to pass through the trabecular interspaces, resulting in an acute rise in intraocular pressure (Figure 7.30). A vitrectomy in addition to an anterior chamber washout is required for treatment.

Angle recession

The inner uveal layer of the trabecular meshwork is supported by the oblique and circular layers of the ciliary muscle. At this potential point of weakness, shockwave movement from blunt trauma on the iris root can result in the formation of a split in the ciliary body (Figure 7.31). The consequence is a posterior displacement of the iris root and collapse of the trabecular meshwork. The migration of corneal endothelial cells across the inner surface of the trabecular meshwork and the subsequent formation of a secondary Descemet's membrane play a part in traumatic outflow obstruction. In early trauma, there may be infiltration by lymphocytes, particularly if there is an anterior uveitis, and this may explain an acute rise in intraocular pressure.

Figure 7.26 A thin plastic section (toluidine blue stain) provides better detail of the extent of infiltration by macrophages into the uveal and corneoscleral layers of the meshwork. The cells are large and have a foamy vesiculated cytoplasm and an eccentric nucleus.

Figure 7.27 In this specimen, blunt trauma caused anteroposterior compression of the corneoscleral envelope. On one side, the iris root has separated from the ciliary body (iridodialysis). On the other side, there is a complete tear in the face of the ciliary body (angle recession). The anterior chamber is completely filled with blood. There is also blood in the vitreous and the lens is cataractous.

Figure 7.28 In prolonged hyphaema, the inner surface of the meshwork is lined by the breakdown products of blood and macrophages. The intertrabecular spaces of the uveal layer are blocked. There is little penetration into the corneoscleral layer, where the intertrabecular spaces are patent.

Figure 7.29 Two mechanisms can lead to obstruction of the outflow system after prolonged haemorrhage. Large macrophages filled with red cell debris are unable to pass through the intratrabecular spaces: intact red cells are malleable

and pass easily through the trabecular meshwork (left – plastic section, toluidine blue stain). Transmission electron microscopy shows that the macrophages containing the red cell debris are confined to the corneoscleral layer (right).

Figure 7.30 A longstanding haemorrhage in the vitreous adopts a yellow appearance ("ochre membrane" – upper left) and an abrupt release of lysed red cells causes an acute obstruction to aqueous outflow (ghost cell glaucoma). The toluidine blue stained section (right) shows a thick layer of lysed red cells on the inner surface of the trabecular meshwork. These inflexible swollen cells (scanning EM, bottom left) are too large to pass through the intertrabecular spaces.

Figure 7.31 Recognition of a recessed angle is aided by the identification of Schlemm's canal and the scleral spur. A vertical line drawn through these two structures should end at the iris root. In this example, there is a tear into the anterior face of the ciliary body. The trabecular meshwork is collapsed. The inset shows a later stage of trabecular collapse when the compressed tissue is lined by an endothelial layer (derived from corneal endothelial cells) and a thin secondary Descemet's membrane.

Epithelial downgrowth

Any form of perforating trauma through the cornea or limbus, whether surgical or civil, may be complicated by epithelial migration especially if the wound edges are not accurately opposed (Figure 7.32). Cells resembling corneal or conjunctival epithelium migrate easily over the posterior corneal surface, trabecular meshwork, iris stroma, and onto the vitreous face (Figure 7.33).

Neoplastic

Melanomas of the iris can infiltrate the trabecular meshwork leading to a secondary glaucoma (Figure 7.34; see Figure 11.5). Infiltration can proceed as far as Schlemm's canal and the collector channels before the onset of glaucoma. When glaucoma occurs secondary to an iris melanoma, enucleation is the sole option – filtering surgery enhances extraocular spread of the tumour.

A ciliary body melanoma can also invade the angle and spread in the anterior chamber, but glaucoma is much more likely to be due to lens displacement and pupil block with secondary angle closure (see Figures 11.9, 11.10).

A retinoblastoma may become necrotic and release a shower of viable tumour cells and tumour debris causing a pseudohypopyon, simulating an acute inflammatory process: the intraocular pressure may be raised.

Miscellaneous

Silicone oil

Silicone oil used in retinal detachment surgery can emulsify and escape as tiny globules into the upper part of the anterior chamber. The globules are rapidly ingested by macrophages, which become trapped in the intertrabecular spaces of the meshwork (Figure 7.35). The trabecular endothelial cells are also able to phagocytose very small globules. Breakdown of anterior uveal tissue with the release of melanosomes occurs in complicated end-stage globes after failed detachment surgery. This explains the presence of melanosomes in endothelial cells and macrophages (Figure 7.35). The intraocular complications of emulsification of silicone oil are described in Chapter 10.

Inflammatory (open angle): trabeculitis

Non-granulomatous inflammation in the iris secondary to chronic keratitis is complicated by lymphocytic infiltration in the trabecular meshwork (Figures 7.36, 7.37). The use of topical steroids to control the inflammation is advantageous, but paradoxically it can increase outflow resistance in individuals who are steroid responders (see “Primary open angle” section, p. 138).

A specific clinical entity with trabeculitis is seen in Fuchs' heterochromic iridocyclitis in which there is a unilateral, intermittent, low-grade iritis of unknown aetiology, associated with glaucoma, cataract, keratic precipitates, and iris heterochromia. The pathology is non-specific in both the iris and trabecular meshwork.

Figure 7.32 After a routine cataract extraction, there was a prolonged dehiscence in the corneal wound and this provided an opportunity for the corneal epithelium to migrate into the anterior chamber. The epithelium extends across the angle onto the iris surface. The absence of goblet cells in the epithelial downgrowth indicates a corneal epithelial origin as opposed to a conjunctival origin.

Figure 7.33 In this example, the epithelial downgrowth lines the iris and the anterior vitreous face in an aphakic eye.

Figure 7.34 A low power micrograph showing ring spread of a poorly cohesive iris melanoma. In this example, the tumour lines the inner surface of the meshwork and has spread onto the posterior surface of the cornea and the anterior surface of the iris. The inset shows the macroscopic appearance of ring spread in an iris melanoma.

Figure 7.35 Silicone oil globules in the trabecular meshwork are seen as empty spaces in a paraffin section (left). The location of oil droplets within the macrophages and endothelial cells is better demonstrated in an electron micrograph (right). This figure is taken from an eye in which there were many secondary complications following retinal detachment surgery including breakdown of iris pigment epithelium. This explains the presence of numerous melanin granules within the macrophages.

Figure 7.36 An inconspicuous lymphocytic infiltrate in the outflow system may obstruct aqueous drainage and lead to secondary open angle glaucoma. A detail of the cells in the trabecular meshwork is shown in Figure 7.37.

Figure 7.37 The small size of the lymphocytes permits easier infiltration of the trabecular meshwork. This explains the greater density of lymphocytes in the corneoscleral and juxtacanalicular layers. Compare this with a macrophagic infiltration (see Figures 7.26, 7.28).

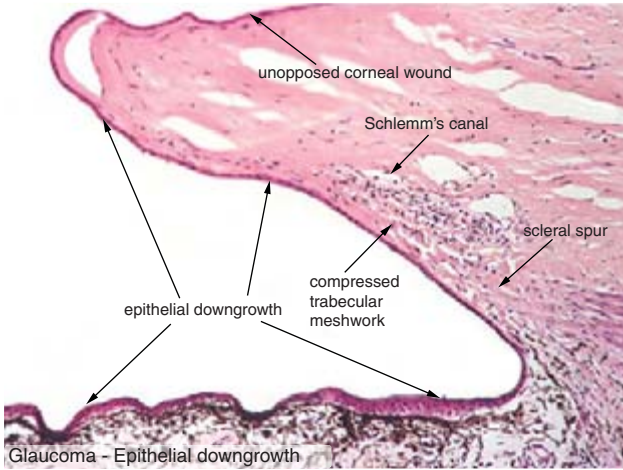


Figure 7.32

Glaucoma - Epithelial downgrowth

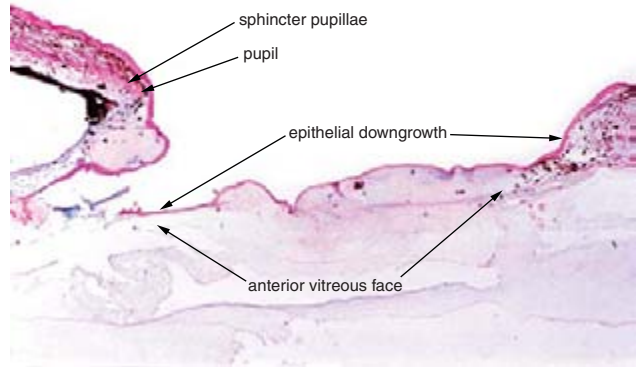


Figure 7.33

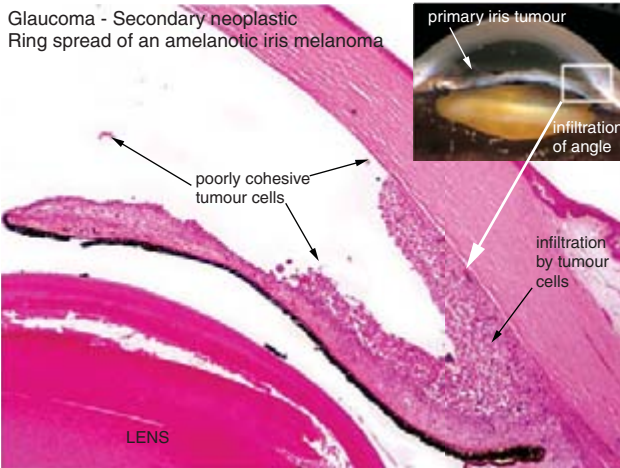


Figure 7.34

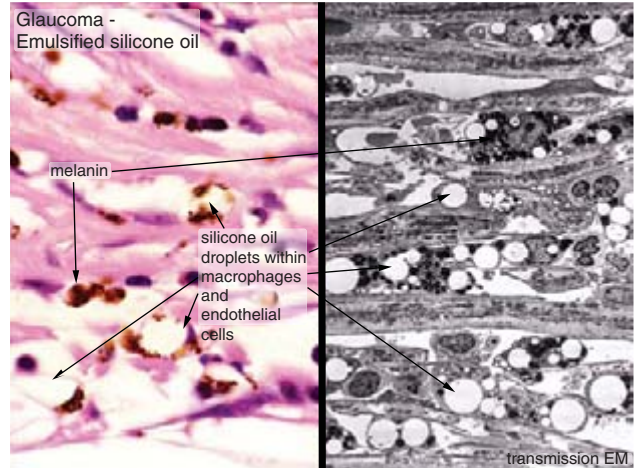


Figure 7.35

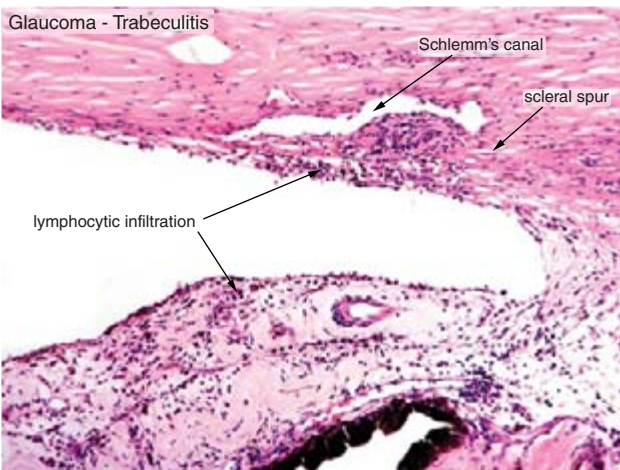


Figure 7.36

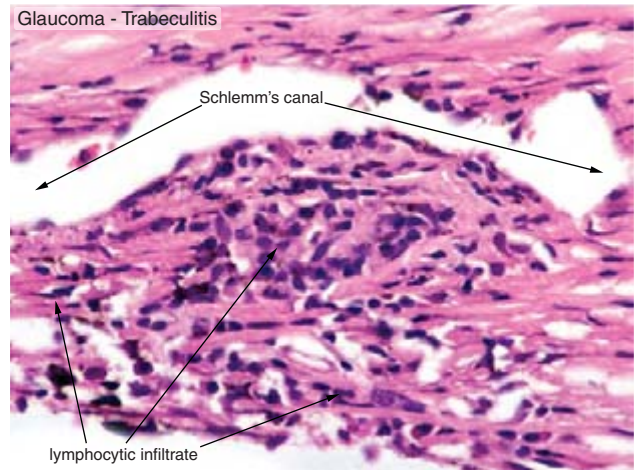


Figure 7.37

Secondary closed

Neovascular

Neovascular glaucoma is commonly seen in enucleation specimens.

Clinical presentation

Early

- 1 The development of neovascularisation first occurs in the angle and this can be seen by gonioscopy; later new vessels are seen on the anterior iris surface.
- 2 The initial pressure rise is due to a neovascular membrane on the inner surface of the trabecular meshwork.

Late

- 1 Contraction of the fibrovascular tissue in the angle leads to iridotrabecular and iridocorneal contact. Gonioscopy reveals closed angles.
- 2 Fibrovascular proliferation on the iris surface rotates the pupil margin forward so that the pigmented epithelium is visible (ectropion uveae).
- 3 There may be evidence of glaucomatous decompensation in the cornea (see "Tissue effects" below).
- 4 A primary cause for ischaemia must always be sought (for example for central retinal vein occlusion or diabetes).

Pathogenesis

Any process which leads to the release of vascular endothelial growth factor (VEGF) into the aqueous could potentially cause neovascularisation of the iris. The sub-categories of possible sources of VEGF are:

- 1 Ischaemic tissue: for example central retinal vein occlusion, diabetic retinopathy, and prolonged retinal detachment.
- 2 Neoplasia: for example intraocular melanomas or retinoblastomas.
- 3 Inflammation: prolonged uveitis of any cause.

Possible modes of treatment

This depends on the primary disease, but the following options are available:

- 1 Removal of cause: for example panretinal photocoagulation of an ischaemic retina.
- 2 Medical treatment for inflammation and glaucoma.
- 3 Ciliary body ablation.
- 4 Surgical treatment by drainage procedures with or without setons.
- 5 Enucleation of the painful blind eye for comfort.

Macroscopic

In an enucleation specimen the following changes may be identified (Figure 7.38):

- bullous keratopathy
- peripheral corneal pannus
- ectropion uveae
- cataract
- retinal changes relevant to vascular disease or tumour.

Microscopic

It is important to appreciate that the neovascular membrane consists of small capillaries and fibroblasts. At the earliest stage, the capillaries and fibroblasts are identified on the iris surface and on the inner surface of the trabecular meshwork (Figure 7.39). Fibroblasts proliferate in the chamber angle and subsequently contract to pull the peripheral iris towards the meshwork (Figure 7.40).

The angle eventually closes and the peripheral iris comes into contact with the cornea (Figure 7.41). Contraction of the fibrovascular membrane on the iris surface results in flattening. NB: Any loss of normal iris folds or the presence of ectropion uveae should alert the examiner to the possibility of neovascularisation.

In some cases, the corneal endothelium migrates across the surface of the neovascular membrane (Figure 7.42).

Pathological evidence of treatment

Evidence of surgery or laser as described above, especially pan-retinal photocoagulation (see Figure 10.48).

Tumour

Mechanical displacement of the iris and lens by tumours of the ciliary body, choroid and retina can lead to a pupil block (see Figures 11.9, 11.10, 11.33, 11.43).

Uveitis/inflammation

In inflammation of the anterior uvea, release of a sticky fibrinous exudate promotes the formation of peripheral anterior and central posterior synechiae with resultant secondary angle closure glaucoma. With prolonged inflammation, neovascularisation may also contribute to a rise in intraocular pressure (see above).

Trauma

With civil or surgical trauma involving decompression and perforation of the cornea or limbus, hypotonia and reactionary fibrosis result in anterior synechia formation.

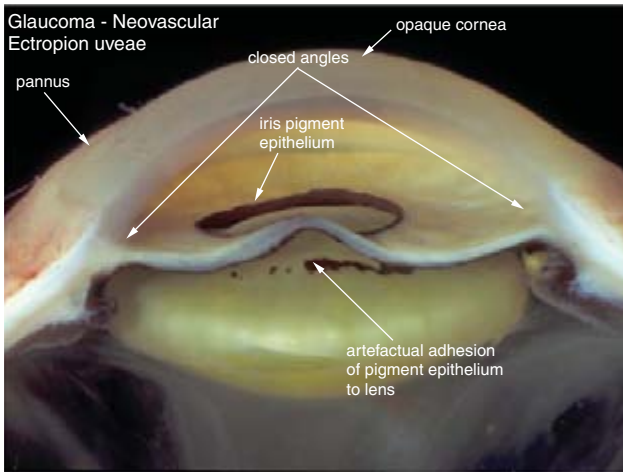


Figure 7.38

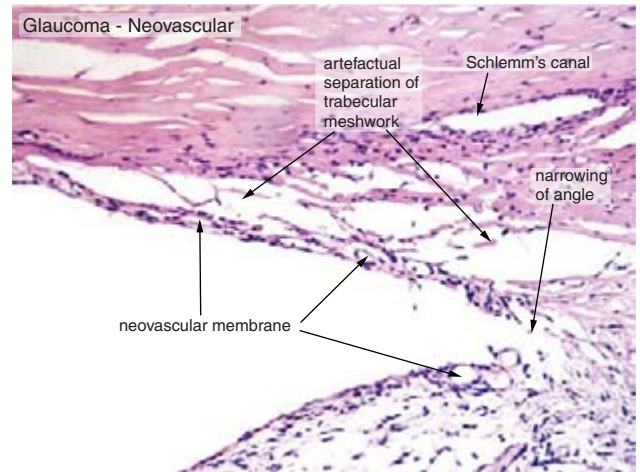


Figure 7.39

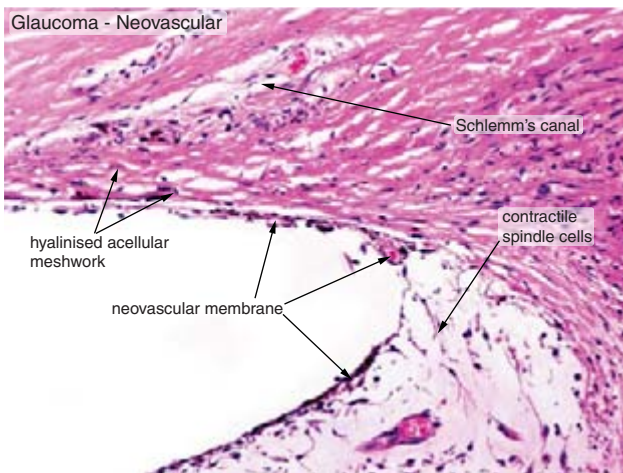


Figure 7.40

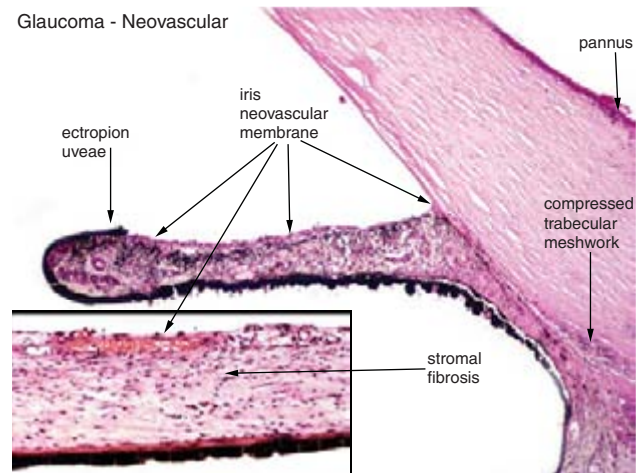


Figure 7.41

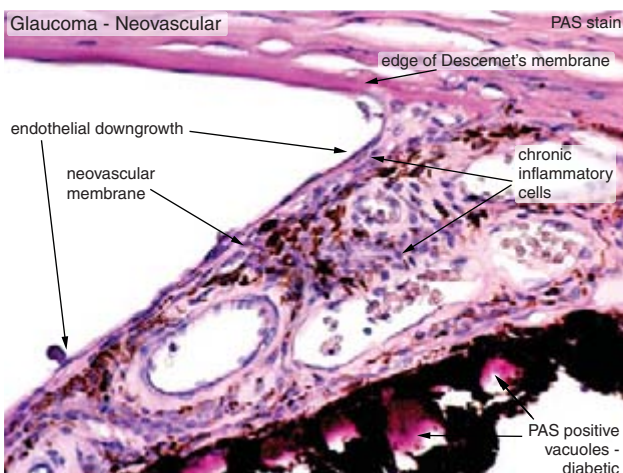


Figure 7.42

Figure 7.38 The macroscopic appearance of the anterior segment in neovascular glaucoma. The iris surface is smooth and the angles are closed. The pigment epithelium of the iris is retracted around the pupil (ectropion uveae). Pigmentation on the lens surface is artefactual but, *in vivo*, occurs in inflammation in the anterior segment.

Figure 7.39 In early neovascular glaucoma, the aqueous outflow is obstructed by a layer of fibrovascular tissue on the inner surface of the meshwork. Similar capillaries are present on the iris surface. This example shows the early stages of secondary angle closure.

Figure 7.40 As the disease progresses, the fibroblastic proliferation and contraction in the chamber angle pulls the peripheral iris forwards. The capillaries are not conspicuous in this example which emphasises the importance of the fibroblast component in angle closure.

Figure 7.41 In late neovascular glaucoma, there is a layer of fibrovascular tissue between the iris stroma and the cornea, the angle is closed, and an ectropion uveae is easily identified. On the iris surface, the neovascular membrane contains capillaries and fibroblasts (inset). The spindle-shaped fibroblasts are responsible for the tissue contraction and pupillary distortion. Note that the iris stromal surface is smooth.

Figure 7.42 In this example of the false angle in neovascular glaucoma, a layer of endothelial cells has migrated across the neovascular membrane (endothelial downgrowth). The presence of PAS-positive lakes within the iris pigment epithelium is a diagnostic feature of diabetes (PAS stain).

Treatment of glaucoma and its complications

Trabeculectomy

Pathological experience is limited to specimens in which surgical treatment of glaucoma has failed. Many procedures were devised to produce a controlled fistula and, of these, a trabeculectomy has proved to be the most commonly employed. The original recommendation was to remove a small block of tissue from the inner sclera, trabecular meshwork, and inner cornea. Currently, a more anterior approach with excision of a small block from the cornea and the anterior part of the trabecular meshwork is favoured. Drainage of aqueous is via the sub-Tenon's space.

Unsuccessful control of intraocular pressure by a fistulising procedure is usually due to fibrosis and scar tissue formation: antimetabolites (5-fluorouracil and mitomycin-C) are used to minimise this complication. Iris prolapse is rare, but bleb complications such as leakage and infection are not uncommon (Figures 7.43, 7.44).

Argon laser trabeculoplasty (ALT)

The original intention of ALT was to create a fistula through the trabecular meshwork into Schlemm's canal, but the effects resulting from this pressure lowering were short

lived due to fibrosis. Current ALT therapy uses considerably less power and the intention is to stimulate the trabecular endothelial cells. Pathological studies are rare, but in failed cases evidence of ALT is seen in the trabecular meshwork as loss of endothelial cells and fusion of trabecular beams (Figure 7.45).

Transcleral ciliary body ablation – cryotherapy and diode

Destruction of the ciliary processes by transcleral laser or cryotherapy in order to decrease aqueous production appears as areas of ciliary body depigmentation in end-stage glaucomatous eyes (Figure 7.46). In successful ablation, the ciliary processes are fragmented and fibrous tissue containing pigment-laden cells is present in the scar (Figure 7.47).

Tissue effects

While it is convenient to describe the tissue effects of glaucoma under two headings, acute (implying primary angle closure) and chronic (implying primary open angle glaucoma), there is often a considerable overlap between cause and effect.

Table 7.1 summarises the histopathological features in acute and chronic glaucoma.

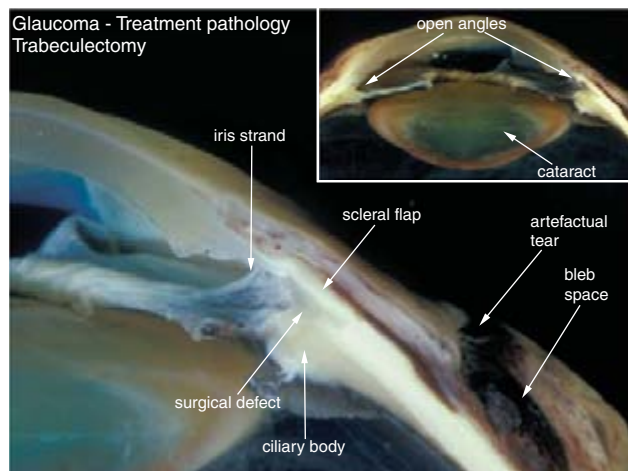


Figure 7.43

Figure 7.43 When the globe is sectioned in the correct plane, it is possible to identify the defect made during a trabeculectomy procedure. The inner limbal defect is located anterior to the ciliary body. In this example iris strands project into the defect. A bleb was present and was artefactually torn. The inset is a lower power view of the anterior segment.

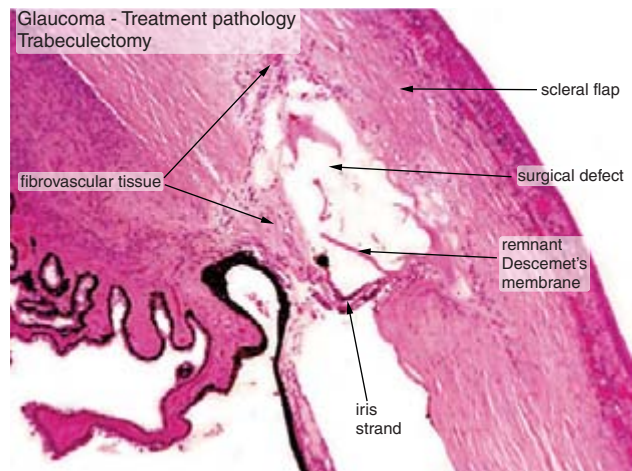
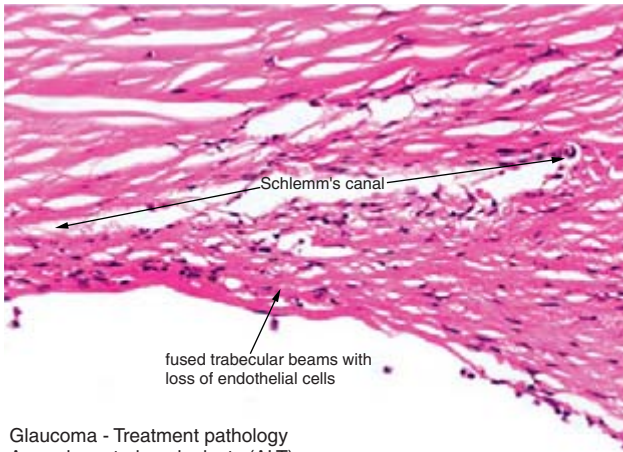


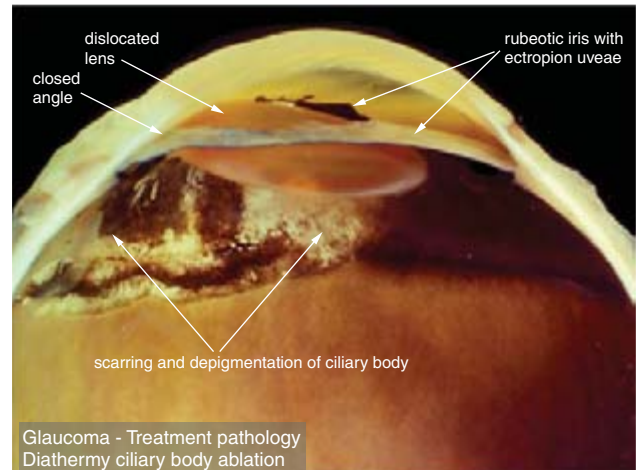
Figure 7.44

Figure 7.44 This figure illustrates some of the potential causes of failure in a trabeculectomy. Fibrovascular scar tissue has drawn the iris over the surgical defect and there is fibrovascular proliferation in the wall of the defect, which contains a strip of Descemet's membrane. The flap is fibrotic and a bleb did not form in this case.



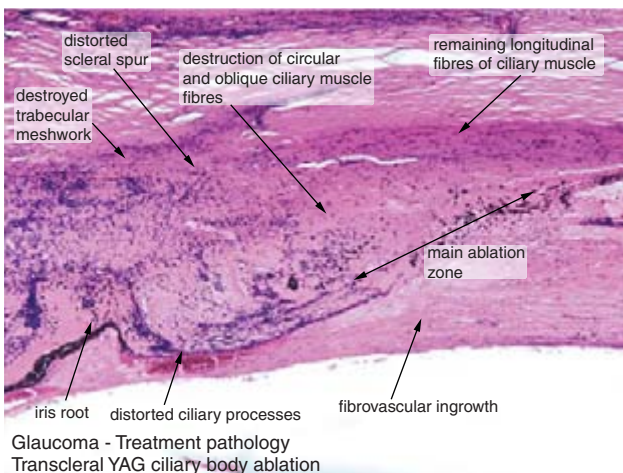
Glaucoma - Treatment pathology
Argon laser trabeculoplasty (ALT)

Figure 7.45



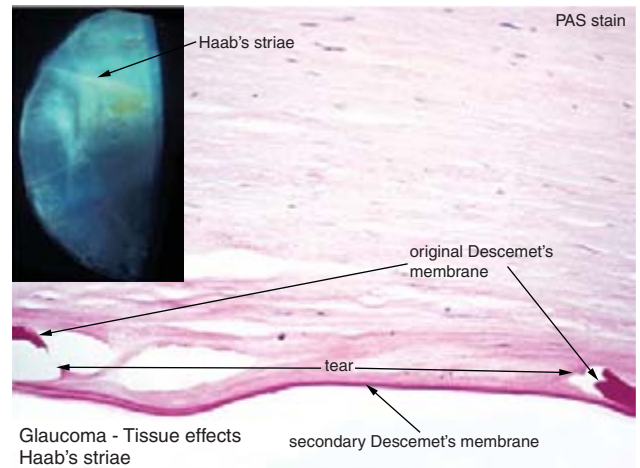
Glaucoma - Treatment pathology
Diathermy ciliary body ablation

Figure 7.46



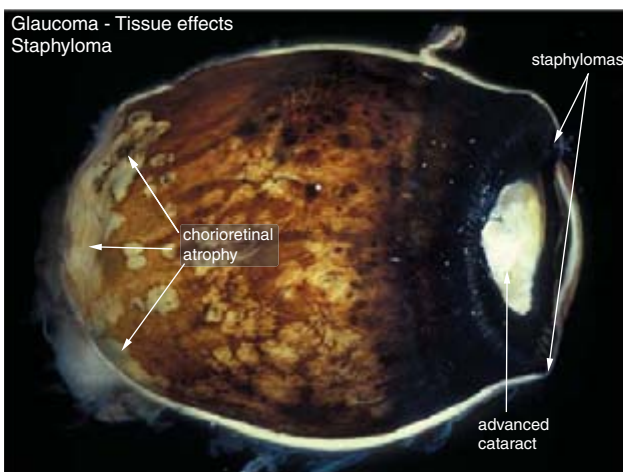
Glaucoma - Treatment pathology
Transcleral YAG ciliary body ablation

Figure 7.47



Glaucoma - Tissue effects
Haab's striae

Figure 7.48



Glaucoma - Tissue effects
Staphyloma

Figure 7.49

Figure 7.45 In this example of failure of an argon laser trabeculoplasty (ALT), there is a loss of trabecular endothelial cells and collapse of the meshwork with fusion of the beams.

Figure 7.46 The regions of diathermy ablation can be identified by areas of depigmentation.

Figure 7.47 Transcleral ablation of the ciliary body can be excessively destructive as in this example in which a YAG laser was used. The epicentre of the ablation zone was positioned too far posteriorly. However, sufficient laser energy was applied to destroy the inner layers of the ciliary muscle and the ciliary processes. An exuberant fibrovascular reaction extended across the retina.

Figure 7.48 The inset shows a hemisection of a corneal disc of a patient with a previous history of infantile glaucoma. Slit lamp microscopy shows these fine horizontal lines as tears in Descemet's membrane (Haab's striae). Microscopy of the tears confirms the defect in the original Descemet's membrane. The bare stroma is re-covered by endothelial sliding and there is subsequent formation of a secondary Descemet's membrane. The endothelium is sparse at this end stage and poorly demonstrated in a PAS section.

Figure 7.49 Elongation of the globe and chorioretinal atrophy are features of axial myopia. However, the presence of staphylomas in the region of the ciliary body (intercalary) in this case of secondary angle closure glaucoma indicates longstanding raised intraocular pressure.

Table 7.1 Summary of the histopathological features in acute and chronic (long term) glaucoma.

	Acute	Chronic
Cornea	<i>Epithelial oedema with or without bulla formation</i> (see Figure 4.7): prolonged high pressure may lead to loss of endothelium and stromal oedema	<i>Degenerative keratopathy</i> : may result if there is sufficiently high pressure (see Figures 4.8, 4.9, 4.11). This may be secondary to endothelial decompensation <i>Haab's striae</i> : a sustained rise in intraocular pressure in the neonatal or infantile eye can stretch the cornea to such an extent that linear tears occur in Descemet's membrane. The endothelium covers the bare stromal surface by sliding to form a secondary Descemet's membrane (Figure 7.48). Clinically the tears are horizontal (Figure 7.48, inset)
Sclera	–	<i>Staphylomas</i> : occur in the region of scleral canals for vessels and nerves (Figure 7.49) <i>Buphthalmos</i> : generalised stretching and thinning of the corneoscleral envelope, which is more elastic in infancy (Figure 7.50)
Iris	<i>Infarction</i> : reflex vascular spasm leads to sectorial infarction of the iris stroma and musculature. Clinically this is seen as a sluggish and irregular pupil. Histologically the infarct appears as an acellular sector with loss of muscle and atrophy of the iris pigment epithelium (Figure 7.51)	–
Lens	<i>Localised epithelial infarction (Glaukomflecken)</i> : focal necrosis of lens epithelial cells (rare pathologically) is seen as white flecks in the anterior cortex	
Retina	Macular and retinal oedema	<i>Inner retinal atrophy and gliosis</i> : retrograde atrophy of the ganglion cell layer is due to interruption of nerve fibres at the disc. Consequently, there is a marked reduction in the thickness of the inner retina and preservation of the outer retina (Figure 7.52)
Optic disc	<i>Papilloedema</i> : if the intraocular pressure rises rapidly, compression of the nerve head obstructs axoplasmic flow and widespread swelling of the prelaminar nerve fibre layer occurs (Figure 7.53)	<i>Optic disc cupping</i> : its distinctive clinical appearance is due to loss of prelaminar axonal tissue (Figures 7.54–7.57). Two main causes are implicated: (1) Mechanical pressure on the prelaminar tissue interferes with axoplasmic flow. The bowing of the lamina cribrosa distorts axons as they pass through the pores in the lamina cribrosa (2) Vascular: it is assumed that in the ageing eye there is diminished blood flow to the optic nerve head. The raised intraocular pressure may interfere with the blood flow from prelaminar capillaries which are supplied by the circle of Zinn
Choroid	Congested	Atrophic

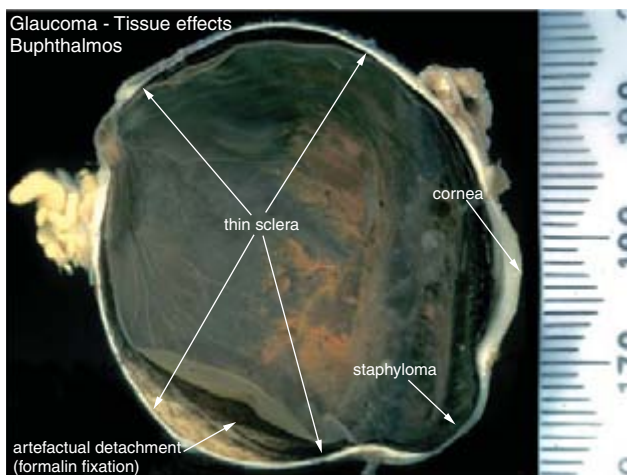


Figure 7.50

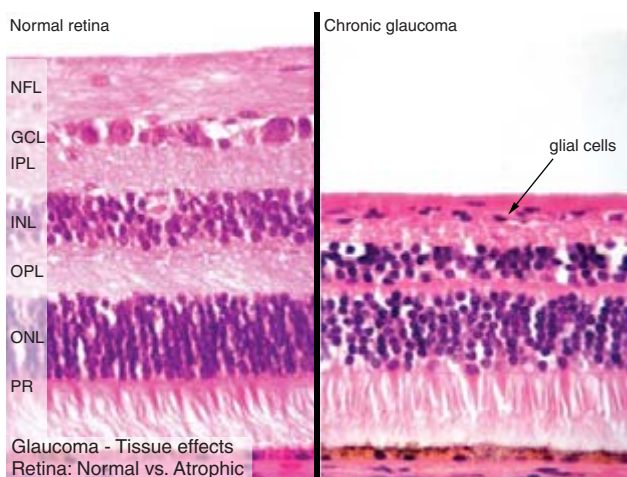


Figure 7.52

Figure 7.50 The patient had a history of a congenital cataract which was treated with lensectomy surgery in infancy. Glaucoma developed later as a complication. This is an extreme example of buphthalmos – the globe measures nearly 40 mm in diameter. Despite the generalised enlargement of the globe, a co-existing localised staphyloma has occurred.

Figure 7.51 In an infarcted sector of the iris, the stroma is acellular. Macrophages containing melanin derived from necrotic stromal melanocytes are scattered throughout the tissue. The hallmark feature of iris infarction is the loss of the dilator pupillae muscle. The pigment epithelium is disrupted or atrophic. Macroscopically (inset) the infarcted area is white.

Figure 7.52 The extent of inner retinal atrophy in longstanding glaucoma (right) is best demonstrated by comparison with normal retinal tissue (left) from a corresponding region. The thickness of the outer nuclear layer and the distribution of rods and cones in the photoreceptor layer are essentially the

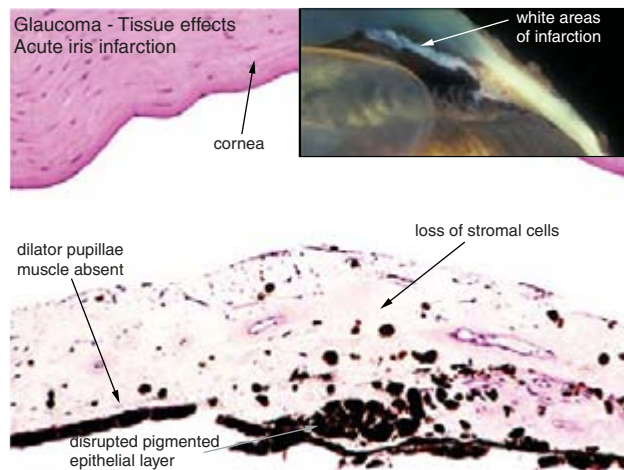


Figure 7.51

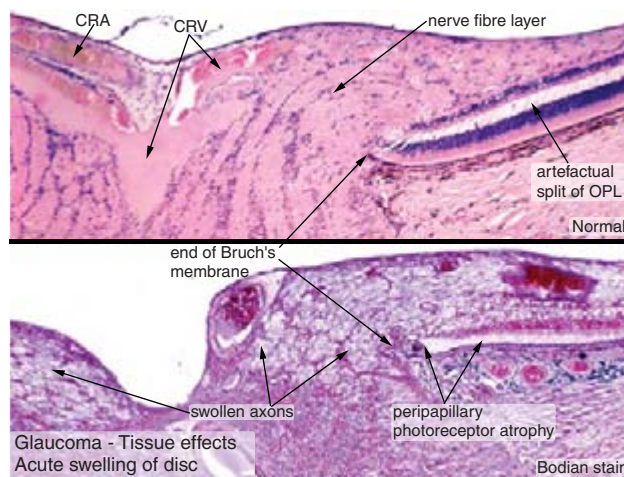


Figure 7.53

same. The striking abnormality is the absence of recognisable inner retinal layers with glial cell proliferation in the atrophic neural tissue. NFL = nerve fibre layer, GCL = ganglion cell layer, IPL = inner plexiform layer, INL = inner nuclear layer (bipolar cells), OPL = outer plexiform layer, ONL = outer nuclear layer (photoreceptor nuclei), PR = photoreceptors.

Figure 7.53 Upper: normal nerve head; lower: acute glaucoma. An acute glaucoma developed in a patient with a necrotic ciliary body melanoma and the outflow system was blocked by macrophages containing melanin granules. A rapid elevation in intraocular pressure results in optic disc swelling – this is histologically seen as swelling of the nerve fibre layer from an interruption of anterograde axoplasmic flow in the prelaminar part of the optic nerve. The Bodian stain reveals distension of axons and the swollen nerve fibre layer displaces the peripapillary photoreceptor layer. The branches of the central retinal artery (CRA) and vein (CRV) are patent. OPL = outer plexiform layer.

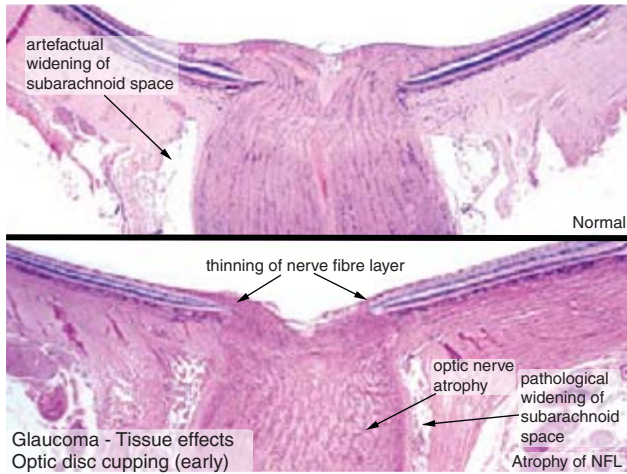


Figure 7.54

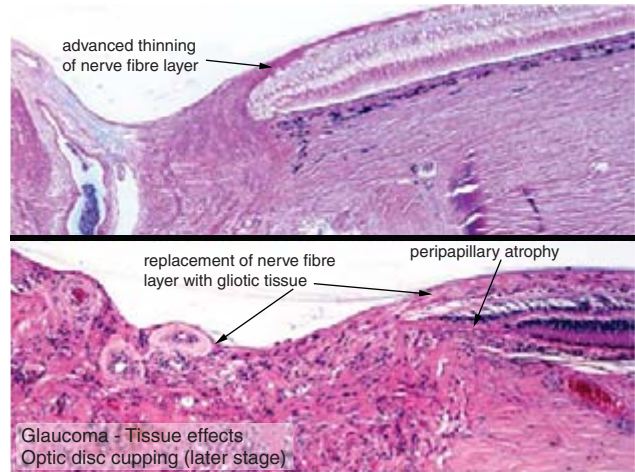


Figure 7.55

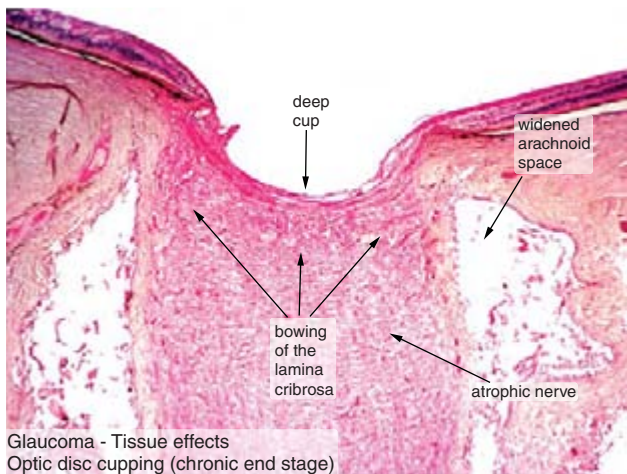


Figure 7.56

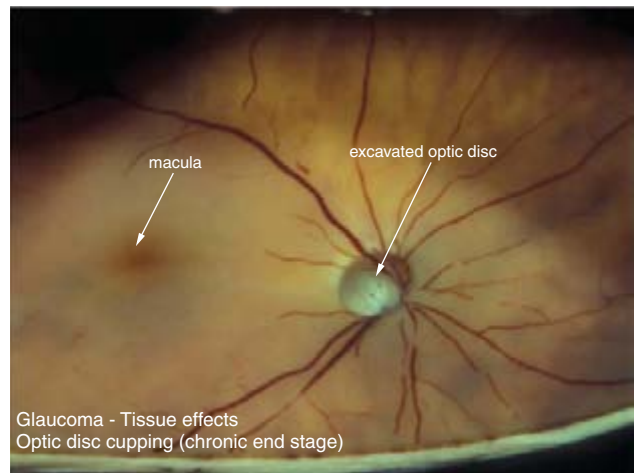


Figure 7.57

Figure 7.54 The lower figure shows early glaucomatous atrophy of the nerve fibre layer (NFL) by comparison with the normal tissue above. The optic nerve itself is atrophic because of the dropout of axonal tissue and there is enlargement of the subarachnoid space.

Figure 7.55 In the later stages of chronic glaucoma, the nerve fibre layer is extremely thin (upper). Ultimately the optic cup is filled with disorganised gliotic tissue and axonal tissue is absent in the prelaminar portion of the optic nerve (lower).

Figure 7.56 At the end stage of chronic glaucoma, the prelaminar neural tissue is absent and the lamina cribrosa is bowed. The optic nerve is atrophic and the arachnoid space is enlarged.

Figure 7.57 A pathologist's view of advanced optic disc cupping. The macula is easily identified by the presence of luteal pigment and its location within the vascular arcades.