OPHTHALMOLOGY

Lecture Notes

Bruce James
Anthony Bron

11th Edition

with website

WILEY-BLACKWELL

Ophthalmology

Lecture Notes

We dedicate this book to Chris Chew, co-contributor and our esteemed friend and colleague, who died in 2004. We valued his insightful contributions, and his company is missed.

Ophthalmology
Lecture Notes

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Companion website

This book has an accompanying website that contains all of the images in the book in Powerpoint format. It is available at:

www.wiley.com/go/james/ophthalmology

Preface to eleventh edition

Welcome to the 11th edition of *Ophthalmology Lecture Notes*! As in the past, our aim has been to make the diagnosis and management of eye disease a palatable process and once again we stress the value of a good history and careful clinical examination of the eye.

The eye is remarkably accessible. Optical and digital techniques give access to the structures of the eye at cellular level. Specular microscopy can image the corneal endothelial cells which regulate corneal hydration and transparency; digital fluorescein angiography allows the retinal capillary bed to be explored in ischaemic retinal disease; optical coherence tomography allows the layers of the retina to be dissected and confocal microscopy provides a three-dimensional view of the optic nerve head. The shape of the cornea can be plotted digitally and, outside the globe, orbital structures and the visual pathway can be viewed by neuroimaging.

Therapeutically, lasers are used to relieve acute, angle closure glaucoma, to lower ocular pressure in chronic glaucoma, to open up an opaque lens capsule following cataract surgery and to seal retinal holes. Sight-threatening diabetic retinopathy can be treated effectively by retinal photocoagulation, to remove the angiogenic stimulus to vasoproliferation. More recently it has become possible to inhibit new vessel formation in diabetic retinopathy, macular degeneration and other retinal vascular disorders by intravitreal injections of anti-angiogenic drugs.

These techniques are matched by technological innovations in microsurgery, responsible for dramatic advances in cataract and vitreoretinal surgery. Cataracts are now removed by phacoemulsification, using an oscillating ultrasonic probe, and optical function is restored by insertion of a lens which unfolds within the eye. Vitreoretinal surgery employs inert gases to flatten the detached retina and endoscopic probes which allow manipulations in the vitreous space and the dissection of microscopic membranes from the retinal surface.

Despite these advances, most ophthalmic diagnoses can still be made from a good history and clinical examination of the eye. This book aims to teach skills which will be useful to anyone engaged in medical practice. Many systemic disorders have ocular features which are critical in diagnosis. This book covers the ophthalmic features of systemic hypertension, diabetes, sarcoidosis, endocarditis, demyelinating disease and space-occupying lesions of the brain. It also explains how to recognize iritis, distinguish various forms of retinopathy and understand the difference between papilloedema and papillitis.

As in the tenth edition, each chapter provides a set of learning objectives and a summary of key points, as well as bullet lists for emphasis. You can test your understanding with the multiple choice questions and picture quizzes at the end of each chapter. In this edition, we have updated all the chapters and added new extended matching questions (EMQs) to bring this small volume up to date.

Chapter 19 offers classical case histories, which will let you test your diagnostic skills. The final section of the book provides a list of further reading and the details of attractive websites which offer an expanded view of the speciality. Try some of these out.

We hope that you will have as much fun reading these Lecture Notes as we did putting them together.

Bruce James
Anthony Bron

Preface to first edition

This little guide does not presume to tell the medical student all that he needs to know about ophthalmology, for there are many larger books that do. But the medical curriculum becomes yearly more congested, while ophthalmology, still the 'Cinderella' of medicine, is generally left until the last, and only too readily goes by default. So it is to these harassed final-year students that the book is principally offered, in the sincere hope that they will find it useful; for nearly all eye diseases are recognized quite simply by their appearance, and a guide to ophthalmology need be little more than a gallery of pictures, linked by lecture notes.

My second excuse for publishing these lecture notes is a desire I have always had to escape from the traditional textbook presentation of ophthalmology as a string of small isolated diseases, with long unfamiliar names, and a host of eponyms. To the nineteenth-century empiricist, it seemed proper to classify a long succession of ocular structures, all of which emerged as isolated brackets for yet another sub-catalogue of small and equally isolated diseases. Surely it is time now to try and harness these miscellaneous ailments, not in terms of their diverse morphology, but in simpler clinical patterns; not as the microscopist lists them, but in the different ways that eye diseases present. For this, after all, is how the student will soon be meeting them.

I am well aware of the many inadequacies and omissions in this form of presentation, but if the belaboured student finds these lecture notes at least more readable, and therefore more memorable, than the prolix and time-honoured pattern, perhaps I will be justified.

Patrick Trevor-Roper

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Numerous colleagues have provided valuable advice in their specialist areas, for which we are most grateful. The authors wish to thank Tom Meagher and Manoj Parulekar for providing additional pictures for the eleventh edition. We are particularly grateful to Professor Allen Foster at the London School of Hygiene and Tropical Medicine, who kindly provided the illustrations for the chapter on tropical ophthalmology. Asha Sharma kindly provided orthoptic advice. Thanks are due also to our editors and the staff at Wiley Blackwell for their encouragement, efficiency and patience during the production of this edition. We are also grateful to our copy-editor, Joanna Brocklesby, for her meticulous reading of the text.

Bruce James
Anthony Bron

Abbreviations

AIDS	acquired immunodeficiency syndrome
AION	anterior ischaemic optic neuropathy
AMD	age-related macular degeneration
ARM	age-related maculopathy
CMV	cytomegalovirus
CNS	central nervous system
CRVO	central retinal vein occlusion
CSF	cerebrospinal fluid
CT	computed tomography
DCR	dacryocystorhinostomy
ENT	ear, nose and throat
ERG	electroretinogram
ESR	erythrocyte sedimentation rate
GCA	giant cell arteritis
GI	gastrointestinal
GPC	giant papillary conjunctivitis
HAART	highly active anti-retroviral therapy
HIV	human immunodeficiency virus
HLA	human leucocyte antigen
HSV	herpes simplex
ICG	indocyanine green angiography
INR	international normalized ratio
IOL	intraocular lens
KP	keratic precipitate
LASEK	laser-assisted subepithelial keratomileusis
LASIK	laser-assisted in situ keratomileusis
LGB	lateral geniculate body
MLF	medial longitudinal fasciculus
MRA	magnetic resonance angiogram
MRI	magnetic resonance imaging
NSAID	non-steroidal anti-inflammatory drug
OCT	optical coherence tomogram
PAS	peripheral anterior synechiae
PEE	punctate epithelial erosions

PHMB	polyhexamethylene biguanide
PMN	polymorphonuclear leucocyte
PPRF	parapontine reticular formation
PRK	photorefractive keratectomy
PS	posterior synechiae
PVR	proliferative vitreoretinopathy
RAPD	relative afferent pupil defect
RPE	retinal pigment epithelium
TB	tuberculosis
TNF	tumour necrosis factor
UV	ultraviolet
VA	visual acuity
VEGF	vascular endothelial growth factor
VKH	Vogt–Koyanagi–Harada disease

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Anatomy

Learning objective

✓ To learn the anatomy of the eye, the orbit and the third, fourth and sixth cranial nerves, to permit an understanding of medical conditions affecting these structures.

Introduction

A knowledge of ocular anatomy and function is important to the understanding of eye diseases. A brief outline is given below.

Gross anatomy

The eye (Figure 1.1) comprises:

- A tough outer coat which is transparent anteriorly (the *cornea*) and opaque posteriorly (the *sclera*). The junction between them is called the *limbus*. The extraocular muscles attach to the outer sclera while the optic nerve leaves the globe posteriorly.
- A rich vascular coat (the *uvea*) forms the *choroid* posteriorly and the *ciliary body* and *iris* anteriorly. The choroid lines the retina, to which it is firmly attached and nourishes its outer two-thirds.
- The ciliary body contains the smooth *ciliary muscle*, whose contraction allows the lens to take up a more curved shape which permits focusing for near objects. The ciliary epithelium secretes *aqueous humour* and maintains the ocular pressure. The ciliary body provides attachment for the *iris*, which forms the pupillary diaphragm.
- The *lens* lies behind the iris, supported by the *zonular fibrils*, which run from the lens equator to the ciliary body. When the eye is focused for distance, tension in the zonule maintains a flattened profile of the lens.

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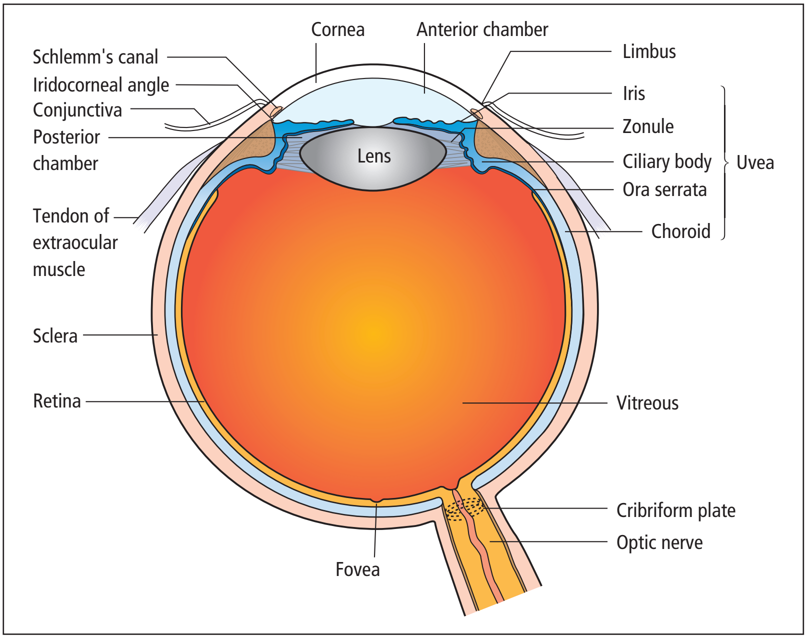

Figure 1.1 The basic anatomy of the eye.

- The cornea anteriorly and the iris and central lens posteriorly form the *anterior chamber*, whose periphery is the *iridocorneal angle* or *drainage angle*. The angle is lined by a meshwork of cells and collagen beams called the *trabecular meshwork*, through which aqueous drains into *Schlemm's canal* and thence into the venous system via the *aqueous veins*. This is the basis of aqueous drainage.
- Between the iris, lens and ciliary body lies the *posterior chamber*, a narrow space distinct from the *vitreous body*. Both the anterior and posterior chambers are filled with aqueous humour. Between the lens and the retina lies the vitreous body, occupying most of the posterior segment of the eye.

Anteriorly, the *bulbar conjunctiva* of the globe is reflected from the sclera into the fornices and thence onto the posterior surface of the lids where it forms the *tarsal conjunctiva*. A connective tissue layer (*Tenon's capsule*) separates the conjunctiva from the sclera and is prolonged backwards as a sheath around the rectus muscles.

The orbit

The eye lies within the bony orbit, which has the shape of a four-sided pyramid (Figure 1.2). At its posterior apex is the *optic canal*, which transmits the optic

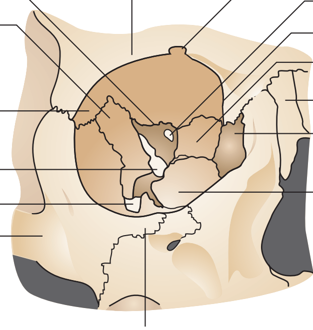

Figure 1.2 The anatomy of the orbit.

nerve to the chiasm, tract and lateral geniculate body. The *superior and inferior orbital fissures* allow the passage of blood vessels and cranial nerves which supply orbital structures. The *lacrimal gland* lies anteriorly in the superolateral aspect of the orbit. On the anterior medial wall lies the fossa for the *lacrimal sac*.

The eyelids (tarsal plates)

The eyelids (Figure 1.3):

- offer mechanical protection to the anterior globe;
- spread the tear film over the conjunctiva and cornea with each blink;
- contain the *meibomian oil glands*, which provide the lipid component of the tear film;
- through closure and blinking prevent drying of the eyes;
- contain the puncta through which the tears flow into the lacrimal drainage system.

They comprise:

- an anterior layer of skin;
- the *orbicularis muscle*, innervated by the seventh nerve;
- a tough collagenous layer (the *tarsal plate*) which houses the oil glands;
- an epithelial lining, the tarsal conjunctiva, which is reflected onto the globe via the *fornices*.

Contraction of the peripheral fibres of the orbicularis muscle results in a protective, forced eye closure, while that of the inner, palpebral muscle results in the blink.

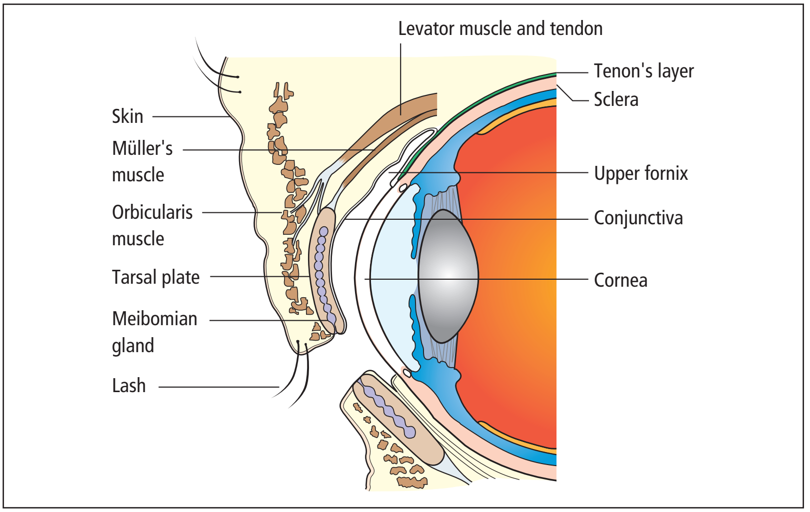

Figure 1.3 The anatomy of the eyelids.

The *levator muscle* passes forwards to the upper lid and inserts by an aponeurosis into the tarsal plate. It is innervated by the third nerve. Damage to the nerve or weakening of the aponeurosis in old age results in drooping of the eyelid (*ptosis*). A flat, *smooth muscle*, innervated by the sympathetic nervous system, arises from the deep surface of the levator and inserts into the tarsal plate. If the sympathetic supply is damaged, a slight ptosis results (*Horner's syndrome*).

The meibomian oil glands deliver their oil to the skin of the lid margin, just anterior to the *mucocutaneous junction*. This oil spreads onto the anterior surface of the tear film with each blink, to form a lipid layer which retards evaporation. Far medially on the lid margins, two puncta form the initial part of the lacrimal drainage system.

The lacrimal drainage system

Tears drain into the upper and lower *puncta* and then into the *lacrimal sac* via the upper and lower *canaliculi* (Figure 1.4). They form a common canaliculus before entering the lacrimal sac. The *nasolacrimal duct* passes from the sac to the nose. Failure of the distal part of the nasolacrimal duct to fully canalize at birth is the usual cause of a watering, sticky eye in an infant. Tear drainage is an active process. Each blink helps to pump tears through the system.

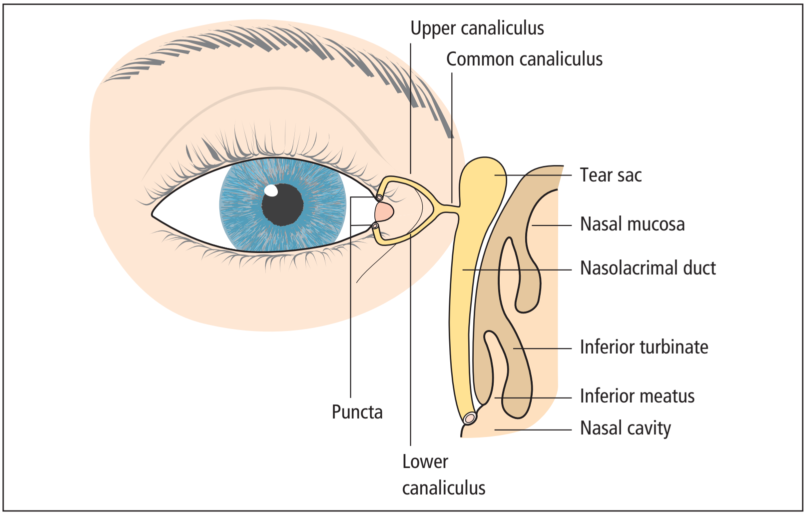

Figure 1.4 The major components of the lacrimal drainage system.

Detailed functional anatomy

The tear film

The ocular surface is bathed constantly by the tears, secreted mainly by the lacrimal gland but supplemented by conjunctival secretions. They drain away via the nasolacrimal system.

The epithelial cells of the ocular surface express a *mucin glycocalyx* which renders the surface wettable. When the eyes are open, the exposed ocular surface (the cornea and exposed wedges of bulbar conjunctiva) are covered by a tear film, 3 μm thick. This comprises three layers:

1. a *mucin gel layer* produced by the conjunctival goblet cells, in contact with the ocular surface;
2. an *aqueous layer* produced by the lacrimal gland;
3. a surface *oil layer* produced by the meibomian glands and delivered to the lid margins.

Functions of the tear film

- It provides a smooth air/tear interface for distortion-free refraction of light at the cornea.
- It transmits oxygen to the avascular cornea.
- It removes debris and foreign particles from the ocular surface through the flow of tears.

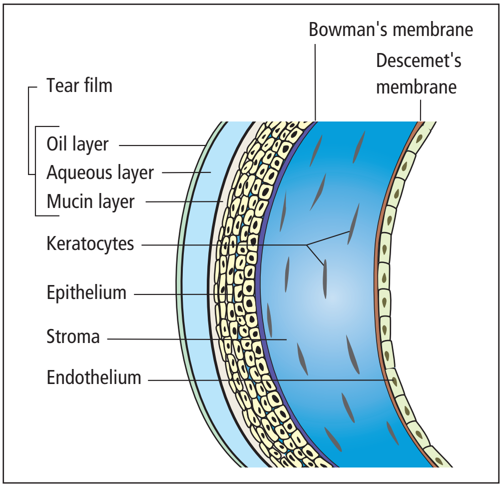

Figure 1.5 The structure of the cornea and precorneal tear film (schematic, not to scale – the stroma accounts for 95% of the corneal thickness).

- It has antibacterial properties through the action of lysozyme, lactoferrin, defensins and the immunoglobulins, particularly secretory IgA.

The tear film is replenished with each blink.

The cornea

The cornea (Figure 1.5) is 0.5 mm thick and comprises:

- The *epithelium*, an anterior non-keratinized squamous layer, thickened peripherally at the *limbus* where it is continuous with the conjunctiva. The limbus houses the germinative *stem cells* of the corneal epithelium.
- An underlying *stroma* of collagen fibrils, ground substance and fibroblasts. The regular packing, small diameter and narrow separation of the collagen fibrils account for corneal transparency. This orderly architecture is maintained by regulating stromal hydration.
- The *endothelium*, a monolayer of non-regenerating cells which actively pump ions and water from the stroma, controlling corneal hydration and hence transparency.

The difference between the regenerative capacity of the epithelium and endothelium is important. Damage to the epithelial layer, by an abrasion for example, is rapidly repaired by cell spreading and proliferation. Endothelial damage, by disease or surgery, is repaired by cell spreading alone, with a loss of cell density. A point is reached when loss of its barrier and pumping functions leads to over-hydration (oedema), disruption of the regular packing of its stromal collagen and corneal clouding.

The nutrition of the cornea is supplied almost entirely by the aqueous humour, which circulates through the anterior chamber and bathes the posterior surface of the cornea. The aqueous also supplies oxygen to the posterior stroma, while the anterior stroma receives its oxygen from the ambient air. The oxygen supply to the anterior cornea is reduced but still sufficient during lid closure, but a too-tightly fitting contact lens may deprive the anterior cornea of oxygen and cause corneal, especially epithelial, oedema.

Functions of the cornea

- It protects the internal ocular structures.
- Together with the lens, it refracts and focuses light onto the retina. The junction between the ambient air and the curved surface of the cornea, covered by its optically smooth tear film, forms a powerful refractive interface.

The sclera

- The sclera is formed from interwoven collagen fibrils of different widths lying within a ground substance and maintained by fibroblasts.
- It is of variable thickness, 1 mm around the optic nerve head and 0.3 mm just posterior to the muscle insertions.

The choroid

- The choroid (Figure 1.6) is formed of arterioles, venules and a dense, fenestrated capillary network.
- It is loosely attached to the sclera.
- It has a remarkably high blood flow.
- It nourishes the deep, outer layers of the retina and may have a role in its temperature homeostasis.
- Its basement membrane, together with that of the retinal pigment epithelium (RPE), forms the acellular Bruch's membrane, which acts as a diffusion barrier between the choroid and the retina.

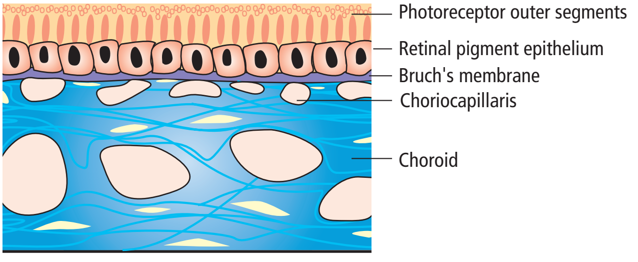

Figure 1.6 The relationship between the choroid, RPE and retina.

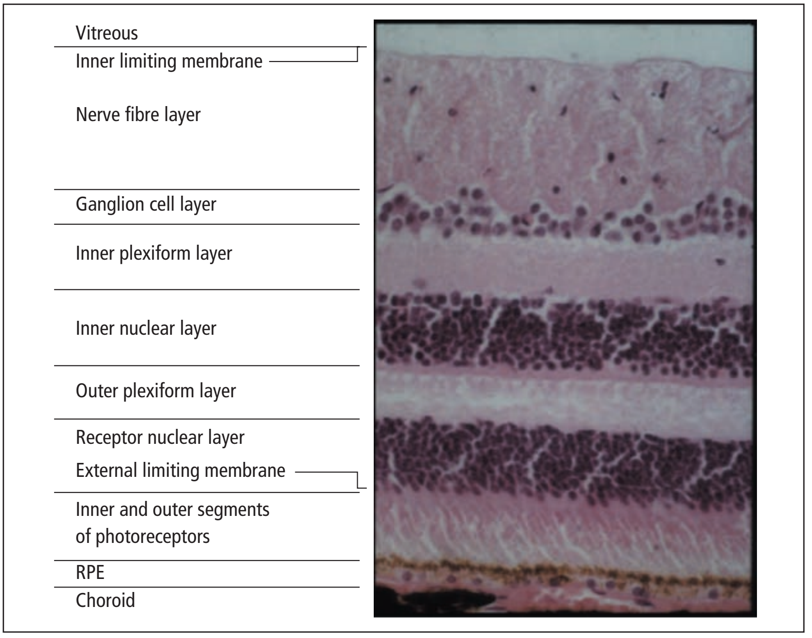

Figure 1.7 The structure of the retina.

The retina

The retina (Figure 1.7) is a highly complex structure derived embryologically from the primitive optic cup. Its outermost layer is the retinal pigment epithelium (RPE) while its innermost layer forms the neuroretina, consisting of the photoreceptors (*rods* and *cones*), the bipolar nerve layer (and horizontal nerve cells) and the *ganglion cell* layer, whose axons give rise to the innermost, nerve fibre layer. These nerve fibres converge to the optic nerve head, where they form the *optic nerve*.

The retinal pigment epithelium (RPE):

- is formed from a single layer of cells;
- is loosely attached to the neuroretina except at the periphery (*ora serrata*) and around the optic disc;
- forms microvilli which project between and embrace the outer segment discs of the rods and cones;
- phagocytoses the redundant external segments of the rods and cones;
- facilitates the passage of nutrients and metabolites between the retina and choroid;
- takes part in the regeneration of rhodopsin and cone opsin, the photoreceptor visual pigments, and in recycling vitamin A;

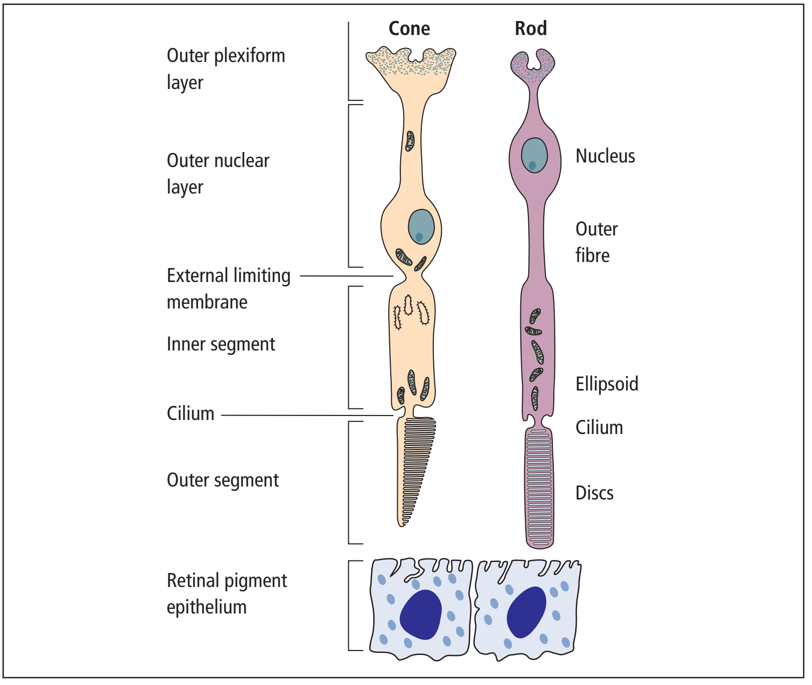

Figure 1.8 The structure of the retinal rods and cones (schematic).

- contains melanin granules which absorb light scattered by the sclera thereby enhancing image formation on the retina.

The photoreceptor layer

The photoreceptor layer is responsible for converting light into electrical signals. The initial integration of these signals is also performed by the retina.

- *Cones* (Figure 1.8) are responsible for daylight and colour vision and have a relatively high threshold to light. Different subgroups of cones are responsive to short, medium and long wavelengths (blue, green, red). They are concentrated at the fovea, where they provide high resolution and the detailed vision required to read.
- *Rods* are responsible for night vision. They have a low light threshold and do not signal wavelength information (colour). They form the large majority of photoreceptors in the remaining retina.

The vitreous

- The vitreous is a clear gel occupying two-thirds of the globe.
- It is 98% water. The remainder is gel-forming hyaluronic acid traversed by a fine collagen network. There are few cells.

- It is firmly attached anteriorly to the peripheral retina, *pars plana* and around the optic disc, and less firmly to the macula and retinal vessels.
- It has a nutritive and supportive role.

Collapse of the vitreous gel (vitreous detachment), which is common in later life, puts traction on points of attachment and may occasionally lead to a peripheral retinal break or hole, where the vitreous pulls off a flap of the underlying retina.

The ciliary body

The ciliary body (Figure 1.9) is subdivided into three parts:

1 the *ciliary muscle*;
2 the ciliary processes (*pars plicata*);
3 the *pars plana*.

The ciliary muscle

- This comprises smooth muscle arranged in a ring overlying the ciliary processes.
- It is innervated by the parasympathetic system via the third cranial nerve.
- It is responsible for changes in lens thickness and curvature during *accommodation*. The *zonular fibres* supporting the lens are under tension during distant viewing, giving the lens a flattened profile. Contraction of the muscle *relaxes* the zonule and permits the elasticity of the lens to *increase* its curvature and hence its refractive power.

The ciliary processes (pars plicata)

- There are about 70 radial *ciliary processes* arranged in a ring around the posterior chamber. They are responsible for the secretion of aqueous humour.
- Each ciliary process is formed by an epithelium two layers thick (the outer *pigmented* and the inner *non-pigmented*) with a vascular stroma.
- The stromal capillaries are fenestrated, allowing plasma constituents ready access.
- The *tight junctions* between the non-pigmented epithelial cells provide a barrier to free diffusion into the posterior chamber. They are essential for the active secretion of aqueous by the non-pigmented cells.
- The epithelial cells show marked infolding, which significantly increases their surface area for fluid and solute transport.

The pars plana

- This comprises a relatively avascular stroma covered by an epithelial layer two cells thick.
- It is safe to make surgical incisions through the scleral wall here to gain access to the vitreous cavity.

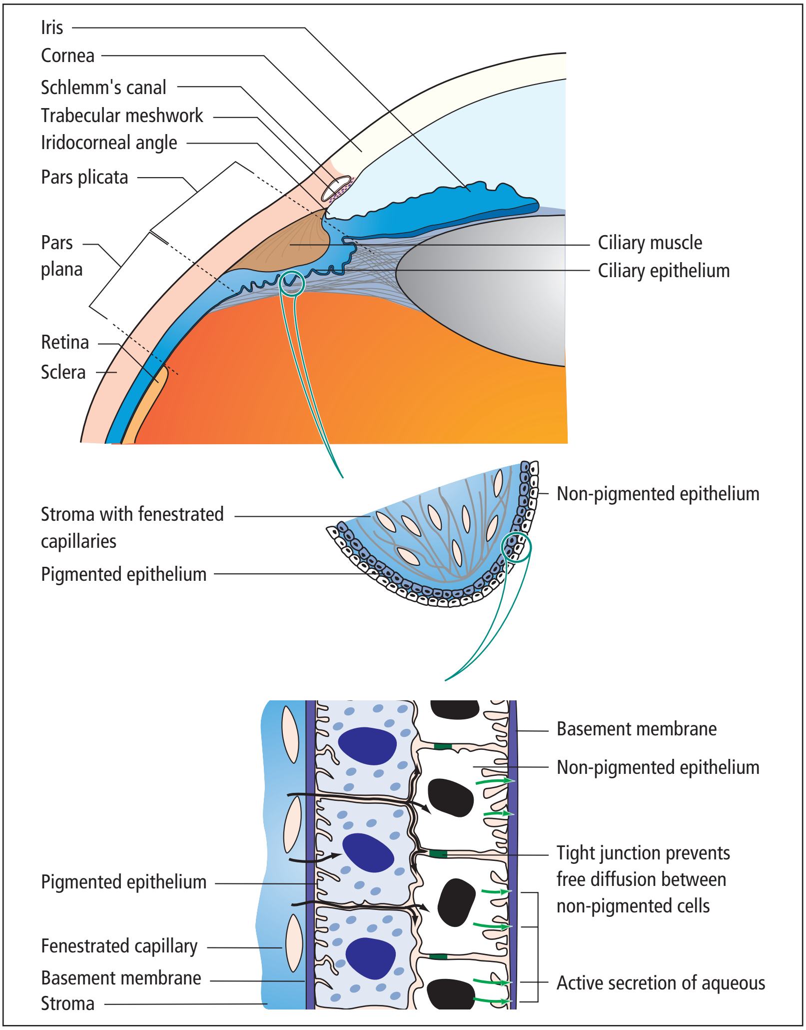

Figure 1.9 The anatomy of the ciliary body.

The iris

- The iris is attached peripherally to the anterior part of the ciliary body.
- It forms the *pupil* at its centre, the aperture of which can be varied by the circular *sphincter* and radial *dilator* muscles to control the amount of light entering the eye.
- It has an anterior border layer of fibroblasts and collagen and a cellular stroma in which the sphincter muscle is embedded at the pupil margin.

- The sphincter muscle is innervated by the *parasympathetic* system.
- The smooth dilator muscle extends from the iris periphery towards the sphincter. It is innervated by the *sympathetic* system.
- Posteriorly the iris is lined by a pigmented epithelium two layers thick.

The iridocorneal (drainage) angle

This lies between the iris, the anterior tip of the ciliary body and the cornea. It is the site of aqueous drainage from the eye via the trabecular meshwork (Figure 1.10).

The trabecular meshwork

This overlies Schlemm's canal and is composed of a lattice of collagen beams covered by trabecular cells. The spaces between these beams become increasingly small as Schlemm's canal is approached. The outermost zone of the meshwork accounts for most of the resistance to aqueous outflow. Damage here raises the resistance and increases intraocular pressure in primary open angle glaucoma. Some of the spaces may be blocked and there is a reduction in the number of cells covering the trabecular beams (see Chapter 10).

Fluid passes into Schlemm's canal both through giant vacuoles in its endothelial lining and through intercellular spaces.

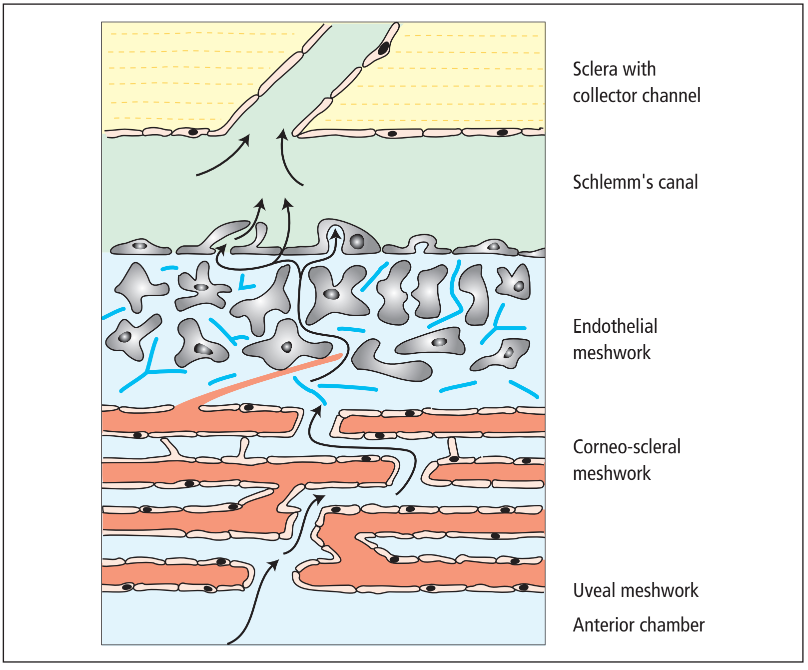

Figure 1.10 The anatomy of the trabecular meshwork.

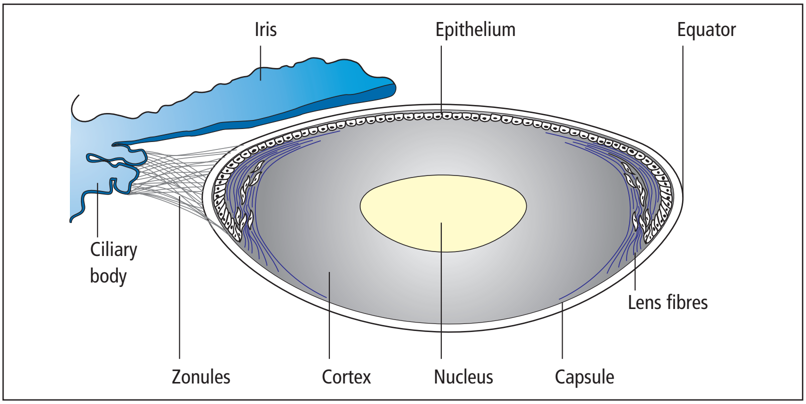

Figure 1.11 The anatomy of the lens.

The lens

The lens (Figure 1.11) is the second major refractive element of the eye; the cornea, with its tear film, is the first.

- It grows throughout life.
- It is supported by zonular fibres running between the ciliary body and the lens capsule.
- It comprises an outer collagenous capsule under whose anterior part lies a monolayer of epithelial cells. Towards the *equator* the epithelium gives rise to the lens fibres.
- The zonular fibres transmit changes in the ciliary muscle, allowing the lens to change its shape and refractive power.
- The *lens fibres* make up the bulk of the lens. They are elongated cells arranged in layers which arch over the lens equator. Anteriorly and posteriorly they meet to form the lens *sutures*. With age the deeper fibres lose their nuclei and intracellular organelles.
- The oldest central fibres represent the fetal lens and form the lens *nucleus*; the peripheral fibres make up the lens *cortex*.
- The high refractive index of the lens arises from the high protein content of its fibres.

The optic nerve

- The optic nerve (Figure 1.12) is formed by the axons arising from the *retinal ganglion cell layer*, which form the *nerve fibre layer* of the retina.

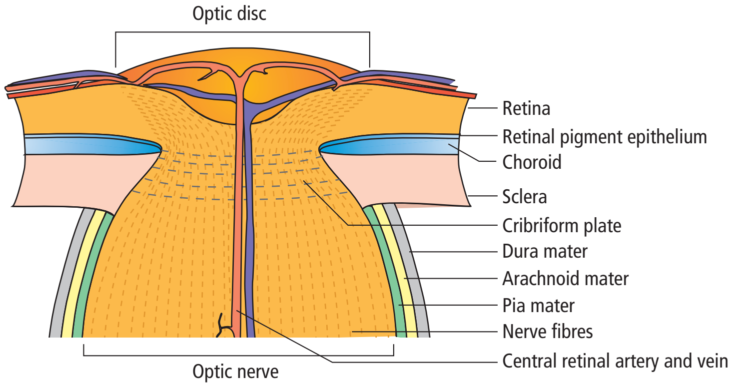

Figure 1.12 The structure of the optic nerve.

- It passes out of the eye through the cribriform plate of the sclera, a sieve-like structure.
- In the orbit the optic nerve is surrounded by a sheath formed by the dura, arachnoid and pia mater, continuous with that surrounding the brain. It is bathed in cerebrospinal fluid (CSF).

The central retinal artery and vein enter the eye in the centre of the optic nerve.

The extraocular nerve fibres are myelinated; those within the eye are not.

The ocular blood supply

The eye receives its blood supply from the ophthalmic artery (a branch of the internal carotid artery) via the retinal artery, ciliary arteries and muscular arteries (Figure 1.13). The conjunctival circulation anastomoses anteriorly with branches from the external carotid artery.

The anterior optic nerve is supplied by branches from the ciliary arteries. The inner retina is supplied by arterioles branching from the central retinal artery. These arterioles each supply an area of retina, with little overlap. Obstruction results in ischaemia of most of the area supplied by that arteriole. The fovea is so thin that it requires no supply from the retinal circulation. It is supplied indirectly, as are the outer layers of the retina, by diffusion of oxygen and metabolites across the retinal pigment epithelium from the choroid.

The endothelial cells of the retinal capillaries are joined by tight junctions so that the vessels are impermeable to proteins. This forms an '*inner blood–retinal barrier*', with properties similar to that of the blood–brain barrier. The capillaries of the choroid, however, are fenestrated and leaky. The retinal pigment

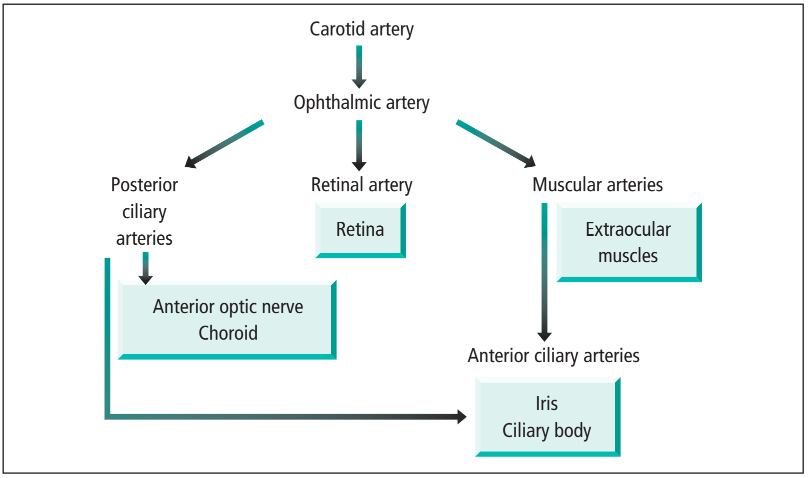

Figure 1.13 Diagrammatic representation of the ocular blood supply.

epithelial cells are also joined by tight junctions and present an '*external blood–retinal barrier*' between the leaky choroid and the retina.

The breakdown of these barriers causes the retinal signs seen in many vascular diseases.

The third, fourth and sixth cranial nerves

The structures supplied by each of these nerves are shown in Table 1.1.

Central origin

The nuclei of the third (oculomotor) and fourth (trochlear) cranial nerves lie in the midbrain; the sixth nerve (abducens) nuclei lie in the pons. Figure 1.14 shows some of the important relations of these nuclei and their fascicles.

Nuclear and fascicular palsies of these nerves are unusual. If they do occur they are associated with other neurological problems. For example if the third nerve fascicles are damaged as they pass through the red nucleus the ipsilateral third nerve palsy will be accompanied by a contralateral tremor. Furthermore a nuclear third nerve lesion results in a contralateral palsy of the superior rectus as the fibres from the subnucleus supplying this muscle cross.

Peripheral course

Figure 1.15 shows the intracranial course of the third, fourth and sixth cranial nerves.

Table 1.1 **The muscles and tissues supplied by the third, fourth and sixth cranial nerves.**

Third (oculomotor)	Fourth (trochlear)	Sixth (abducens)
Medial rectus	Superior oblique	Lateral rectus
Inferior rectus		
Superior rectus (innervated by the contralateral nucleus)		
Inferior oblique		
Levator palpebrae (both levators are innervated by a single midline nucleus)		
Preganglionic parasympathetic fibres run in the third nerve end in the ciliary ganglion. Here postganglionic fibres arise and pass in the short ciliary nerves to the sphincter pupillae and the ciliary muscle		

Third nerve

The third nerve leaves the midbrain ventrally between the cerebral peduncles. It then passes between the *posterior cerebral* and *superior cerebellar arteries* and then lateral to the *posterior communicating artery*. Aneurysms of this artery may cause a third nerve palsy. The nerve enters the cavernous sinus in its lateral wall and enters the orbit through the superior orbital fissure.

Fourth nerve

The nerve decussates and leaves the *dorsal* aspect of the midbrain below the inferior colliculus. It first curves around the midbrain before passing like the third nerve between the posterior cerebral and superior cerebellar arteries to enter the lateral aspect of the cavernous sinus inferior to the third nerve. It enters the orbit via the superior orbital fissure.

Sixth nerve

Fibres leave from the inferior border of the pons. It has a long intracranial course passing upwards along the pons to angle anteriorly over the petrous bone and into the cavernous sinus where it lies infero-medial to the fourth nerve in proximity to the internal carotid artery. It enters the orbit through the superior orbital fissure. This long course is important because the nerve can be involved in numerous intracranial pathologies including base of skull fractures, invasion by nasopharyngeal tumours and raised intracranial pressure.