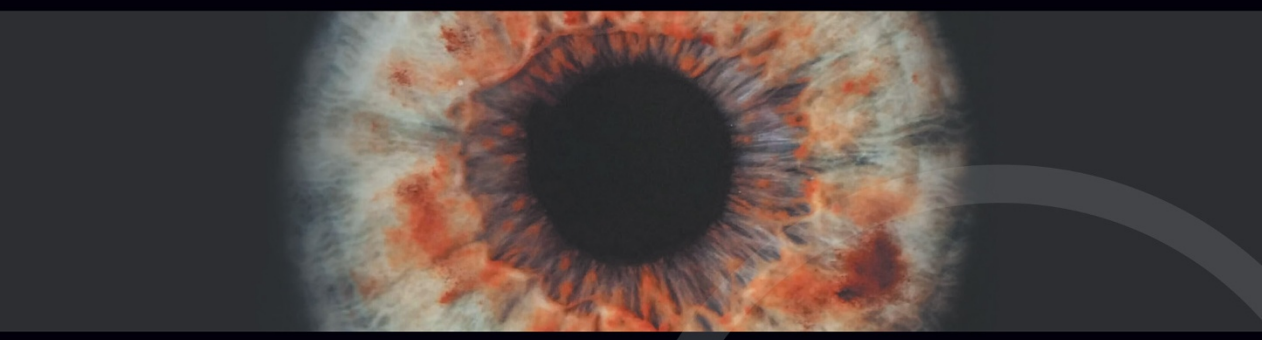
OPHTHALMOLOGY

Lecture Notes



Bruce James
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12th Edition

with website

WILEY Blackwell

Ophthalmology
Lecture Notes

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Twelfth Edition

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WILEY Blackwell

This edition first published 2017 © 2017 by Bruce James, Anthony Bron and Manoj V Parulekar

Previous editions 1960, 1965, 1968, 1971, 1974, 1980, 1986, 1997, 2003, 2007, 2011

Registered office: John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
Editorial offices: 9600 Garsington Road, Oxford, OX4 2DQ, UK
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
111 River Street, Hoboken, NJ 07030-5774, USA

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Library of Congress Cataloging-in-Publication Data

Names: James, Bruce, 1957- author. | Bron, Anthony J., author. | Parulekar, Manoj V., author.
Title: Lecture notes. Ophthalmology / Bruce James, Anthony Bron, Manoj V. Parulekar.
Other titles: Ophthalmology
Description: 12th edition. | Chichester, West Sussex ; Hoboken, NJ : John Wiley & Sons, Inc., 2017. | Includes bibliographical references and index.
Identifiers: LCCN 2016026509 (print) | LCCN 2016027367 (ebook) | ISBN 9781119095903 (pbk.) | ISBN 9781119095927 (pdf) | ISBN 9781119095941 (epub)
Subjects: | MESH: Eye Diseases | Handbooks | Problems and Exercises
Classification: LCC RE50 (print) | LCC RE50 (ebook) | NLM WW 39 | DDC 617.7–dc23
LC record available at https://lccn.loc.gov/2016026509

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Set in 8.5/11pt UtopiaStd-Regular by Thomson Digital, Noida, India

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Preface to twelfth edition

Welcome to the twelfth 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 continue to develop giving increasingly detailed access to the structures of the eye at cellular level. Specular microscopy can image the corneal endothelial cells which regulate corneal hydration and transparency; optical coherence tomography allows the layers of the retina to be dissected and recently allows the retinal vasculature to be imaged without the need for injection of fluorescein. 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. They have an established role in reshaping the cornea to treat refractive errors of the eye and their role is now extending to use in cataract surgery itself. 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 antiangiogenic drugs. Roles for these drugs in treating oedema of the retina, see for example in diabetes, are also becoming established.

These techniques are matched by technological innovations in microsurgery, responsible for dramatic advances in cataract and vitreoretinal surgery. Optical function in cataract surgery is restored by insertion of a lens which unfolds within the eye. These are becoming increasingly complex allowing for the treatment of astigmatism and restoring near and distance vision in some patients without the need for glasses. Vitreoretinal surgery employs inert gases and silicone oil 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. Glaucoma surgery is developing tiny drainage implants to reduce intraocular pressure.

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 eleventh 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 questions and picture quizzes at the end of each chapter. In this edition, we have updated all the chapters and added to the extended matching questions (EMQs) and multiple choice questions to bring this small volume up to date.

Chapter 20 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
Manoj V. Parulekar

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

Acknowledgements

Numerous colleagues have provided valuable advice in their specialist areas, for which we are most grateful. The authors wish to thank Tom Meagher and Ramona Khooshabeh for providing additional pictures for the twelfth edition. Tom Butler provided substantial input to the chapter on clinical optics. 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. Richard James, Chris King and Ajay Mohite worked on the questions and assessments. Thanks are due also to Karen Moore and the staff at Wiley Blackwell for their encouragement, efficiency and patience during the production of this edition. We are also grateful to Shikha Pahuja and the copyediting team of Thomson Digital, for meticulous reading and production of the text.

Bruce James
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Abbreviations

AIDS	acquired immunodeficiency syndrome
AION	anterior ischaemic optic neuropathy
AMD	age-related macular degeneration
ARM	age-related maculopathy
CCTV	closed circuit television
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

About the companion website

Don't forget to visit the companion website for this book:

www.lecturenoteseries.com/ophthalmology

There you will find valuable material designed to enhance your learning, including:

- Interactive MCQs
- Interactive EMQs
- Figures from the book

Scan this QR code to visit the companion website.

1

Anatomy

Learning objective

✓ To learn the anatomy of the eye, the orbit and the third, fourth and sixth cranial nerves, as a background to the medical conditions affecting them.

Introduction

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

Surface anatomy of the face

The eyes are disposed symmetrically about the face and their forward-looking arrangement permits a large overlap in visual fields, the basis of stereopsis. Lying within the bony orbits, they are protected from trauma by the orbital walls and rims and by the eyelids, by blinking and eye closure. With the eyes open and looking straight ahead, all but the upper and lower corneal margins are exposed in the *palpebral aperture*, together with two small white triangles of bulbar conjunctiva, overlying the sclera. The medial and lateral ends of the fissure are known as the medial and lateral *canthi* (Figure 1.1).

The lids and the upper and lower orbital rims are overlain by the orbicularis muscle which sweeps over these structures in an ellipse, from a region just medial to the medial orbital rim. It acts as the palpebral sphincter (Figure 1.2). Like all other muscles of the face, it is supplied by the seventh cranial nerve. Contraction of its orbital part results in protective, forced eye closure, while contraction of its palpebral part is employed in the downstroke of the upper lid during a blink. The levator palpebrae muscle, the elevator of the upper lid (see below), is concerned with the upstroke of the blink (third cranial nerve). These synchronized contractions are completed within just 300 ms. The contents of the orbit are separated from those of the lid by a connective tissue sheet, or orbital septum, which extends from the orbital rim to the tarsal plate, deep to orbicularis.

Sensory innervation of the face: the fifth cranial nerve

The sensory innervation of each half of the face is provided by the trigeminal nerve (Figure 1.3). The eye, upper lid, eyebrow, forehead and nose are supplied by its ophthalmic division (V1), via its lacrimal, frontal and nasociliary branches, which enter the orbit through the superior orbital fissure. The maxillary division (V2), lying inferolaterally to V1 in the cavernous sinus, exits the cranial cavity via the foramen rotundum and, at the inferior orbital fissure, gives rise to the infraorbital and zygomatic nerves. These supply, chiefly, the lower lid and the

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Published 2017 by John Wiley & Sons, Ltd.
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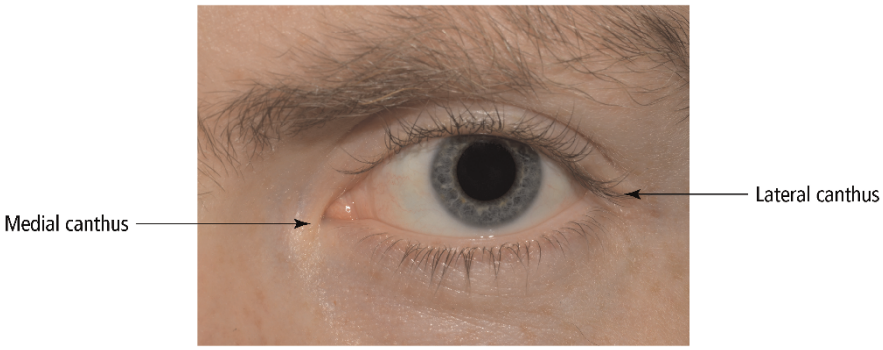

Figure 1.1 The eye, looking straight ahead.

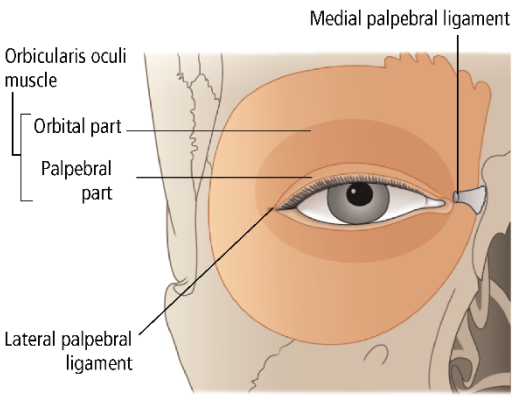

Figure 1.2 Disposition of the orbicularis is muscle.

upper lip and cheek. The mandibular division (V3), exiting the skull via the foramen ovale, supplies the lower lip, chin and jaw and the preauricular skin and temporal region. It is also motor to the muscles of mastication.

The neurons of the three divisions of the trigeminal nerve converge upon the trigeminal ganglion, whose sensory roots enter the pons to be distributed to the trigeminal nuclei in the brainstem. The mesencephalic nucleus is concerned with proprioception, the main sensory nucleus with touch and the medullary nucleus of the spinal tract with pain and temperature sensibility. Fibres from the ophthalmic division go to the lowest part of this nucleus, those from the mandibular division to its highest part.

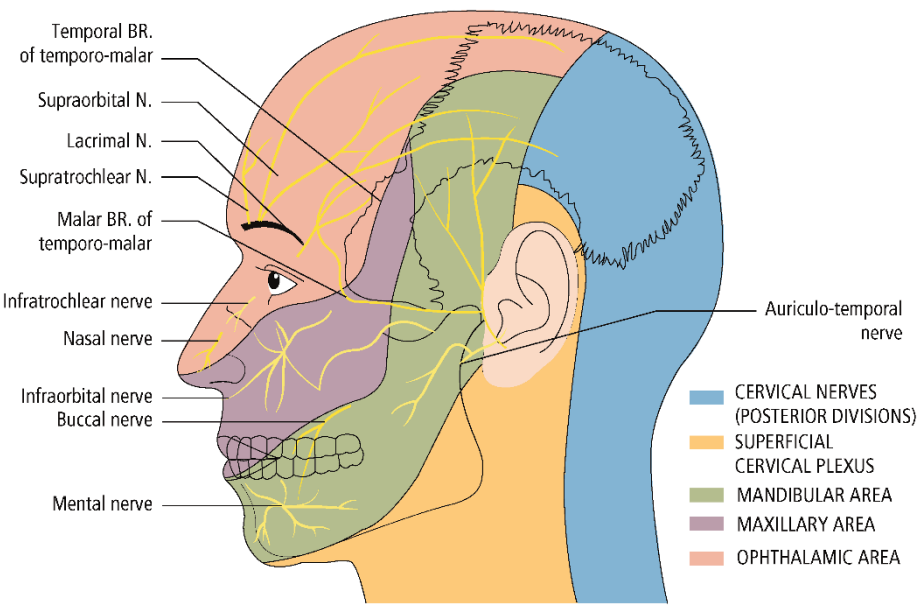

Figure 1.3 Sensory innervation of the face by the trigeminal nerve.

Gross anatomy of the eye

The eye comprises (Figure 1.4):

- A tough, collagenous 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. Internal to the choroid lies the retina, to which it is firmly attached and whose outer two-thirds it nourishes.
- The ciliary body contains the smooth *ciliary muscle*, whose contraction controls focusing by altering lens shape. The *lens* lies behind the iris, supported by the *zonules*, whose fine fibres 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. When the ciliary body contracts, tension is relaxed, the lens takes up a more curved shape and focusing for near objects is achieved.
- The ciliary body also provides attachment for the *iris*, which forms the pupillary diaphragm. The *ciliary epithelium* secretes *aqueous humour* and maintains the ocular pressure.
- The space between the cornea anteriorly and the iris and central lens posteriorly, filled with aqueous humour, is the anterior chamber, whose periphery is the iridocorneal angle or drainage angle. The angle gives access to 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* behind. 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. The posterior segment refers to the posterior two-thirds of the eye, lying behind the anterior vitreous face. The anterior segment comprises all those structure lying *anterior* to the vitreous.

Anteriorly, the *bulbar conjunctiva* of the globe passes from the limbus into the fornices of the conjunctival sac and thence onto the posterior surface of the lids, where it becomes 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.

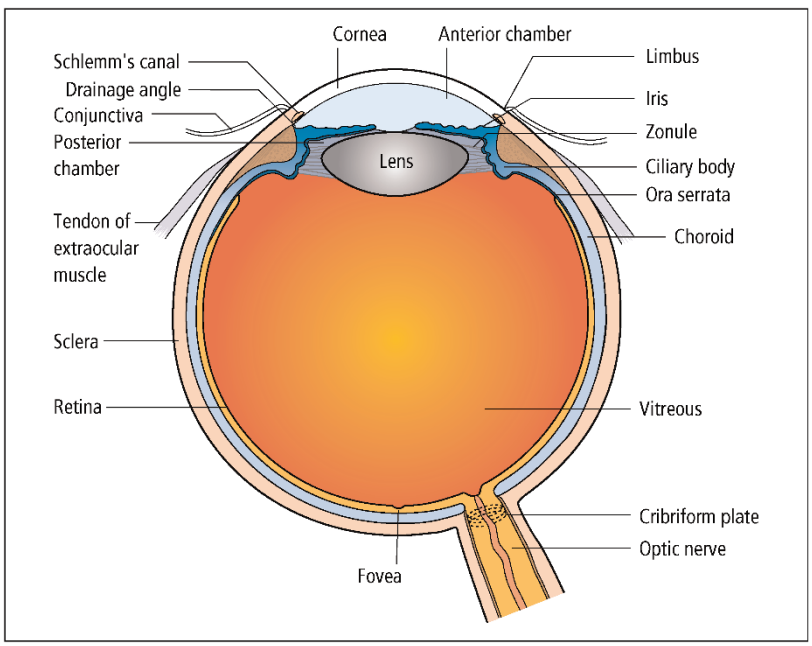

Figure 1.4 The basic anatomy of the eye.

The orbit

The eye, or globe, lies within the bony orbit, which has the shape of a four-sided pyramid (Figure 1.5). At its posterior apex is the *optic canal*, which transmits the optic nerve to the chiasm, tract and lateral geniculate body. The *superior and inferior orbital fissures* transmit the blood vessels and cranial nerves that supply the orbital structures. The *lacrimal gland* lies anteriorly in the superolateral aspect of the orbit. On the anterior part of the medial wall lies the fossa for the *lacrimal sac*.

The eyelids (the tarsus)

The eyelids (Figure 1.6):

- offer mechanical protection to the globe;
- spread the tears over the conjunctiva and cornea with each blink.

The levator muscle is the main elevator of the upper lid. It passes forwards from an attachment on the sphenoid bone, above the optic foramen, to an aponeurosis which inserts into the tarsal plate. It is innervated by the third cranial nerve. Damage

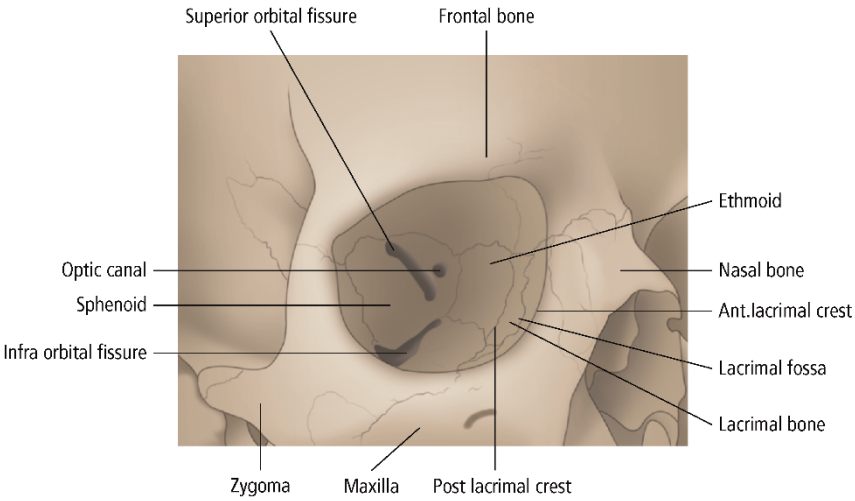

Figure 1.5 The anatomy of the orbit.

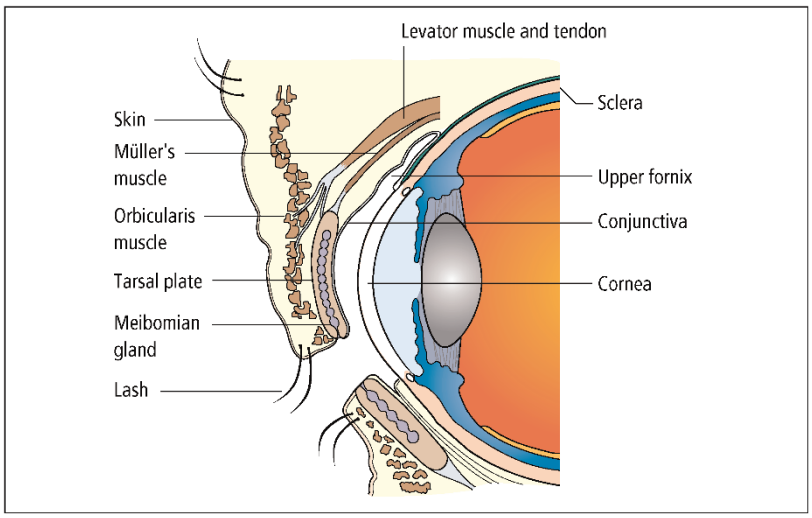

Figure 1.6 The anatomy of the eyelids.

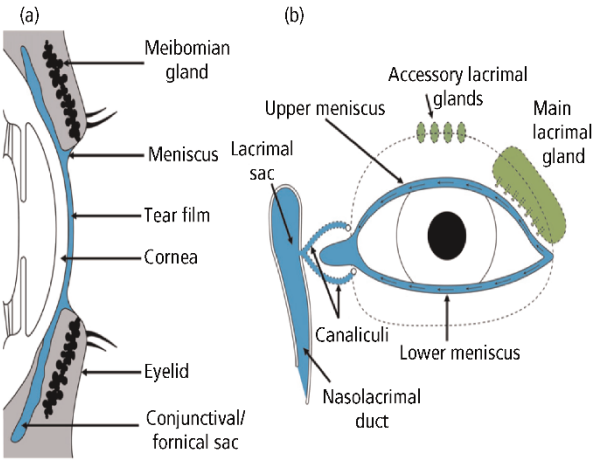

Figure 1.7 Drawing of the eye: (a) in cross section, (b) in frontal view to illustrate the distribution of the tears. (*Source:* Gaffney EA et al. Progress in Retinal and Eye Research 2010; **29**(1):59–78. Reproduced with permission of Elsevier.)

to the nerve or weakening of the aponeurosis in old age results in drooping of the upper eyelid (ptosis). A flat, smooth muscle, (the superior tarsal, or Müller's muscle) innervated by the sympathetic nervous system, arises from the deep surface of the levator and inserts into the tarsal plate. Müllers muscle also contributes to a lesser extent to elevation of the lid, and if the sympathetic supply is damaged, a slight ptosis results as part of Horner's syndrome.

Each eyelid comprises:

- an anterior layer of skin;
- the palpebral part of the *orbicularis muscle*;
- a tough collagenous layer (the *tarsal plate*) which houses the meibomian oil glands;
- an epithelial lining, the *tarsal conjunctiva*;
- the lash-bearing, lid margins.

The tarsal conjunctiva is reflected, via the fornices, onto the anterior surface of the globe, where it becomes the bulbar conjunctiva. When the eyes are closed, this lining forms the conjunctival sac, which contains the tears. When the eyes open, a tear film is formed which covers and protects the exposed cornea and conjunctiva. At the lid margins, the tear film is bordered by the tear menisci (Figure 1.7).

The lid margins exhibit a narrow, posterior conjunctival zone, continuous with the tarsal conjunctiva and a cutaneous zone anteriorly, which bears the lashes. These zones are separated by the mucocutaneous junction which forms the anterior boundary of each tear meniscus (Figure 1.8). At the medial ends of each lid margin, dipping into a lake of tears at the nasal canthus, are the lacrimal puncta, through which tears drain from the tear menisci into the lacrimal drainage system.

The meibomian oil glands, embedded in the tarsal plates (Figure 1.8), deliver their oil to the skin of the lid

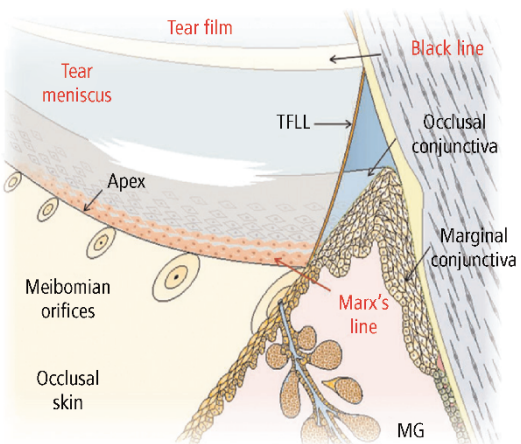

Figure 1.8 Diagram of lid margin to show meibomian orifices, meniscus and tear film lipid layer (TFLL). (*Source:* Bron et al. Ocul Surf 2011; **9**(2):70–91. Reproduced with permission of Elsevier.)

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 and stabilizes the tear film.

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 1.9). They form a common canaliculus before entering the lacrimal sac. The *nasolacrimal duct* passes from the sac to the nasal cavity which enters at the *inferior meatus*. Failure of the distal part of the

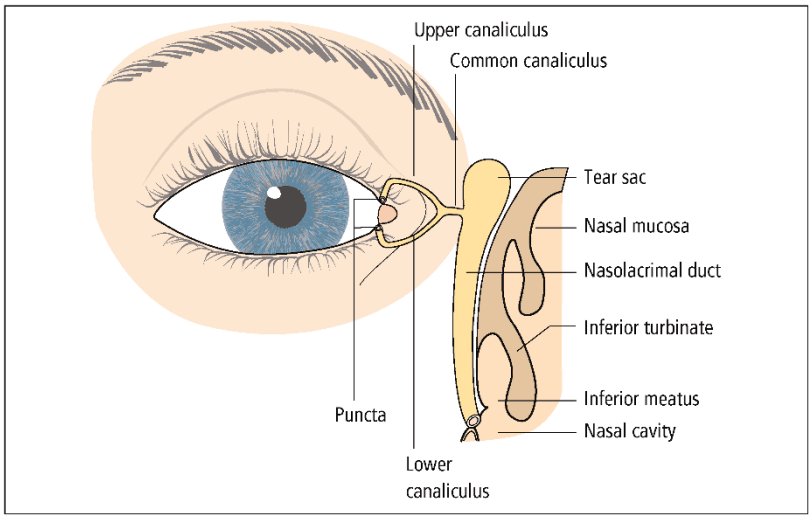

Figure 1.9 The major components of the lacrimal drainage system.

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.

Detailed functional anatomy

The tear film

The eye is bathed constantly by the tears, secreted by the lacrimal gland into the upper fornix of the conjunctival sac. There is a small contribution from the conjunctiva. Tears are lost from the surface in part by evaporation and in part by drainage via the nasolacrimal system. Lacrimal secretion is under parasympathetic control through a feedback loop from the cornea, via the trigeminal nerve, to the superior salivatory nucleus and thence to the lacrimal gland. This ensures that tear production is regulated reflexly in response to signals from the ocular surface.

The most superficial epithelial cells of the ocular surface express a *mucin-rich glycocalyx* which renders the surface wettable. When the eyes are open, the exposed ocular surface is covered by a tear film, 3 µm thick. This has two layers:

- A *mucoaqueous layer* containing gel mucin from the conjunctival goblet cells and *aqueous tear fluid* from the lacrimal gland, directly in contact with the ocular surface.
- A thin surface *oil layer* (100 nm) produced by the meibomian glands and delivered to the tear film from the lid margins.

Functions of the tear film

- It moistens the eye, preventing dehydration of its surface.
- It provides a smooth, air/tear, optical 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 and drainage of the tears and the action of the blink.
- It has antibacterial properties by means of lysozyme, lactoferrin, defensins and the immunoglobulins, particularly secretory IgA.

The tear film is replenished with each blink.

The cornea

The cornea is 0.5 mm thick and comprises (Figure 1.10):

- The epithelium, an anterior, non-keratinised squamous layer, five cells thick, thickened peripherally at the limbus where it is continuous with the conjunctiva. The limbus houses the germinative *stem cells* which maintain the corneal epithelium. The basal cells of the epithelium are firmly attached to an underlying basal lamina by hemidesmosomes and by anchoring fibrils which extend into Bowman's layer.
- An underlying *stroma* which accounts for over 90% of the corneal thickness. On its most anterior aspect is a tough, *anterior limiting layer* (Bowman's layer), 20 µm thick, which is free of cells and composed of fine, short, tightly interwoven collagen fibrils. The main body of the stroma consists of type I collagen fibrils arranged in

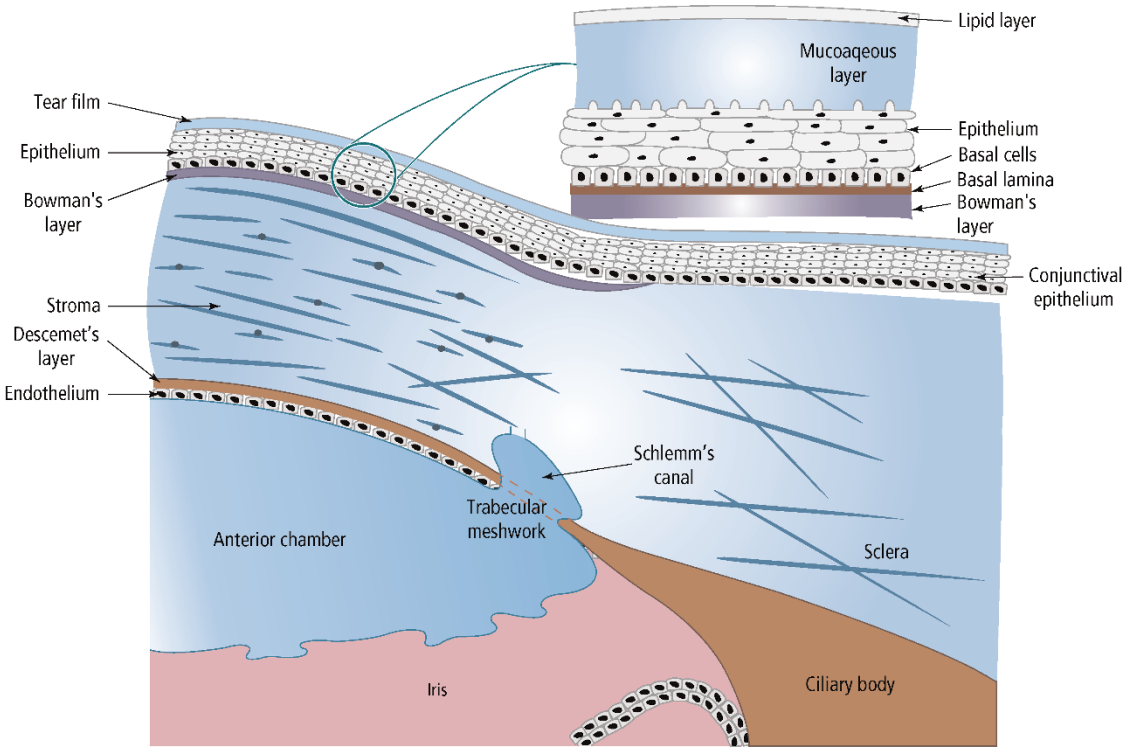

Figure 1.10 The structure of the cornea and precorneal tear film (schematic, not to scale – the stroma accounts for 95% of the corneal thickness).

parallel within lamellae, each fibril surrounded by a ground substance rich in proteoglycans. Between the lamellae are scattered keratocytes which, like fibroblasts, engage in stromal maintenance and repair. The anterior lamellae lie in the plane of the cornea, while posteriorly they have a more woven arrangement. The regular packing of the collagen fibrils, their small diameter and narrow separation (in the region of 200 nm) accounts for corneal transparency. Backscattered light, towards the source, is obliterated by destructive interference and over 90% of the light is transmitted. This orderly architecture is maintained by regulating stromal hydration. The stroma is bounded behind by the *posterior limiting layer* (Descemet's layer), the basal lamina of the corneal endothelium. It is chiefly composed of type IV collagen.

- The *endothelium*, a monolayer of hexagonal, non-regenerating cells (Figure 1.11) which actively pump ions from the stroma into the anterior chamber carrying water with them. This controls corneal hydration and thickness 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. When cell density falls below a critical level, a loss of

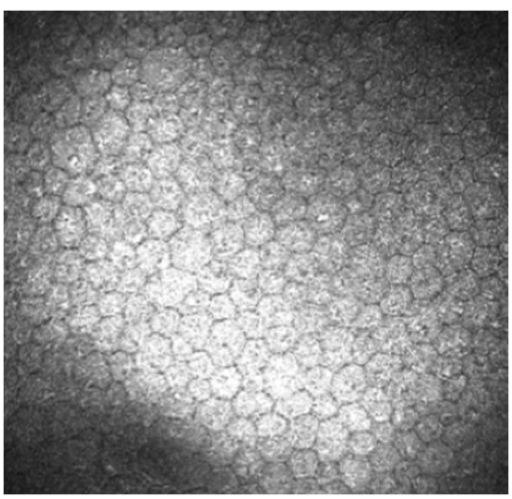

Figure 1.11 Normal corneal endothelium shown by confocal microscopy. (Courtesy of Paula Hedges.)

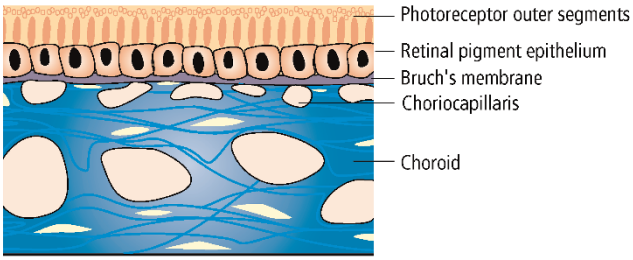

Figure 1.12 The relationship between the choroid, RPE and retina.

barrier and pumping functions leads to corneal overhydration (oedema), stromal swelling, disruption of the regular packing of the collagen fibrils and to corneal clouding. The effect on vision is compounded by an associated epithelial oedema.

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; however, a too tightly fitting contact lens may deprive the anterior cornea of oxygen, causing epithelial oedema and visual loss.

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 the optically smooth tear film, forms a powerful refractive interface.

The sclera

- The sclera is formed from interwoven collagen fibrils lying within a ground substance and maintained by fibroblasts. Because of the coarse weave and the variation in fibril width, the sclera scatters light strongly and appears white and opaque.
- It is of variable thickness, 1 mm around the optic nerve head and 0.3 mm just posterior to the rectus muscle insertions.

The choroid

- The choroid (Figure 1.12) is a vascular layer formed of arterioles and venules and a dense, fenestrated capillary network, fused with the basal lamina of the retina.
- It is loosely attached to the sclera.
- It has a remarkably high blood flow.
- It nourishes the deep, outer two-thirds of the retina and may have a role in its temperature homeostasis.
- Its basal lamina, together with that of the retinal pigment epithelium (RPE), forms the acellular *Bruch's membrane* that acts as a diffusion barrier between the choroid and the retina which facilitates the passage of nutrients and metabolites between the retina and choroid.

The retina

The retina (Figure 1.13) is a highly complex structure derived embryologically from the primitive optic cup. Its outermost layer is the RPE while its innermost layer forms the neuroretina, consisting of the photoreceptors (rods and cones), the bipolar nerve layer (and the amacrine 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.

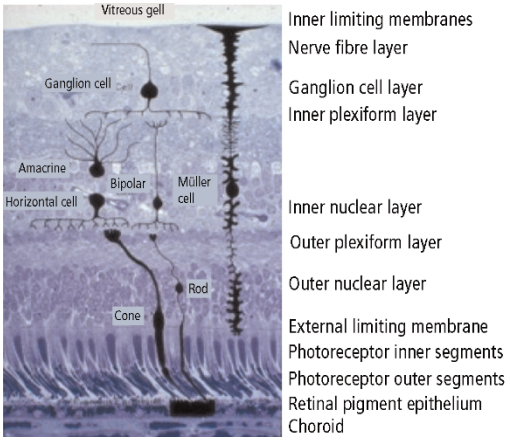

Figure 1.13 The structure of the retina. (Courtesy of Professor John Marshall.)

Müller cells, the principal glial cells of the retina, extend across its thickness and are vital for the health of the retinal neurons.

The retinal pigment epithelium (RPE)

- It is consists of a single layer of cells.
- It is loosely attached to the neuroretina, except at the periphery (*ora serrata*) and around the optic disc.
- It forms microvilli which project between and embrace the outer segment discs of the rods and cones.
- It phagocytoses the redundant, pigment-containing discs, which are replaced by new ones.
- It takes part in the regeneration of rhodopsin and cone opsin, the photoreceptor visual pigments and in recycling vitamin A.
- It 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 impulses. The initial integration of these impulses is also performed by the retina.

- *Cones* (Figure 1.14) 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 (red, green and blue,). They are concentrated at the fovea, where they provide the high resolution required for detailed vision, as in reading.
- *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 physically supportive role and permits the passage of nutrients and metabolites.

Loss of gel structure in later life, with collapse of the vitreous away from the retina (vitreous detachment), 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. This is a risk factor for subsequent retinal detachment.

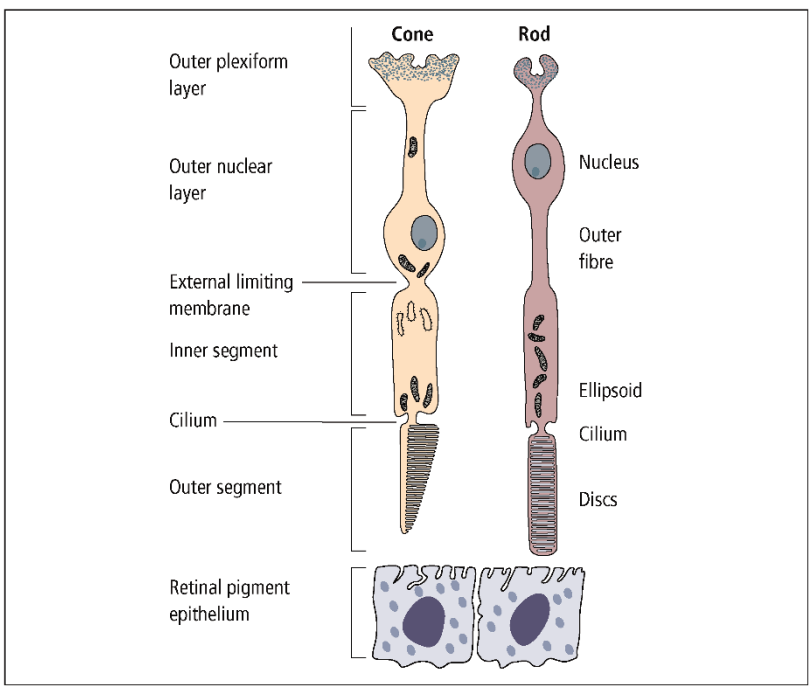

Figure 1.14 The structure of the retinal rods and cones (schematic).

The ciliary body

The ciliary body (Figure 1.15) is subdivided into three parts:

1 the ciliary muscle;
2 the ciliary processes (pars plicata);
3 the pars plana, located posteriorly.

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.
- The lens of the eye is suspended from the ciliary muscle by the ciliary zonule. Contraction of the ciliary muscle is responsible for changes in lens thickness and curvature during accommodation (see below).

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

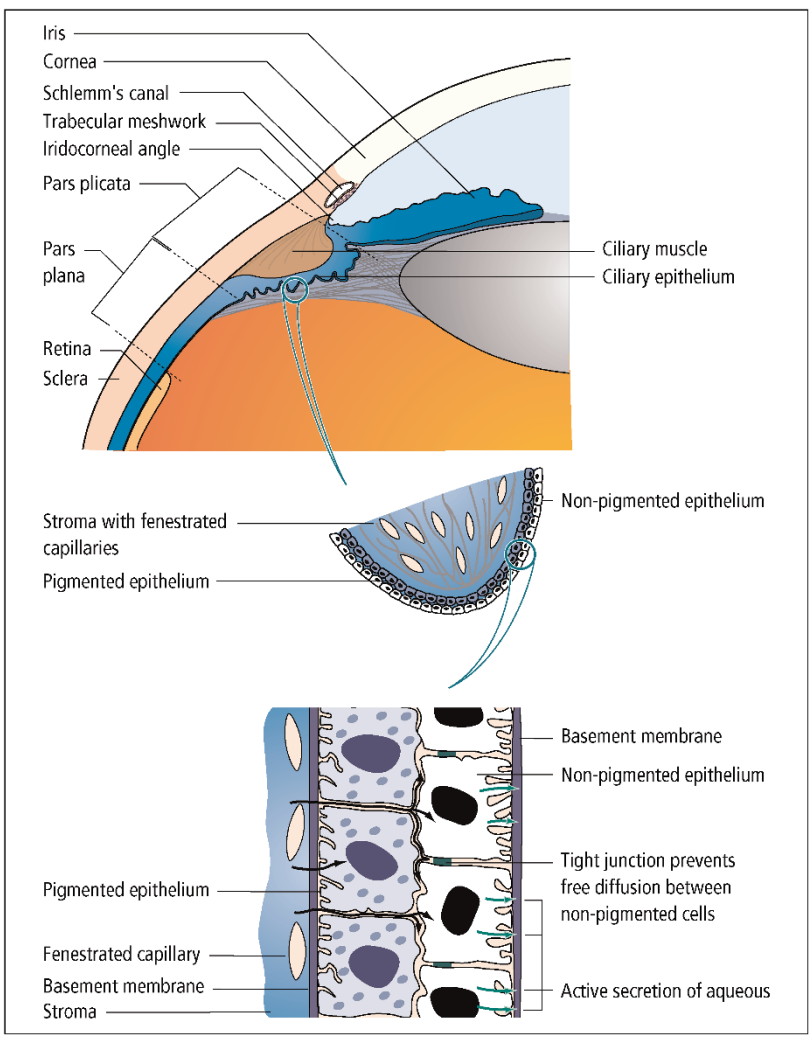

Figure 1.15 The anatomy of the ciliary body.

into the posterior chamber. They are essential for the active secretion of aqueous by these cells.
- The epithelial layers show marked infolding, which 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 in this region to gain access to the vitreous cavity.

The iris

- The iris diaphragm is attached peripherally to the anterior part of the ciliary body.
- It is perforated centrally by the *pupil*, which is constricted or dilated by contraction of the circular *sphincter* or radial *dilator* muscles, respectively, 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 1.16).

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.

The lens

Function

The lens is the second major refractive element of the eye; the cornea being the first. It is a perfectly transparent structure that lies directly behind the iris and pupil, suspended from the ciliary body by the fibres of the ciliary zonule (Figure 1.17). The zonular fibres insert into the lens equator, transmitting forces generated by the ciliary muscle to the lens, to change its shape and refractive power. This allows focusing to be adjusted from distance to near. At rest, during distance viewing, the zonular fibres are under tension, giving the lens a flattened profile. Contraction of the muscle during accommodation for near, relaxes the zonule and permits the elasticity of the lens to increase its curvature and hence its refractive power. This may seem counter-intuitive, but it comes about because the muscle bulges inwards and moves forwards during contraction.

Anatomy

- The lens comprises an outer, tough, collagenous capsule.
- A compact inner mass of lens fibre cells.

The capsule is the basal lamina of the lens epithelium, a monolayer of cells that lies between the capsule and the lens fibres anteriorly. The anterior part of the capsule increases in thickness throughout life but synthesis of the posterior part ceases after birth, so it is thinner and more fragile. This is important during cataract surgery.

The epithelial cells at the lens equator form a germinative zone, where cell division gives rise to the lens fibres that make up the bulk of the lens. Fibres are elongated, spindle-shaped cells arranged in layers which arch over the lens equator. Anteriorly and posteriorly, their tips meet to form the lens which increase in complexity as the lens ages (Figure 1.18).

The high concentration of lens-specific proteins within the fibres (the *lens crystallins*), accounts for the high refractive index of the lens. Their molecular order, together with the regular packing of the lens fibres, accounts for its perfect transparency.

The lens grows throughout life, as shells of new fibres are laid down at the surface of the fibre mass. Thus, the oldest, central fibres that form the *lens nucleus* represent the fetal lens and the fibres external

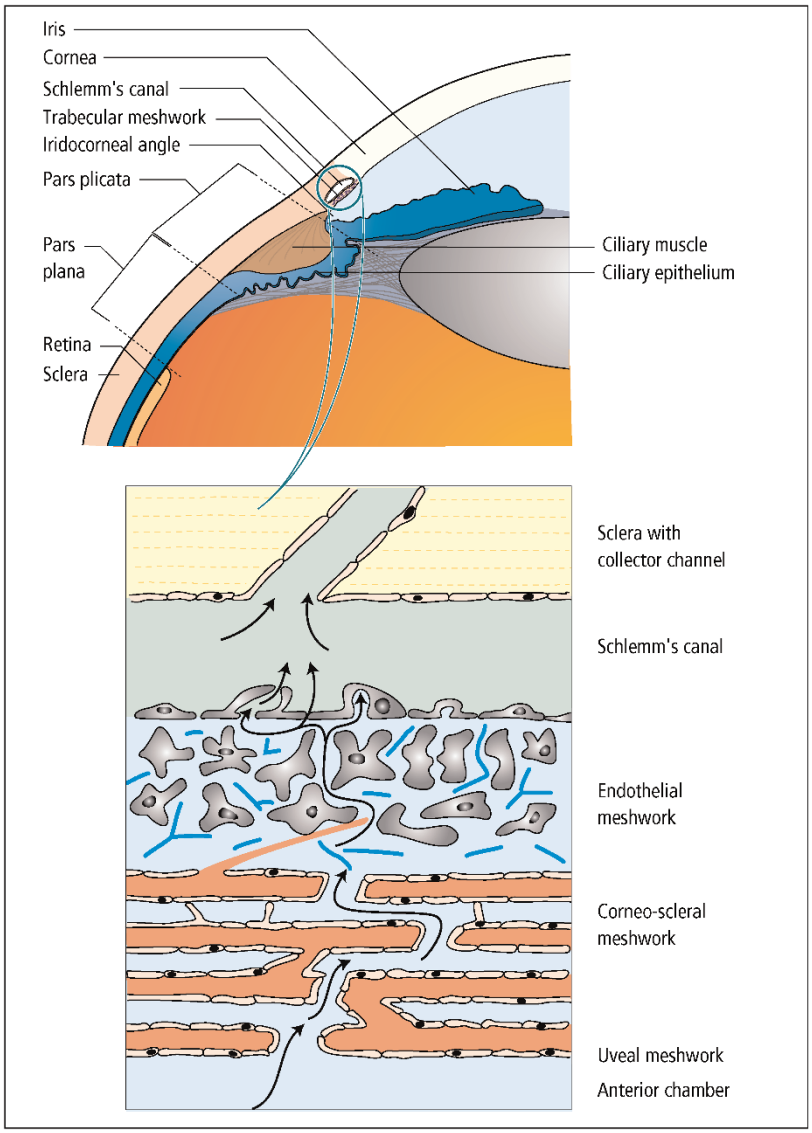

Figure 1.16 The anatomy of the trabecular meshwork.

to this that make up the *lens cortex* are all laid down postnatally. For this reason, the depth of a lens opacity may provide a clue to its time of formation.

With age, the deeper fibres lose their nuclei and intracellular organelles and become inert, so the metabolic work to maintain lens transparency is provided entirely by the lens epithelium and the youngest, most superficial fibres. It is remarkable that these deeper lens fibres, which are essentially dead, retain their transparency into late life. However, over the life span, there is progressive cross-linking of the lens crystallins leading to increasing stiffness of the lens and a loss of deformability. This results in a loss of accommodative power which reaches its peak at around 50 years. This is termed presbyopia.

Crystallin cross-linking, formation of high molecular weight aggregates and additional post-translational modifications to proteins, including pigmentation, also lead to a steady loss of lens transparency, particularly affecting the lens nucleus, which at some point may amount to cataract.

The optic nerve

The optic nerve (Figure 1.19) is formed by the axons arising from the *retinal ganglion cell layer*, which form

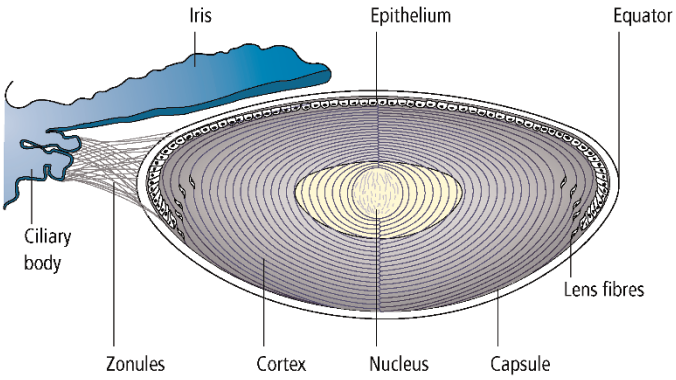

Figure 1.17 The anatomy of the lens.

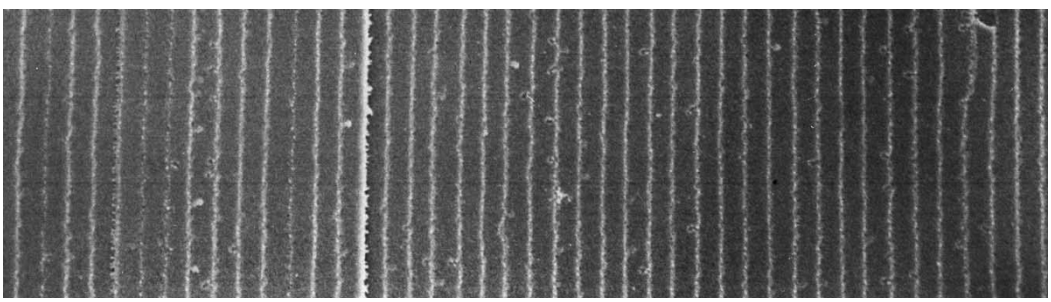

Figure 1.18 Remarkable regularity of rabbit lens fibre packing, shown by surface electron microscopy. (*Source*: Kuzak, J.R., Zoltolski, R.K. & Sivertson, C. *Exp Eye Res* 2004; 78: 673–687. Reproduced with permission from Elsevier.)

the *nerve fibre layer* of the retina. There are approximately 1 million nerve fibres in 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.

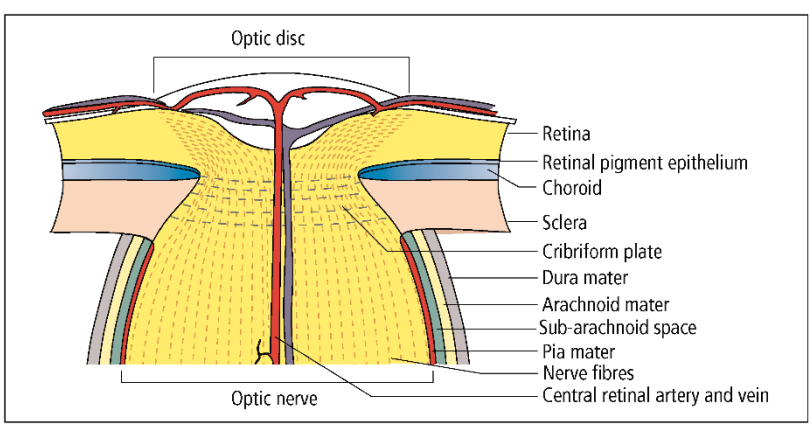

Figure 1.19 The structure of the optic nerve.

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 1.20). 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 choroidal capillaries.

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 those of the blood–brain barrier. The capillaries of the choroid, however, are fenestrated and leaky. The retinal pigment epithelial cells are also joined by tight junctions and present an *external blood–retinal barrier* between the leaky choroid and the retina.

Breakdown of these barriers is responsible for the clinical features of many retinal vascular diseases.

The third, fourth and sixth cranial nerves

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

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 from the Edinger Westphäl nucleus run in the third nerve and end in the ciliary ganglion. Here postganglionic fibres arise and pass in the short ciliary nerves to the sphincter pupillae and the ciliary muscle		

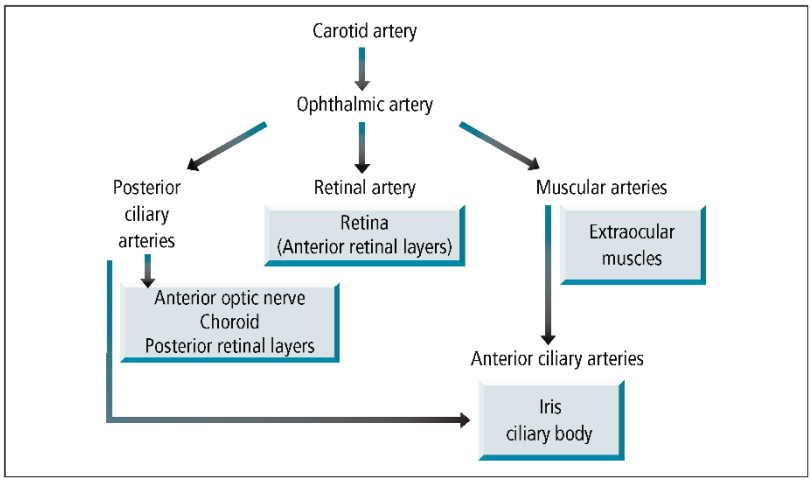

Figure 1.20 Diagrammatic representation of the ocular blood supply.

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 1.21 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 reflecting the accompanying brainstem injury. 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. Also, a nuclear third nerve lesion results in an ipsilateral palsy of the muscles supplied by the third nerve, bilateral ptosis and a palsy of the contralateral superior rectus,

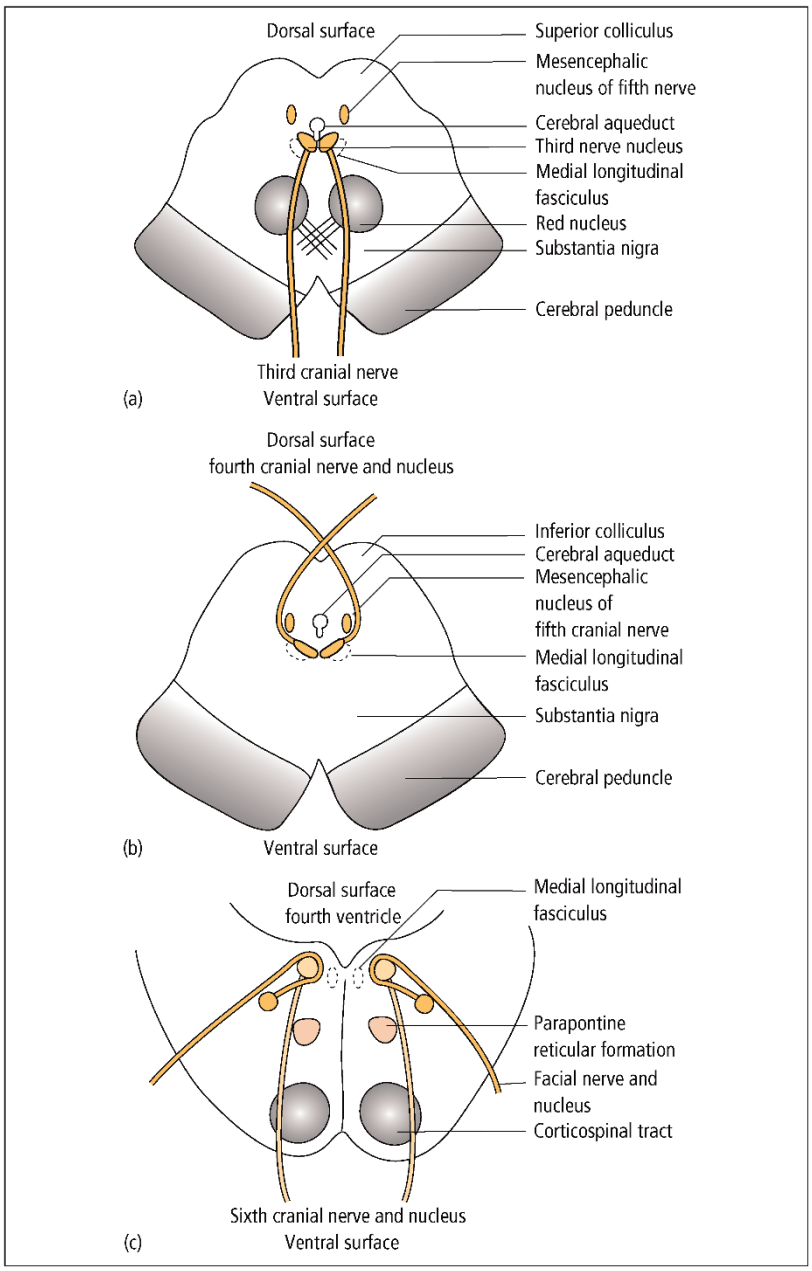

Figure 1.21 Diagrams to show the nuclei and initial course of the (a) third, (b) fourth and (c) sixth cranial nerves.

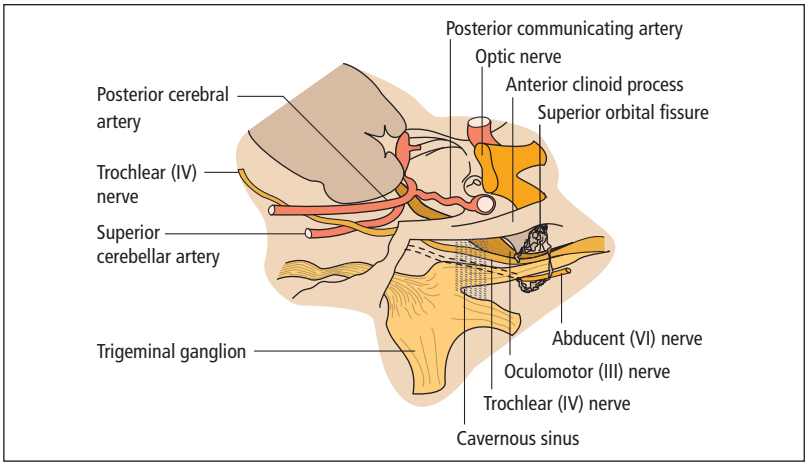

Figure 1.22 The intracranial course of the third, fourth and sixth cranial nerves.

since both sets of crossing fibres from the subnucleus are affected.

Peripheral course

Figure 1.22 shows the intracranial course of the third, fourth and sixth cranial nerves.

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 inferomedial to the fourth nerve in proximity to the internal carotid artery. *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.

The seventh cranial nerve

The seventh cranial nerve arises from a nucleus in the pons, loops over that of the sixth cranial nerve (Figure 1.21c) and leaves the brainstem at the *cerebellopontine angle* where it is joined by the *nervus intermedius*. The two nerves travel together in the internal auditory canal where they fuse to form the geniculate ganglion. From there, the somatic motor fibres issue from the skull through the stylomastoid foramen, to supply the muscles of the face and scalp. The nervus intermedius carries secretomotor fibres to the lacrimal gland via the *nerve of the pterygoid canal*, a mixed autonomic nerve which includes sympathetic fibres from the carotid plexus. The preganglionic, parasympathetic fibres synapse with postganglionic fibres in the *pterygopalatine ganglion* and reach the lacrimal gland via the lacrimal nerve. The nervus intermedius also carries taste fibres and secretomotor fibres to the submandibular and sublingual glands, which run in the chorda tympani.

Assessment questions
True or False

1. The cornea

a Has an endothelial layer that regenerates readily.

b Has an epithelial layer that fails to regenerate.

c The endothelium actively pumps water from the stroma.
d Is an important refractive component of the eye.
e Has a stroma composed of randomly arranged collagen fibrils.

2. The retina

a Is ten layers thick.
b Has ganglion cells whose axons form the optic nerve.
c Has three types of rods responsible for colour vision.
d The neuroretina is firmly attached to the retinal pigment epithelium.
e The RPE delivers vitamin A for rhodopsin production.

3. The lens

a Grows throughout life.
b Is surrounded by a collagenous capsule.
c Cortex and nucleus are rich in organelles.
d Has a high refractive index owing to its protein content.
e Shape becomes more curved during accommodation for near.

4. The suspensory ligament of the lens (the zonule)

a Attaches the lens to the ciliary body.
b Is part of the iridocorneal angle.
c Is composed of smooth muscle.
d Transmits changes in tension to the lens capsule.

5. The posterior chamber

a Is another name for the vitreous body.
b Lies between the iris, lens and ciliary body.
c Contains aqueous humour, secreted by the ciliary processes.
d Is in communication with the anterior chamber.

6. The tear film

a Is 100 μm thick.
b Tears are drained by the nasolacrimal system.
c The mucoaqueous layer is in contact with the cornea.
d Is important in the refraction of light entering the eye.
e Contains lysozyme and secretory IgA.

7. The iridocorneal angle

a Is the site of aqueous production.
b Lies between the cornea and the ciliary body.
c In primary open-angle glaucoma, there is a reduction in the number of cells covering the trabecular meshwork.
d Fluid passes through the trabecular meshwork to Schlemm's canal.

8. The optic nerve

a Axons leave the eyeball through the cribriform plate.
b Is not bathed in CSF until it enters the cranial cavity.
c Anteriorly is supplied by blood from the ciliary arteries.
d Axons are not myelinated in the retrobulbar part of the nerve.
e Is formed by axons of the nerve fibre layer of the retina.

9. The third, fourth and sixth cranial nerves

a All originate in the midbrain.
b A nuclear third nerve palsy will cause a contralateral palsy of the superior rectus.
c The fourth nerve supplies the lateral rectus.
d The sixth nerve has a long intracranial course.
e The third nerve may be affected by aneurysms of the posterior communicating artery.

Answers

1. The cornea

a False. The human endothelium does not regenerate; dead cells are replaced by the spreading of surviving cells.
b False. The epithelial layer readily regenerates.
c True. The endothelial cells pump out ions and the water follows osmotically. Removal of water maintains corneal transparency.
d True. The cornea is a more powerful refractive element than the natural lens of the eye.
e False. The fine, equally spaced, stromal collagen fibrils are arranged in parallel and packed in an orderly manner. This is a requirement for transparency.

2. The retina

a True. See Figure 1.13.
b True. The retinal ganglion cell axons form the retinal nerve fibre layer and exit the eye at the optic nerve head.
c False. The rods are responsible for night vision and three cone types are responsible for daylight and colour vision.

d False. The attachment is loose; the neuroretina separates from the RPE in retinal detachment.
e True. Vitamin A is delivered by the RPE to the photoreceptors and combined with opsin.

3. The lens

a True. It does grow throughout life.
b True. This is of great importance in cataract surgery.
c False. The older, deep cortical and nuclear fibres lose their nuclei and other organelles.
d True. The high protein content accounts for its high refractive index.
e True. See page 11.

4. The suspensory ligament of the lens (the zonule)

a True. Zonular fibres extend from the pars plicata of the ciliary body to the lens equator.
b False. The zonule lies behind the iris and iridocorneal angle.
c False. The ciliary muscle contains smooth muscle, not the zonule, which is acellular.
d True. Contraction of the ciliary muscle relaxes the zonular fibres allowing the lens to increase its curvature and thus its refractive power (this is 'accommodation').

5. The posterior chamber

a False. The vitreous body is quite separate.
b True. See Figure 1.4.
c True. See page 10.
d True. Communication is via the pupil, in the gap between iris and lens at the pupil margin. If this gap is narrowed or closed, pressure in the posterior chamber pushes the iris forward and may close the angle (acute closed-angle glaucoma).

6. The tear film

a False. The tear film is about 3 μm thick.
b True. There is a punctum on the medial aspect of both upper and lower eyelids. These allow tears to drain into the nasolacrimal drainage system.
c True. The mucin layer is produced by goblet cells.
d True. It provides a smooth interface for the refraction of light.
e True. These account for the antibacterial properties of the tear film.

7. The iridocorneal angle

a False. It is the site of aqueous drainage.
b True. See Figure 1.15.
c True. This may reduce aqueous drainage.
d True. Flow depends on the pressure gradient between the anterior chamber and Schlemm's canal and there is also an active component.

8. The optic nerve

a True. This sieve-like structure provides support for the optic nerve as it leaves the eye.
b False. In the orbit, outside its pial sheath, the optic nerve is surrounded by cerebrospinal fluid within the subarachnoid space. This is in continuity with that in the intracranial cavity.
c True. The supply to the anterior part of the optic nerve differs from the supply to the anterior layers of the retina.
d True. This is a most important blood supply for the anterior optic nerve.
e False. They are usually not myelinated *within* the eye.
f True. It is made up from retinal ganglion cell axons.

9. The third, fourth and sixth cranial nerves

a False. The nuclei of the sixth and seventh nerves lie in the pons.
b True. The superior rectus is innervated by the contralateral nucleus.
c False. It supplies the superior oblique.
d True. This makes the sixth nerve susceptible to trauma, which may cause lateral rectus palsy.
e True. It passes lateral to the artery.