1

Anatomy

Learning objective

✔ The anatomy of the eye, 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. An outline is given below.

Surface anatomy

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 margins of the cornea are exposed in the *palpebral aperture,* together with two small white triangles of bulbar conjunctiva, and the underlying sclera. The medial and lateral ends of the aperture are termed 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 facial muscles, 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 and in light eye closure. The levator palpebrae muscle, the elevator of the upper lid, is concerned with the upstroke of the blink (*third cranial nerve*). The synchronized contractions of the blink are completed within just 300 ms.

The contents of the orbit are separated from the overlying skin 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 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.

Centrally, 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

Ophthalmology: Lecture Notes, Thirteenth Edition. Bruce James, Anthony Bron, and Manoj V. Parulekar.

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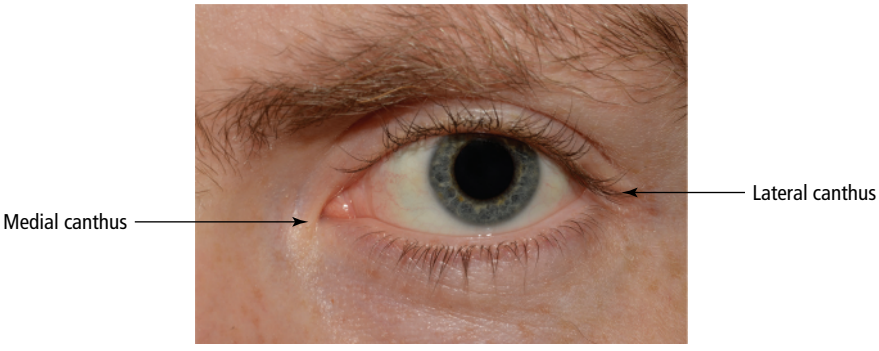


Figure 1.1 The eye, looking straight ahead.

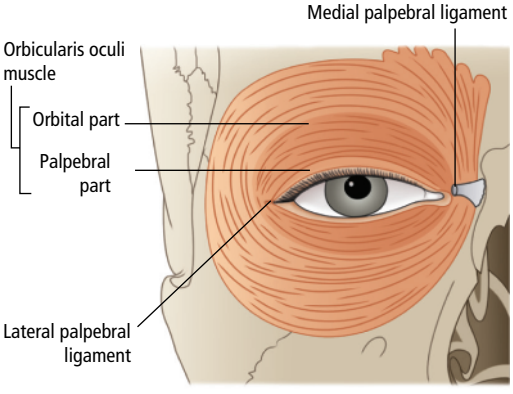


Figure 1.2 Disposition of the orbicularis muscle.

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.

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

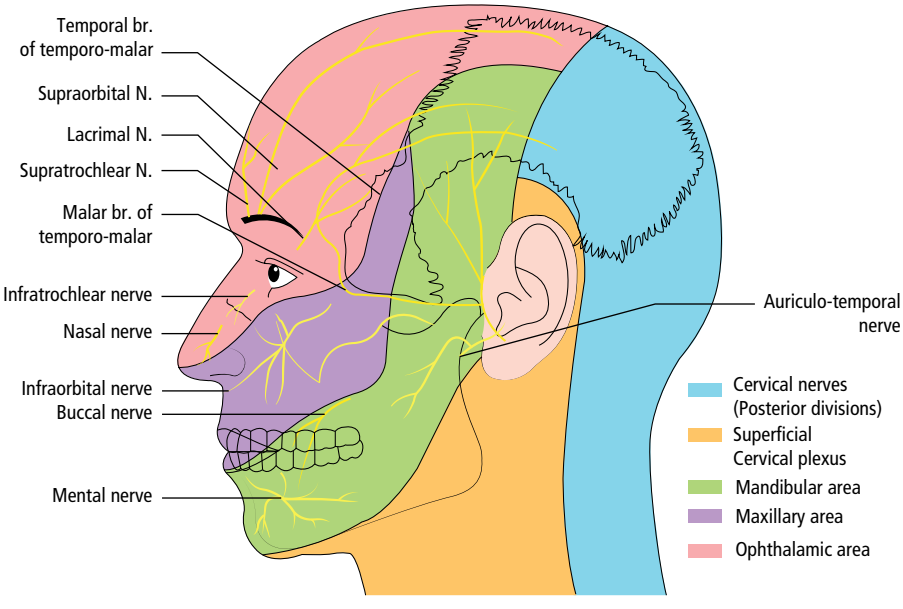


Figure 1.3 Sensory innervation of the face by the trigeminal nerve.

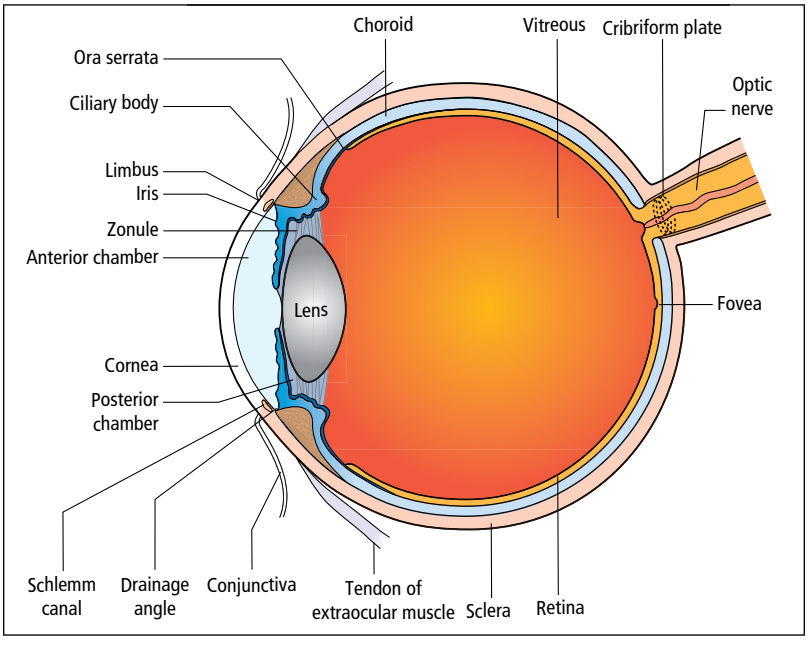


Figure 1.4 The basic anatomy of the eye.

outer sclera, while the optic nerve leaves the globe posteriorly.

- A rich vascular coat (the uvea) forms the choroid posteriorly (lining the inner surface of the sclera) and the ciliary body and iris anteriorly. Internal to the choroid lies the retina, to which it is firmly attached and whose outer third it nourishes.
- The *lens* lies behind the iris, supported by the *zonules,* whose fine fibres run from the lens equator to the ciliary body. The ciliary body contains the smooth *ciliary muscle* whose contraction controls focusing by altering lens shape. When the eye is focused for distance, tension in the zonule is high and maintains the lens in a flattened profile. 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. It is covered by the *ciliary epithelium*, which 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*. Its periphery is the iridocorneal angle or *drainage angle*. The angle gives access to an interlacement of cell-lined collagen beams called the *trabecular meshwork* (Figure 1.24), through which aqueous drains into Schlemm 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 structures 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 capsule*) separates the conjunctiva from the sclera and is prolonged backwards as a sheath around the rectus muscles.

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

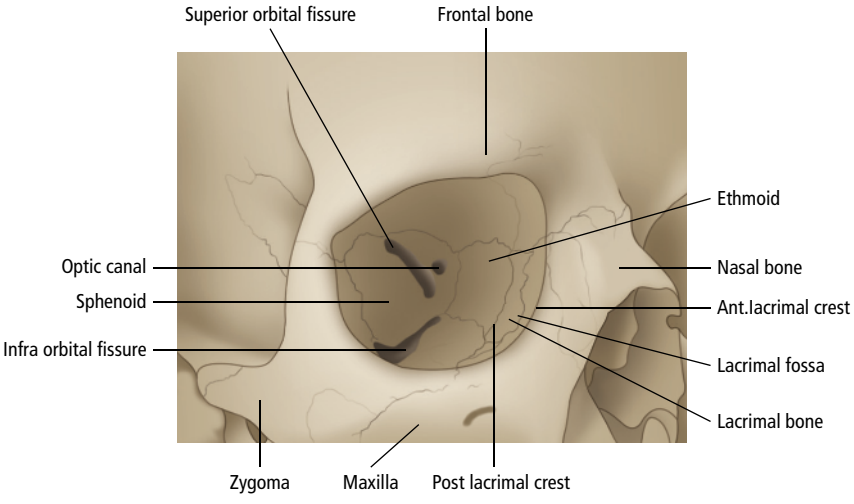


Figure 1.5 The anatomy of the orbit.

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 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 muscle) innervated by the sympathetic nervous system, arises from the deep surface of the levator and inserts into the tarsal plate. Müller muscle contributes to a lesser extent to elevation of the lid and if the sympathetic supply is

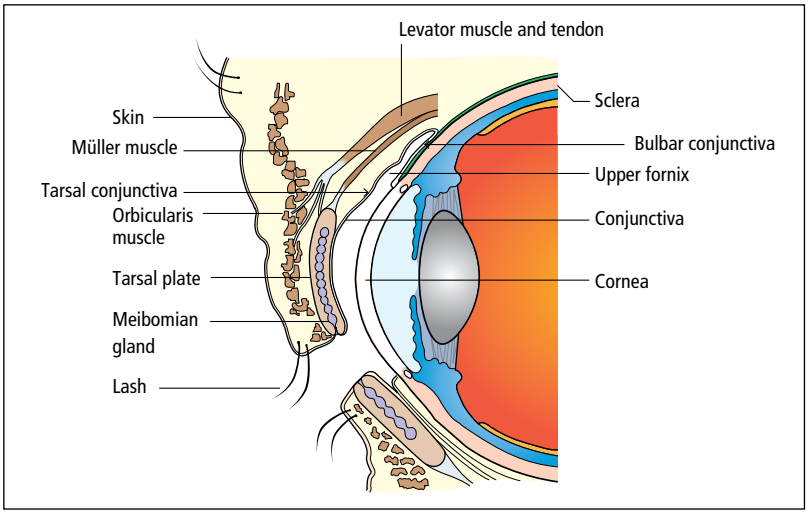


Figure 1.6 The anatomy of the eyelids.

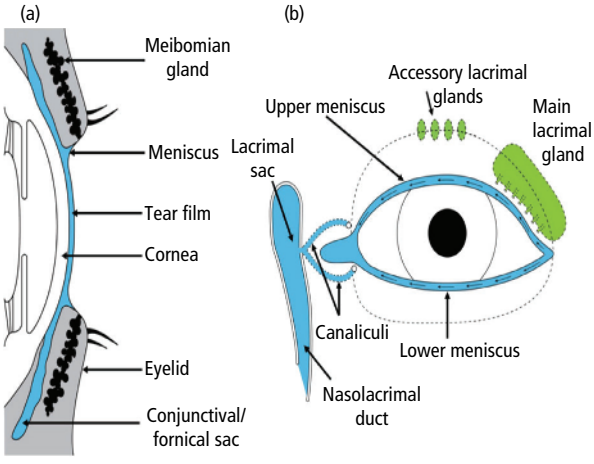


Figure 1.7 Drawing of the eye: (a) in cross section, (b) in frontal view to illustrate the distribution of the tears. (*Source:* Reproduced from Gaffney et al. (2010) / with permission of Elsevier.)

damaged, a slight ptosis results as part of Horner 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 at 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, the tears are spread as a film 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 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 stabilizes the tear film and possibly retards evaporation.

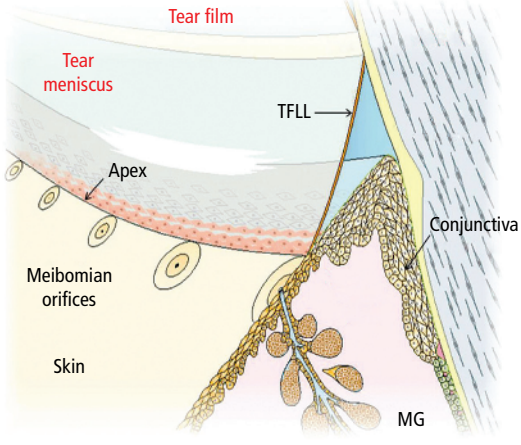


Figure 1.8 Diagram of lid margin to show meibomian gland (MG) orifices, meniscus and tear film lipid layer (TFLL). (*Source:* Reproduced from Bron et al. (2011) / with permission of Elsevier.)

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 into the nasal cavity, entering at the *inferior meatus*. 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.

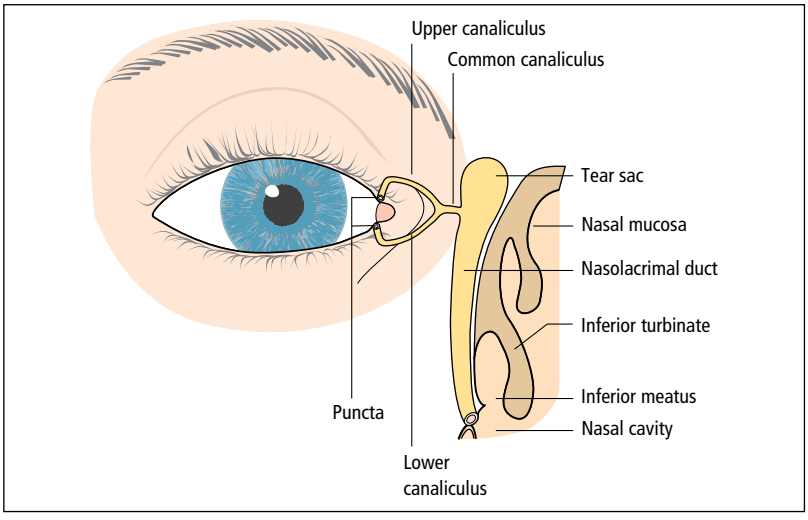


Figure 1.9 The major components of the lacrimal drainage system.

Detailed functional anatomy

The tear film

The eye is bathed constantly by the tears, secreted by the lacrimal gland into the upper, outer 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 in the brainstem and thence to the lacrimal gland. This ensures that tear production is regulated reflexly in response to signals from the ocular surface, arising from the cooling effect of airflow or from atmospheric particles. This reflex system is referred to as the *Lacrimal Functional Unit*.

The most superficial epithelial cells of the ocular surface express a mucin-rich *apical glycocalyx* in their surface membranes which renders the surface wettable by the tears (Figure 1.10). When the eyes are open, the exposed ocular surface is covered by a tear film, 3 µm thick, which has two layers:

- A thin, superficial *lipid layer* (100 nm) produced by the meibomian glands and delivered to the tear film from the lid margins.
- An underlying *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.

Functions of the tear film

- It provides an optically smooth air/tear interface, providing distortion-free refraction of light at the cornea.
- It is replenished with each blink, moistening the eye and preventing dehydration of the exposed ocular surface.
- It removes debris and foreign particles from the ocular surface through the action of the blink and by the flow and drainage of the tears.
- It transmits oxygen to the avascular cornea.
- The tears have antimicrobial properties by means of lysozyme, lactoferrin, defensins and immunoglobulins, particularly *secretory IgA*.

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.
- An underlying *stroma* which accounts for over 90% of the corneal thickness. On its most anterior aspect is a tough, *anterior limiting layer* (Bowman layer), 20 µm thick, which is free of cells and composed of fine, short, tightly interwoven collagen fibrils. The basal cells of the epithelium are firmly attached to an underlying basal lamina by *hemidesmosomes* and to Bowman layer by *anchoring fibrils*.

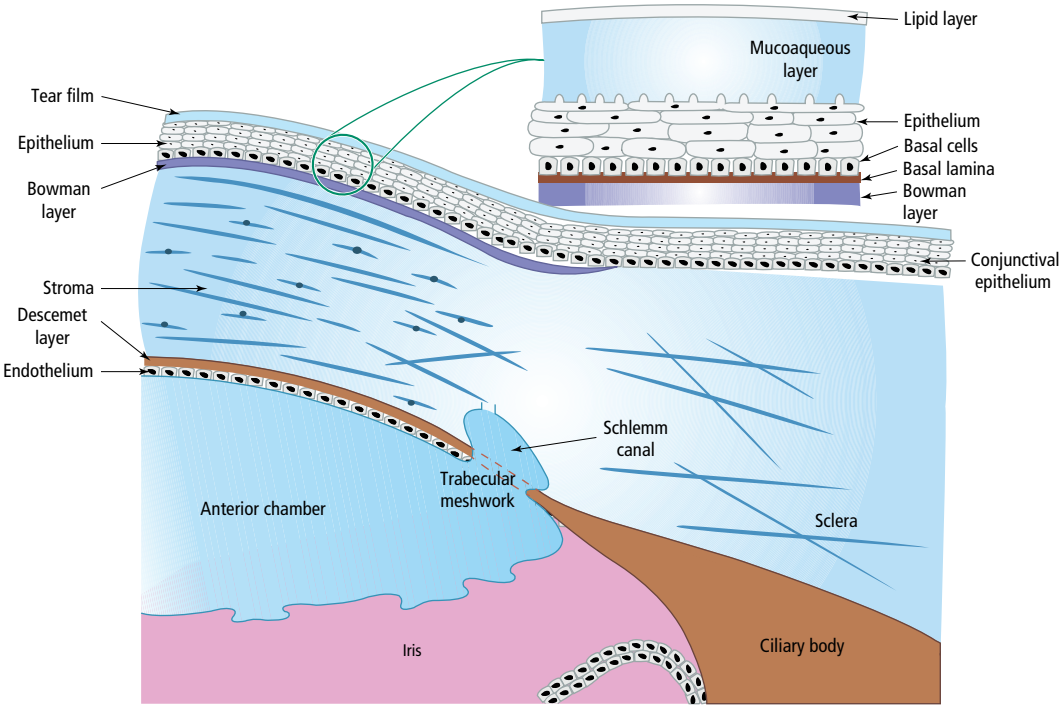


Figure 1.10 The structure of the cornea and precorneal tear film (schematic, not to scale – the stroma accounts for 95% of the corneal thickness).

The main body of the stroma consists of type I collagen fibrils arranged in parallel within multiple lamellae, embedded in 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 between the lamellae. The extraordinarily regular packing of the stromal collagen fibrils, with a small diameter and narrow separation (in the region of 200 nm), accounts for the almost perfect transparency of the cornea. Backscattered light (towards the source), is obliterated by destructive interference so that over 90% of the incident light is transmitted into the eye.

The stroma is bounded behind by the *posterior limiting layer* (Descemet layer), the basal lamina of the corneal endothelium. It is chiefly composed of type IV collagen.

- The orderly architecture of the cornea, on which transparency depends, is maintained by regulating stromal hydration. The *endothelium,* a monolayer of hexagonal, nonregenerating cells covering the posterior aspect of Descemet' layer (Figure 1.11) actively pumps ions from the stroma into the anterior chamber carrying water with them. This controls corneal hydration, thickness and order, and hence

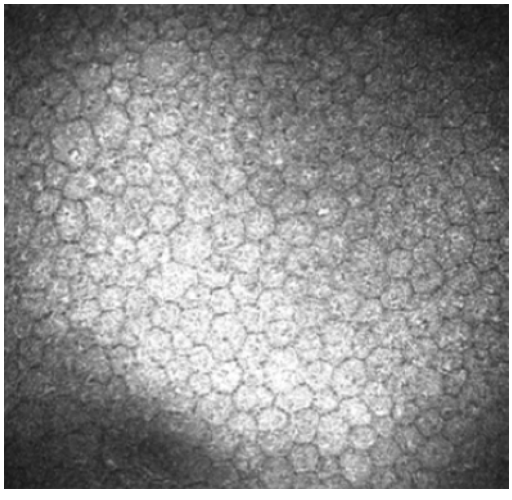


Figure 1.11 Normal corneal endothelium shown by confocal microscopy. (*Source:* Courtesy of Paula Hedges.)

transparency. Failure of endothelial pumping leads to corneal oedema and swelling and a loss of transparency as the orderly structure breaks down.

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 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 cornea is avascular and its nutrition 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, in contrast to the cornea, scatters light strongly and appears white and opaque.
- It is of variable thickness, about 1 mm around the optic nerve head and about 0.3 mm, just behind the rectus muscle insertions.

The choroid

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

The retina

The retina is the thin, light-sensitive, innermost layer of the globe, fused externally with the vascular choroid and closely apposed internally, to the *vitreous gel* (Figure 1.13). On ophthalmoscopy, the retina is the major feature of the *fundus oculi* (Figure 1.14), extending peripherally to its junction with the ciliary body, at the *ora serrata*.

The key landmarks of the fundus oculi are the *optic nerve head* (referred to ophthalmoscopically as the *optic disc*), the retinal *veins and arteries* (actually arterioles) and the *fovea,* the cone-rich centre of the retina, two disc diameters lateral to the temporal margin of the optic disc. At the centre of the fovea is the *foveola*, a declivity marking the thinnest part of the retina, containing only cone photoreceptors. In

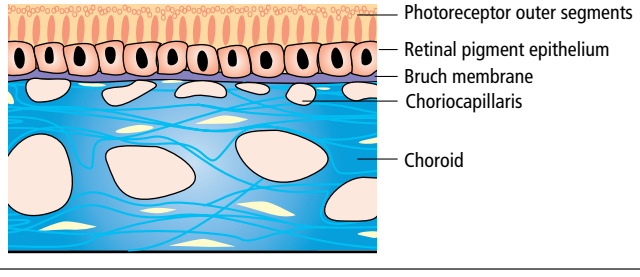


Figure 1.12 The relationship between the choroid, RPE and retina.

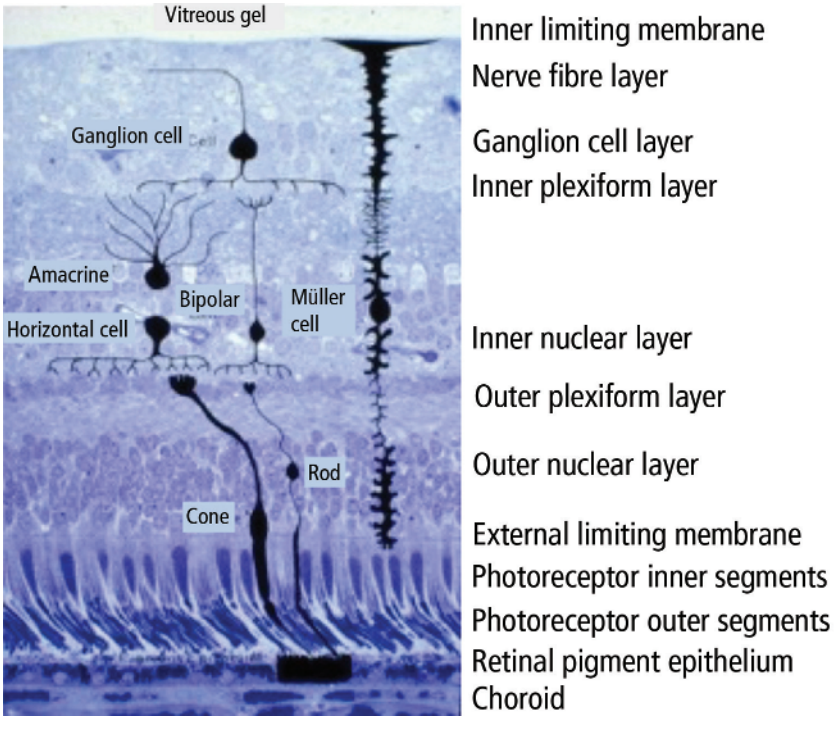


Figure 1.13 The structure of the retina. (*Source:* Courtesy of John Marshall.)

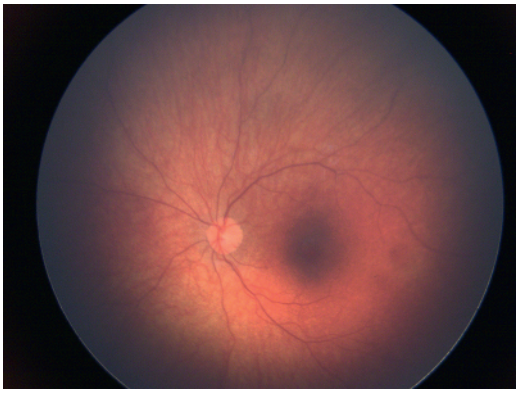


Figure 1.14 Photograph of the fundus oculi.

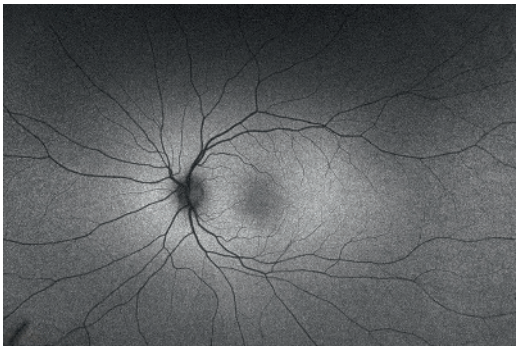


Figure 1.15 Autofluorescence photograph of the macula lutea.

youth, it is visible during ophthalmoscopy as a pinpoint reflection of light from the foveal *pit*.

A barely discernible, broad, disc-shaped zone, 5.5 mm in diameter, centred on the fovea and appearing slightly yellow in colour in appropriate lighting conditions, is termed the *macula* or *macula lutea* ('yellow spot'), whose yellow colour is due to the abundant presence of three xanthophyll, carotenoid pigments, *lutein, zeaxanthin* and *meso-zeathanthin*, in the axons of the cone photoreceptors and therefore in the outer plexiform layer. These macular pigments (MPs) are also present to a lesser extent in the inner plexiform layer of the central retina and also in the retinal glial (Müller) cells (Arunkumar et al. 2020). This zone can be imaged by autofluorescence techniques (Figure 1.15). The macula can be the seat of a

wide range of inherited, degenerative or toxic disorders which may threaten vision or be responsible for blindness. The most common of these is *age-related macular degeneration*, or AMD (Chapter 12).

The MPs protect the receptors and the underlying RPE from the phototoxicity of high-energy blue light, partly acting as an optical filter, absorbing strongly in the wavelengths 445–450 nm, and partly as antioxidant, free-radical scavengers, able to quench the damaging action of reactive oxygen species (ROS), such as hydroxyl or peroxyl radicals, or reactive non-radical compounds such as singlet oxygen, peroxynitrite, or hydrogen peroxide.

The retinal MPs are entirely of dietary origin since they cannot be synthesized in the human body; lutein and zeaxanthin are derived from leafy green vegetables and orange and yellow fruits and vegetables. Kale, spinach and broccoli are rich sources of lutein, while corn products are rich in zeaxanthin. Meso-zeaxanthin is a metabolic product of these ingested carotenoids. There is evidence that foodstuffs and nutritional supplements containing lutein and zeaxanthin can reduce the risk of AMD, while ß-carotenoids, such as those contained in carrots, though a source of vitamin A, afford no such protection.

The vascular architecture of the retina is routinely demonstrated during *fluorescein angiography* which permits the capillary systems of the inner retina to be seen at high resolution (Chapter 3, Figure 1.16). The vascular nutrition of the inner two thirds of the retina is supplied by the retinal capillaries while the outer third of the retina is nourished, across the RPE, by the capillary bed of the choroid (the *choriocapillaris*). At the fovea, however, the retina is sufficiently thin that its nutritional needs are supplied entirely by the choroid.

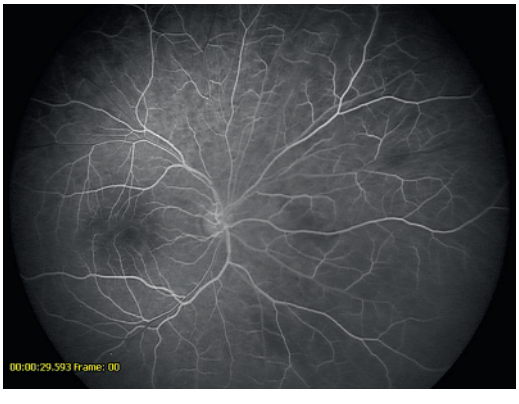


Figure 1.16 A fluorescein angiogram showing the vascular architecture of the retina.

In keeping with this, in terms of its retinal vascular blood supply, the fovea is *capillary-free* (Figure 1.17).

The retina is derived embryologically from the optic vesicle, an outpouching of the forebrain connected to it by the optic stalk, the forerunner of the optic nerve. With development, the optic vesicle invaginates to form the optic cup, whose outermost layer forms the RPE while its innermost layer forms the neuroretina (Figure 1.18). A ventral infolding of the optic stalk forms the choroidal fissure which closes at 5–7 weeks of gestation. Failure to do so may give rise to the congenital defect of *coloboma*.

The layers of the retina

The layers of the retina are, from outside in, the RPE and the neuroretina, the latter consisting of the photoreceptors (rods and cones), the bipolar nerve layer (and the amacrine and horizontal nerve cells) and the retinal ganglion cell (RGC) layer, whose axons give rise to the innermost, nerve fibre layer (Figure 1.13). The RGC axons converge to the optic nerve head, where they form the *optic nerve*. The optic nerve head is visible by ophthalmic examination, when its appearance is referred to as the *optic disc*. The disc displays a small, roughly central depression, the *optic cup*, outside which is the *neuroretinal rim*, which transmits the RGC axons into the nerve. Loss of RGC axons in glaucoma is accompanied by a narrowing of the rim and a widening of the cup in the vertical plane – a diagnostic feature.

Müller cells, the principal glial cells of the retina, extend across its full thickness, from the photoreceptor layer to the RGC layer and are vital for the health of the retinal neurons. The basal lamina of the Müller cells forms the *external limiting membrane* of the retina at the interface of the photoreceptors and outer nuclear layer, and the *internal limiting membrane* (ILM) at the surface of the nerve fibre layer, sometime referred to as the hyaloid membrane. Collagen fibrils of the vitreous inserted into the ILM give attachment between vitreous and retina at selected sites such as the optic disc, fovea and retinal vessels. Insertions at the retinal periphery may transmit forces from the mobile vitreous to the retina that can induce a retinal hole and lead to retinal detachment. This is a particular risk in highly myopic individuals (Chapter 12).

The retinal pigment epithelium (RPE)

- Consists of a single layer of cells.
- Is loosely attached to the neuroretina, except at the periphery (*ora serrata*) and around the optic disc.

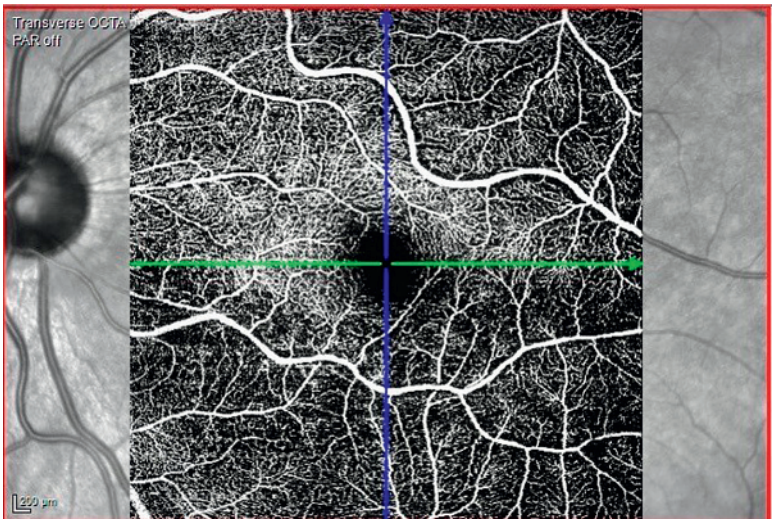
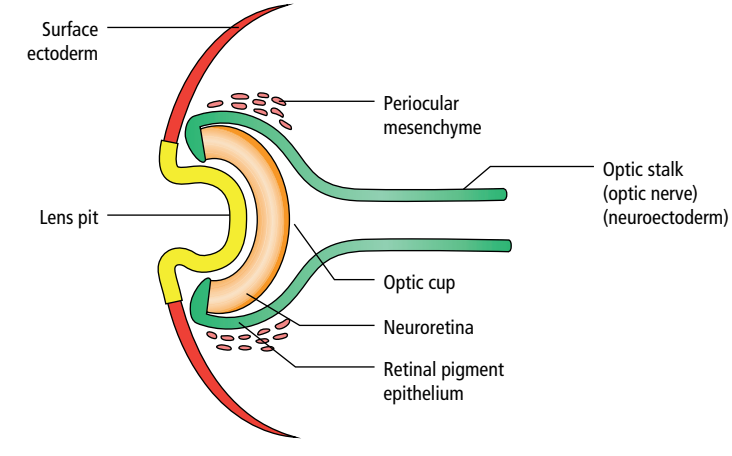
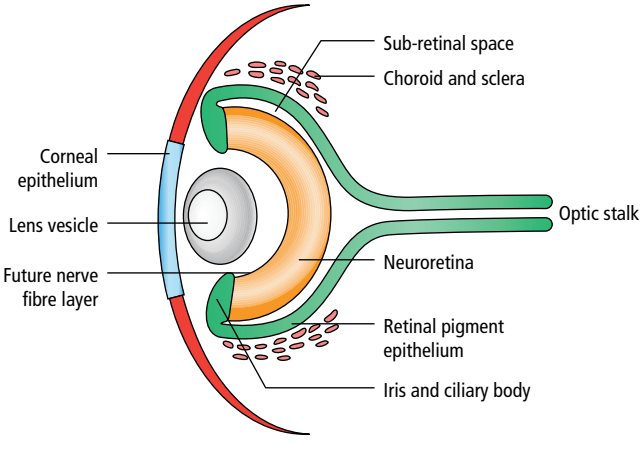


Figure 1.17 An OCT angiogram showing the absence of the capillary network at the fovea. (*Source:* Ambreen Tunio.)



Week 5



Week 6

Figure 1.18 The presumptive regions of the human eye at five and six weeks of development (schematic).

- Forms microvilli which project between and embrace the *outer segment discs* of the rods and cones (Figure 1.19).
- Phagocytoses the redundant, pigment-containing discs, which are replaced by new ones.
- Takes part in the regeneration of the photoreceptor visual pigments, rhodopsin and cone opsin and in recycling vitamin A.
- Contains melanin granules which absorb light scattered by the sclera, thereby enhancing image formation on the retina and reducing glare.
- The RPE plays a key role in maintaining the photoreceptors, transferring nutrients and vitamin-A precursors to them and removing waste products. In particular, as new outer segment discs are formed proximally, the older, spent, distal discs are removed by the interdigitating microvilli.

The photoreceptor layer

The photoreceptor layer is responsible for converting light from the image formed on the retina into electrical impulses that are delivered to the visual cortex. These are transmitted via synaptic connections, from the rods and cones to the bipolar cells and thence to the RGCs, lateral geniculate bodies and finally to the visual cortex. Within the retina, the *amacrine* and *horizontal* cells are involved in preliminary processing of the visual signal.

- *Cones* (Figure 1.20) are responsible for daylight and colour vision and have a relatively high threshold to light. Different subgroups of cones are selectively responsive to short, medium and long wavelengths (blue, green and red light). They are packed in greatest density at the foveola, where they provide the high resolution required for detailed vision, as in reading. Their density falls off towards the periphery and with it, the level of visual resolution which may be achieved. During viewing of a visual scene, the eyes are directed so that the image of an object of interest falls upon the fovea so that it is perceived in colour and in the greatest possible detail. By directing the eyes in a series of saccades over the whole of the visual scene, a detailed picture of the visual world is rapidly built up in the visual cortex and visual

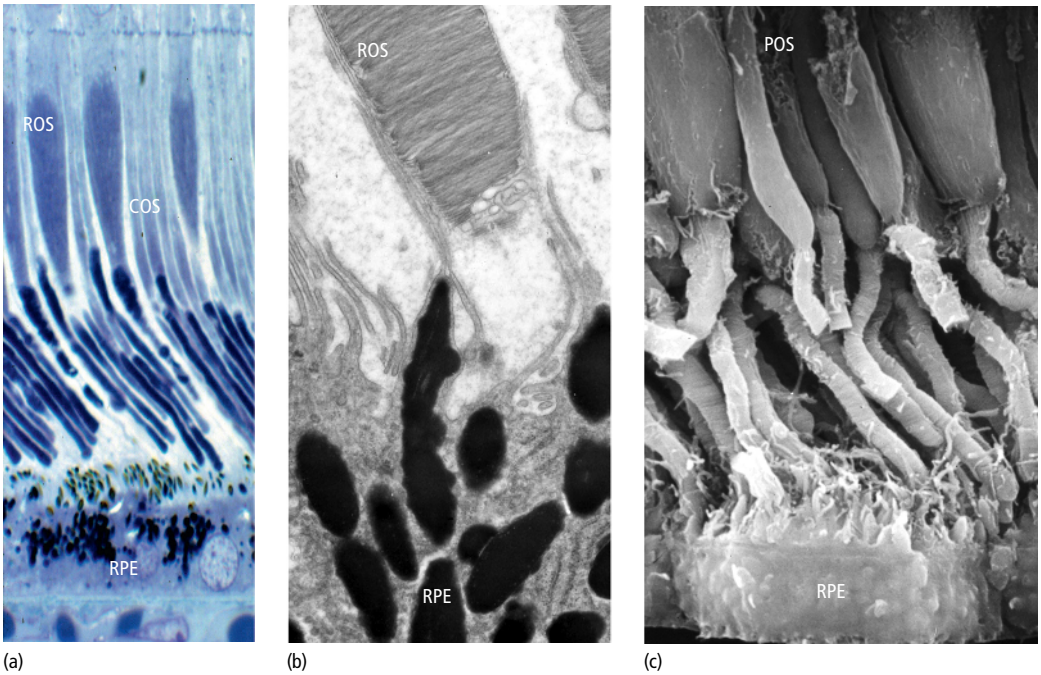


Figure 1.19 Micrograph showing the interface between the retinal pigment epithelium (RPE) and the rod (ROS) and cone (COS) photoreceptor outer segments (POS). (a) light microscopy (LM), (b) electron microscopy (EM) and (c) scanning electron microscopy (SEM). The EM micrograph shows how RPE microvilli engage with the stack of ROS discs to remove the older, redundant ones. (*Source:* Courtesy of John Marshall.)

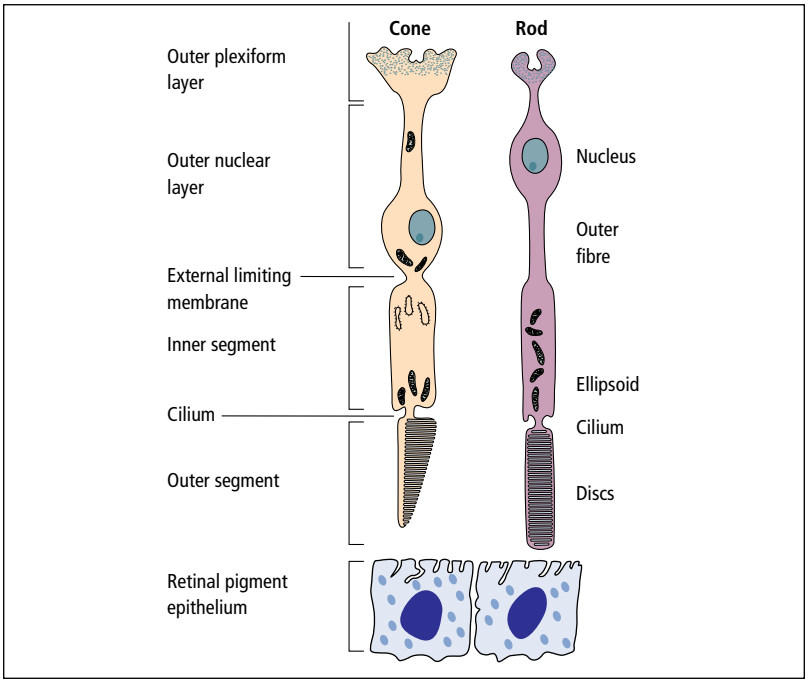


Figure 1.20 The structure of the retinal rods and cones (schematic).

association areas and brought to consciousness in the mind's eye.

- *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, their density being highest in the periphery and falling off towards the fovea, where they are entirely absent.

The layer of bipolar, amacrine and horizontal cells

These nerve cells are in synaptic connection, permitting a preliminary integration of nerve impulses at this level.

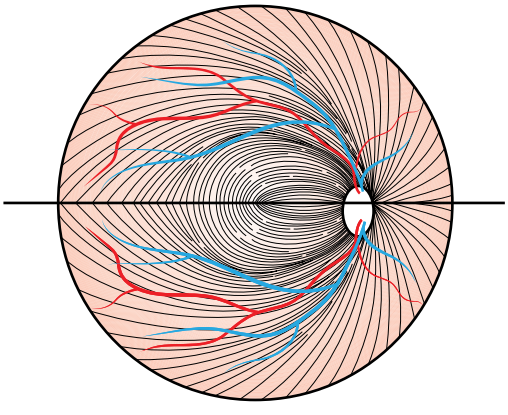


Figure 1.21 Diagram of the retina showing the sweep of the RGC axons towards the optic nerve.

The retinal ganglion cell layer

There are about 1 million RGCs in the retina, each consisting of a *soma,* containing the nucleus and abundant mitochondria and an *axon* which sweeps (in the *nerve fibre layer*) in an arcuate fashion to the optic nerve head, above and below the horizontal, to form the optic nerve (Figure 1.21). In youth, this pattern may be discerned ophthalmoscopically. The topographic arrangement of the RGCs in the retina and nerve head is very precise, and is responsible for a retinotopic projection onto the visual field, such that loss of a bundle of such nerves gives rise to a characteristic arcuate visual field loss, or *nerve fibre bundle defect.* Such a defect is typically found in chronic glaucoma (Chapter 11) when, as a result of raised intraocular pressure, bundles of nerve fibres are damaged locally at the nerve head. In youth this loss may actually be visible in the retina ophthalmoscopically.

About 1–2% of the RGCs contain the visual pigment *melanopsin,* which, activated maximally by

blue light in the range λ 460–480 nm, allows them to signal daily and seasonal, non-image-forming changes in ambient light. These photoreceptor RGCs (pRGCs) thus represent *an additional photoreceptor layer* (Foster 2020). They project, via the retino-hypothalamic tract to the suprachiasmatic nucleus (SCN) of the hypothalamus (Figure 1.22), the *master clock* of the body, which, in turn, projects to about 35 regions of the brain (Nikolaev et al. 2021). Additionally, a sympathetic nervous connection traversing the superior cervical ganglion, extends to the *pineal gland*, where it stimulates the synthesis of the hormone *melatonin*. Melatonin synthesis is triggered by the waning of light at the end of the day, when it is released into the third ventricle and subsequently into the vascular circulation. Its level in the bloodstream rises and falls over a defined period between dusk and dawn, peaking in the early hours of the morning at around 2.00–3.00 hours. Once daylight is established melatonin synthesis ceases. During the night, while its level is raised, it may act immediately on sensitive targets or, after a priming period and a delay, it may act later, when melatonin levels are low. In this way melatonin influences *clock-controlled genes* and cellular time-keepers in the brain, including the SCN and in a range of target tissues, such as the liver, muscle, pancreas, and adipose tissues. Melatonin synchronizes the message of the master clock to control circadian rhythms, sleep and pupillary activity in response to the day/night cycle.

Sleep propensity has a homeostatic component and a time-of-day, or circadian clock, component. Melatonin, acting on MT receptors in the SCN, is

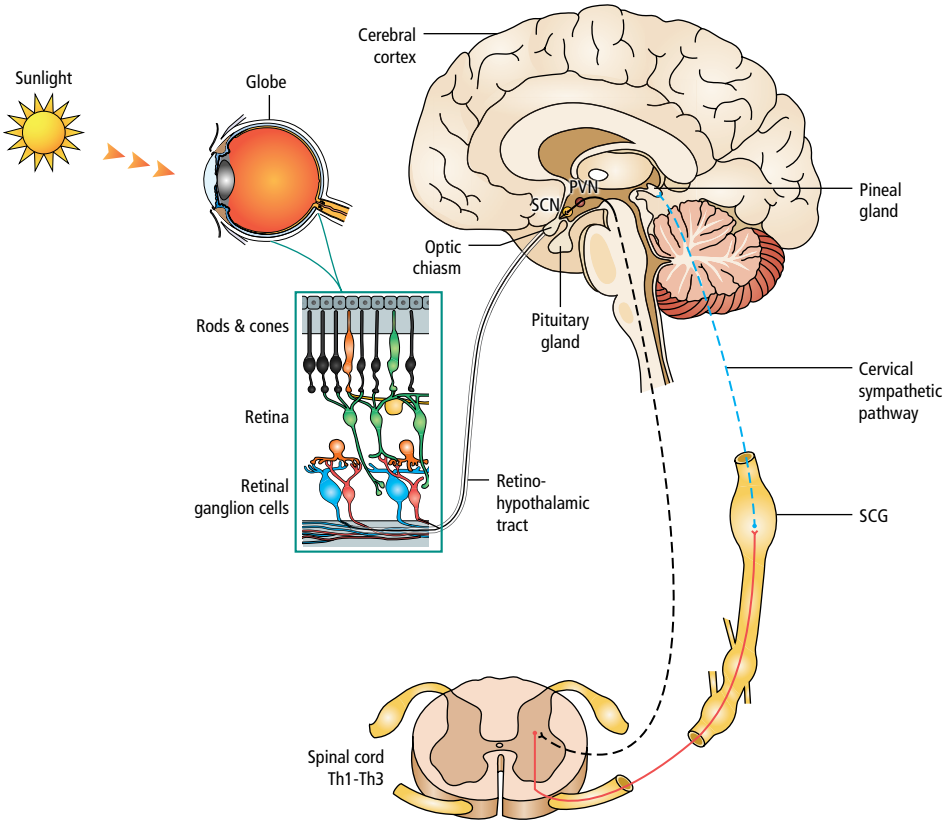


Figure 1.22 Neural pathways concerned with light-dependent biorhythms. Melanopsin-containing photoreceptor RGCs, activated by sunlight, project via the retino-hypothalamic tract to the suprachiasmatic nucleus (SCN) of the hypothalamus which serves as the master clock of the body. Melatonin is produced by the pineal gland under the control of the sympathetic nervous system. Synthesis and release of melatonin is triggered by the waning of light at the end of the day. PVN, para-ventricular nucleus; SCG, superior cervical ganglion. (*Source:* Figure modified from Vasey et al. (2021); and Ptito et al. (2021).)

thought to promote sleep by attenuating the wake-promoting signal of the circadian clock. Because melatonin does not increase the non-Rapid Eye Movement (REM) component of sleep – it is thought to be a marker for homeostatic sleep pressure. It is considered that the sleep-promoting effects of melatonin are due mostly to its action on the circadian component of sleep regulation (Zisapel 2018, Foster 2021).

The vitreous

- The vitreous is a clear gel lying behind the lens and 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 a few cells, or *hyalocytes*.
- 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.

In later life, the homogeneous gel structure of the vitreous is replaced by pools of liquefaction. Inward collapse of the remaining gel, away from the surface of the retina (vitreous detachment), is a common occurrence. Occasionally, this puts traction on the retina at points of peripheral attachment, so that the vitreous pulls off a flap of underlying retina, leading to a retinal break or hole. This is a risk factor for subsequent retinal detachment (Chapter 12).

The ciliary body

The ciliary body (Figure 1.23) 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 fibrils of 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*) and a vascular stroma.
- The stromal capillaries are fenestrated, allowing plasma constituents ready access to the stroma.
- 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 these cells.
- The epithelial layers show marked infoldings, which increase their surface area for fluid and solute transport.

The pars plana

- Situated posteriorly to the ciliary muscle, this comprises a stroma covered by an epithelial layer, two cells thick.
- Because it is relatively avascular, 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 *parasympathetic* nerves.
- The smooth dilator muscle extends from the iris periphery towards the sphincter. It is innervated by *sympathetic* nerves.
- 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 1.24).

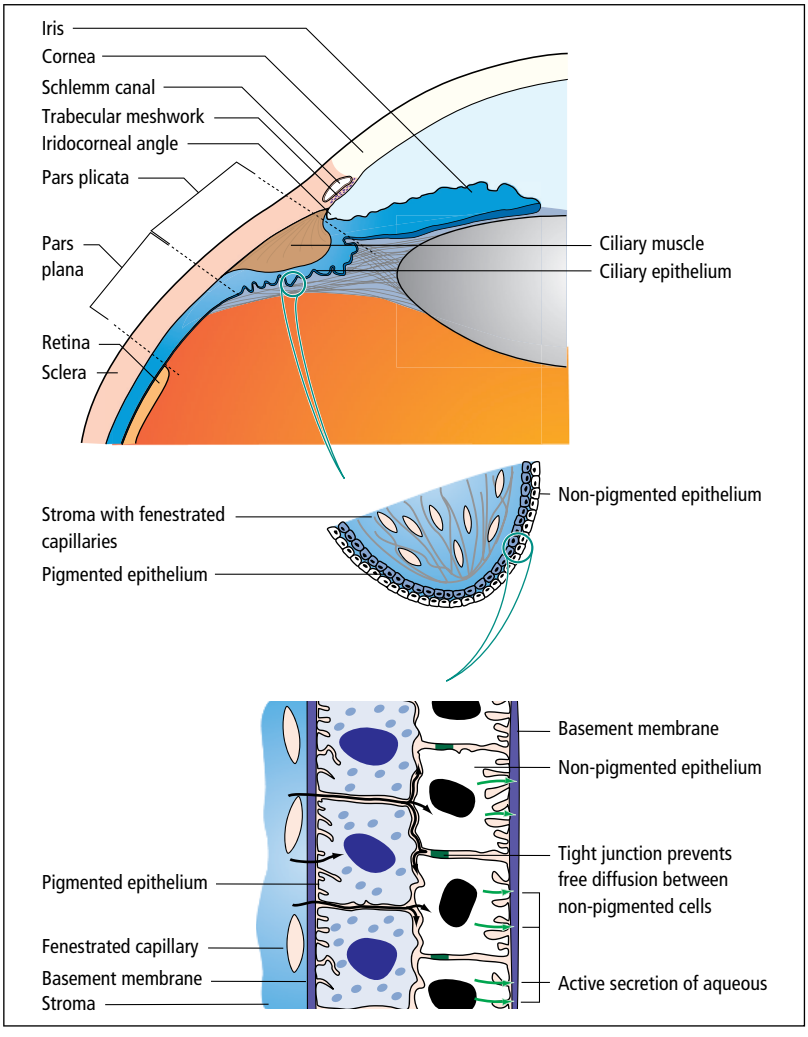


Figure 1.23 The anatomy of the ciliary body.

The trabecular meshwork

This overlies Schlemm canal and is composed of a lattice of collagen beams covered by trabecular cells. The spaces between these beams become increasingly small as Schlemm canal is approached. The outermost zone of the meshwork accounts for most of the resistance to aqueous outflow. Fluid passes into Schlemm canal, both through giant vacuoles in its endothelial lining and through intercellular spaces.

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 11).

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 1.25). 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

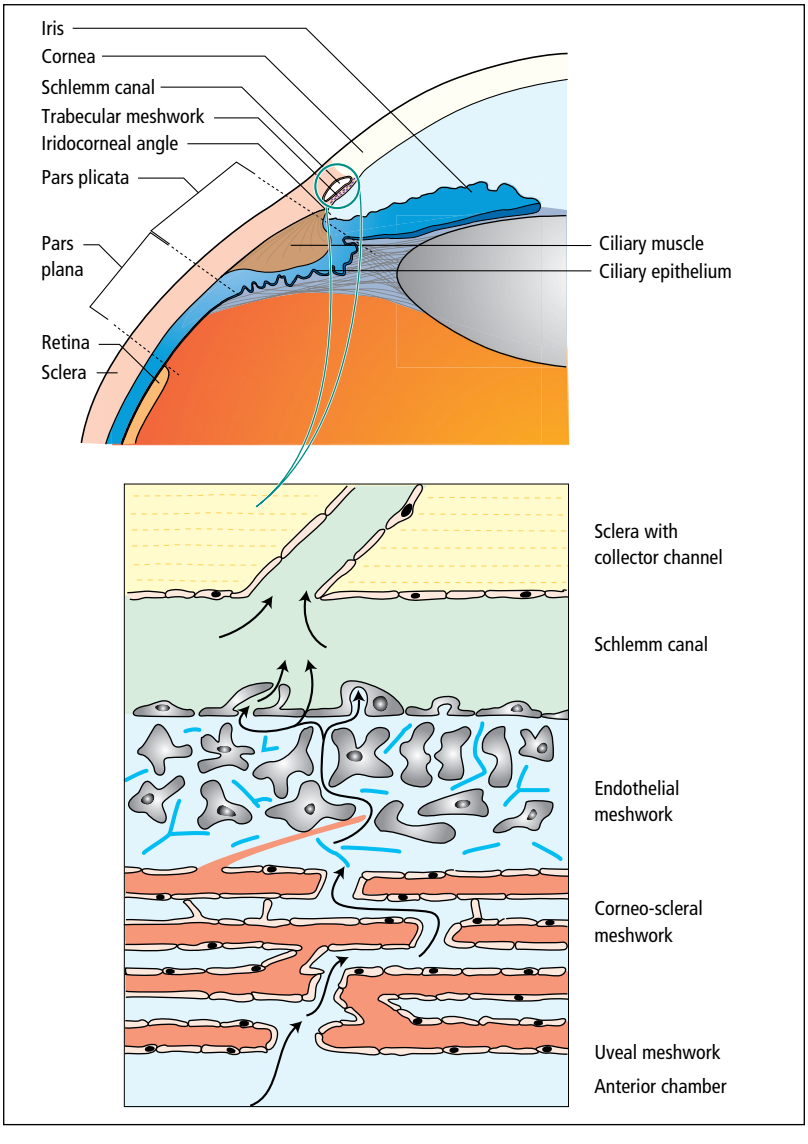


Figure 1.24 The anatomy of the trabecular meshwork.

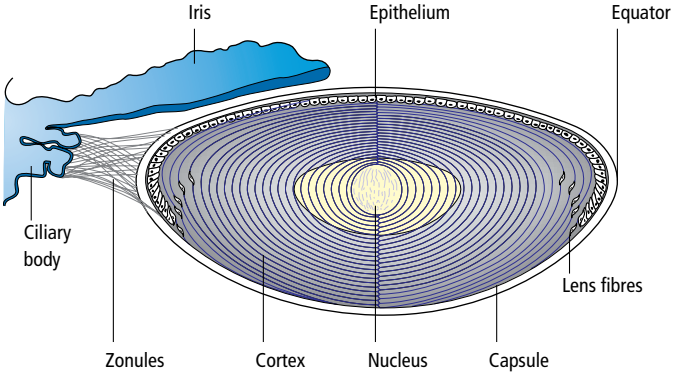


Figure 1.25 The anatomy of the lens.

zonule and permits the elasticity of the lens to increase its curvature and hence its refractive power. This may seem counterintuitive, but it comes about because the muscle bulges inwards and moves forwards during contraction.

Anatomy

The lens comprises:

- a tough, outer collagenous capsule.
- an anterior epithelium.
- A compact inner mass of lens fibre cells.

The capsule is the basal lamina of the lens epithelium, a monolayer of cells lying 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 that it is thinner and more fragile than the anterior part. This is important during cataract surgery when it may be inadvertently torn.

The epithelial cell sheet extends to a germinative zone at the lens equator, where cell division gives rise to the shells of lens fibres that make up the bulk of the lens. Fibres are elongated, spindle-shaped cells disposed with remarkable regularity in layers which arch over the lens equator (Figure 1.26). Anteriorly and posteriorly, their tips meet to form the lens *sutures,* which increase in complexity as the lens ages.

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

The lens grows throughout life, starting *in utero*, 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 foetal lens and the fibres external 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 lens fibres lose their nuclei and intracellular organelles and become inert. As a result, the metabolic work required to maintain lens transparency depends entirely on the activity of the lens epithelium and of the youngest, still nucleated, 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. The resulting loss of accommodative power, leading to a difficulty in focusing on near objects, reaches a peak at around 50 years and is termed *presbyopia*.

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

The optic nerve

The optic nerve is formed by *retinal ganglion cell axons* which make up the *nerve fibre layer* of the retina (Figure 1.27), and come together at the *optic nerve head* (Figure 1.21). There are approximately 1 million nerve fibres in each optic nerve (Figure 1.27).

- It passes out of the eye through the cribriform plate of the sclera, a sieve-like structure which permits the passage of the axons.
- 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).

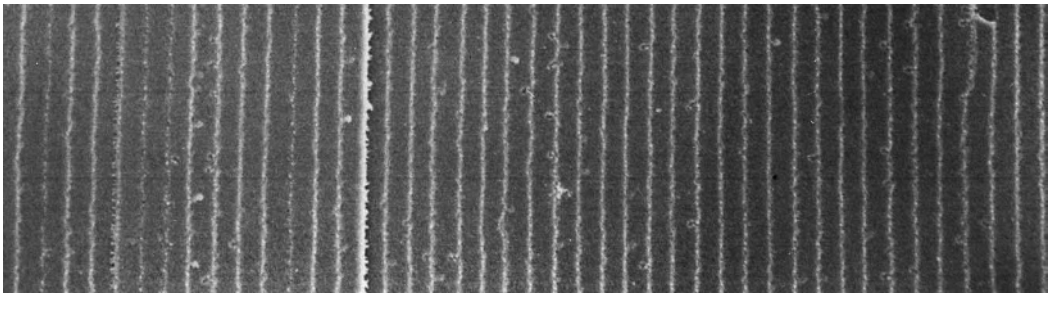


Figure 1.26 Remarkable regularity of rabbit lens fibre packing, shown by surface electron microscopy. (*Source:* Kuzak et al. (2004) / Reproduced with permission from ELSEVIER.)

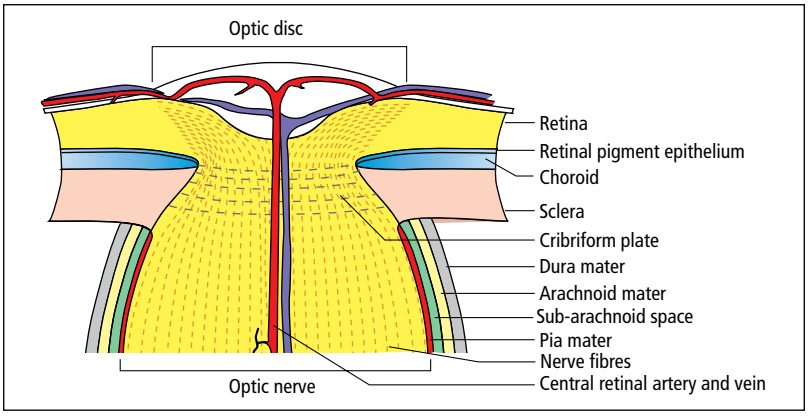


Figure 1.27 The structure of the optic nerve head.

The central retinal artery and vein enter and leave 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 central retinal artery, ciliary arteries and muscular arteries (Figure 1.28). 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 a defined 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 RPE from the choroidal capillaries.

The endothelial cells of the retinal capillaries are connected 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 connected by tight junctions, giving rise to an *external blood–retinal barrier* lying between the leaky choroid and the retina.

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

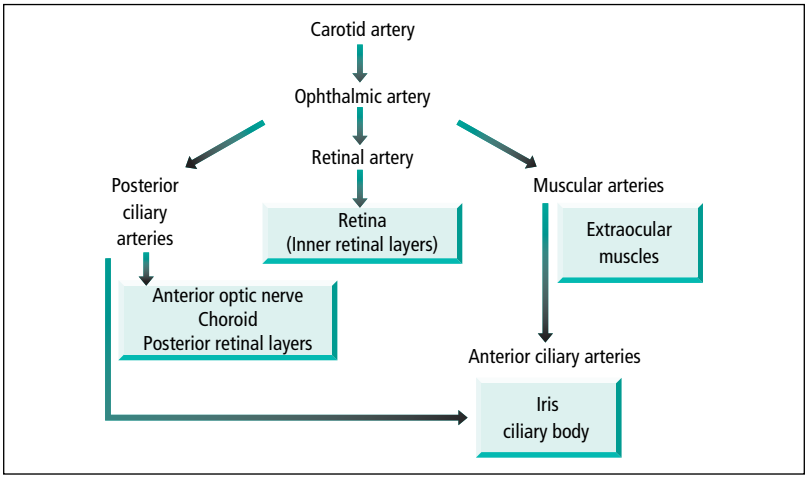


Figure 1.28 Diagrammatic representation of the ocular blood supply.

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 1.29a–c 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, since both sets of crossing fibres from the nucleus are affected.

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		

Peripheral course

Figure 1.30 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. 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.

The seventh cranial nerve

The seventh cranial nerve arises from a nucleus in the pons, loops over that of the sixth cranial nerve (Figure 1.29c) and leaves the brainstem at the *cerebellopontine angle* where it is joined by the *nervus intermedius*. The two nerves travel together in the

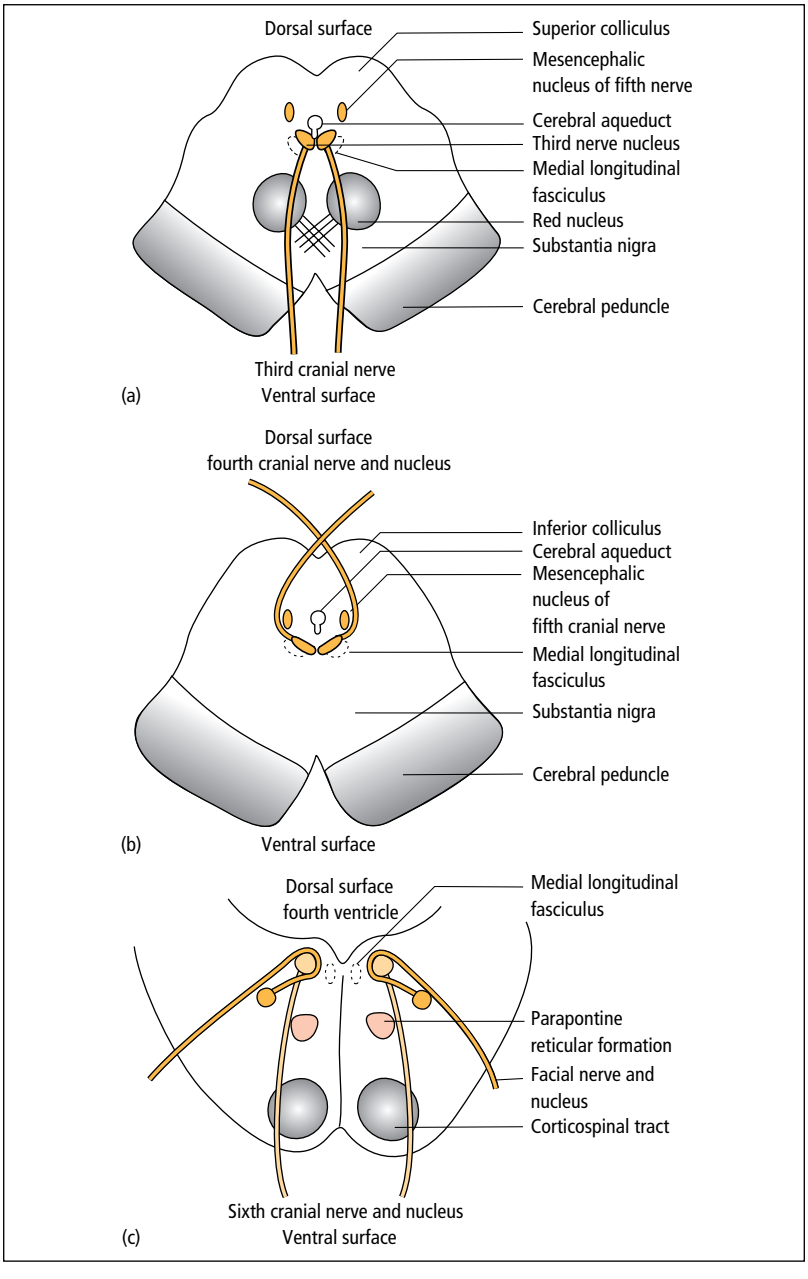


Figure 1.29 Diagrams to show the nuclei and initial course of the (a) third, (b) fourth and (c) sixth cranial nerves.

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

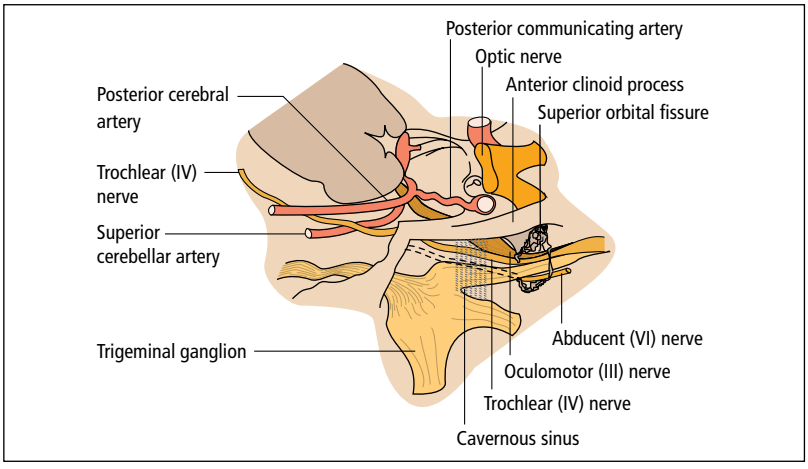


Figure 1.30 The intracranial course of the third, fourth and sixth cranial nerves.

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 The tears contain lysozyme and secretory IgA.

7. The iridocorneal angle

a Is the site of aqueous production.
b Lies between the cornea and the iris.
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 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 normally regenerate; dead cells are replaced by the spreading of surviving cells.
b False. The epithelial layer readily regenerates.
c False. The endothelial cells actively 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. Only the most superficial cortical fibres possess organelles. The older, deeper cortical fibres and nuclear fibres lose their nuclei and other organelles with the passage of time.
d True. The high protein content accounts for its high refractive index.
e True. This increases the power of the lens.

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.
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 contribute to the antibacterial properties of the tear film.

7. The iridocorneal angle

a False. It is the site of aqueous drainage.
b True. See Figure 1.23.

c True. This may reduce aqueous drainage.

d True. Flow depends on the pressure gradient between the anterior chamber and Schlemm 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 False. They are myelinated in the retrobulbar optic nerve but not in the eye. Occasionally, patches of myelination occur at the nervehead and within the retina.

e 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.

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