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1164 • MEDICAL OPHTHALMOLOGY Lacrimal gland/lacrimal drainage The lacrimal gland lies within the periorbita of the anterolateral roof of the orbit. Its secretions (tears) wash away surface irritants and convey emotion. Excess tears drain, via canaliculi in the lids, into the lacrimal sac, nasolacrimal duct and inferior nasal meatus. Extraocular muscles The extraocular muscles (Fig. 27.1) consist of four recti, two obliques and one levator. The recti originate from a circular condensation of periorbita, the annulus of Zinn, which encircles the superior orbital fissure and the optic canal. They extend forwards to insert into the anterior sclera. The levator palpebrae superioris originates above the optic canal and inserts into the tarsal plate and overlying skin of the upper eyelid. The superior tarsal muscle (Müller’s muscle) originates from the inferior aspect of the levator and also inserts into the tarsal plate. The superior oblique originates superonasal to the recti, and runs along the roof of the orbit, its tendon passing horizontally through the trochlea at the orbital rim to insert into the anterior sclera. The inferior oblique originates from the floor of the anterior orbit, just posterior to the lacrimal sac. It turns horizontally, passing beneath the inferior rectus, to insert into the inferior anterior sclera. Eye The optic vesicle develops from the diencephalon. The eye is therefore contiguous with the brain. This is reflected in the three-layer structure of the eye: The ability to see is an important aspect of everyday life. Although rarely a cause of mortality, visual impairment can have a profoundly negative impact on socioeconomic status. Globally, although refractive errors and cataract remain the main causes of visual impairment, significant progress has occurred in prevention and treatment. Public health measures have reduced diseases of poor hygiene and unclean water, such as trachoma and onchocerciasis, and greater access to surgery has reduced the burden of untreated cataract and glaucoma. However, conditions associated with longevity, such as age-related macular degeneration, diabetic retinopathy and retinal vein occlusion, for which scientific advances have led to effective but

expensive therapies requiring frequent and long-term attendance, are increasing in frequency. Traditionally, ophthalmology relied on other specialties to undertake extraocular investigation and treatment. Medical ophthalmology bypasses that co-dependence, allowing patients with visual disorders to receive overarching care within ophthalmology. As such, it requires a good grounding in medicine, particularly dermatology, diabetes and endocrinology, infectious diseases, medical genetics, neurology, rheumatology and stroke medicine. Medical ophthalmology presents a challenge for a medical textbook, as it overlaps with almost all other specialties, but particularly neurology. In this book neuro-ophthalmology is covered in Chapter 25. This chapter concentrates mainly on intraocular inflammation, which was the prime drive to create the specialty, and conditions that require intravitreal injection therapy. It does not therefore represent the totality of the medical ophthalmologist's workload. Ophthalmological conditions that are usually managed within non-ophthalmological specialties are discussed in the corresponding chapters, although for ease of reference the more common ophthalmic features of nonophthalmological conditions are listed throughout this chapter (haematological disease in Box 27.1, diabetes and endocrine disease in Box 27.2, cardiovascular disease in Box 27.3, respiratory disease in Box 27.4, rheumatological/musculoskeletal disease in Box 27.5, gastrointestinal disease in Box 27.6 and skin disease in Box 27.7). Functional anatomy and physiology Visual pathways, innervation of the eye and the control of eye movement are discussed in Chapter 25. Orbit The orbit is the fat-filled cavity in which the eye is suspended. It is shaped like a hollow square pyramid, its base the orbital rim. The orbital periosteum ('periorbita') is continuous with the periosteal layer of cranial dura mater. The dura and arachnoid form the optic nerve sheath, its subarachnoid space containing cerebrospinal fluid in continuity with the third ventricle. Eyelid/orbital septum/conjunctiva In primary gaze, the eyelids just cover the superior and inferior cornea. The eyelids contain the orbital septum and the tarsal plate. Within the tarsal plates, modified sebaceous (Meibomian) glands produce an oily surfactant to slow tear evaporation. The conjunctiva, a mucous membrane, lines the posterior surface of the eyelid, adhering only to the tarsal plates and the scleral/corneal junction. The accessory lacrimal glands provide basal tear production; mucus produced by goblet cells stabilises the tear film by lowering surface tension. 27.1 Ophthalmic features of haematological disease Condition Ophthalmic findings Severe anaemia of any cause (retinopathy of anaemia) Flame haemorrhages Cotton wool spots Roth spots Pre-retinal haemorrhage Megaloblastic anaemia Optic neuropathy Sickle cell anaemia Conjunctival vasculopathy Peripheral retinal neovascularisation Thalassaemia Desferrioxamine-associated pigmentary retinopathy Leukaemia (leukaemic retinopathy) Pseudohypopyon Flame haemorrhages Roth spots Retinal oedema Retinal vein occlusion Lymphoma Non-Hodgkin lymphoma Central nervous system lymphoma Lacrimal gland infiltration Posterior uveitis (atypical choroiditis) Myeloproliferative disorders Hyperviscosity Cerebral venous thrombosis Retinal vein occlusion Papilloedema Paraproteinaemias Waldenström's macroglobulinaemia Multiple myeloma Retinal vein engorgement/ occlusion Thrombophilia Cerebral venous thrombosis Papilloedema

27.3 Ophthalmic features of cardiovascular disease Condition Ophthalmic findings Arteriosclerosis Arteriovenous nipping Retinal vein occlusion, caused by arteriovenous nipping Retinal artery macroaneurysm Ischaemic optic neuropathy Pupil-sparing third and/or sixth nerve palsy, caused by infarction of the vasa nervosum Hypertension Hypertensive retinopathy Cotton wool spots Flame haemorrhages Optic disc oedema, with or without macular oedema Infective endocarditis Flame

haemorrhages Roth spots Endophthalmitis, caused by haematogenous spread of infection Drugs Vortex keratopathy (corneal epithelial deposits), caused by amiodarone (also seen in Fabry's disease, p. 370) Bilateral optic neuropathy, caused by amiodarone Thromboembolic disorders (including thromboembolus from atrial fibrillation) Retinal artery occlusion, caused by artery-to-artery embolism Homonymous hemianopia, caused by embolic stroke (p. 1088) 27.2 Ophthalmic features of diabetes and other endocrine disease Condition Ophthalmic findings Diabetes Proliferative retinopathy Macular oedema Small pupils (autonomic neuropathy) Cataract (including 'snowflake' cataract) Thyrotoxicosis (any cause) Eyelid retraction Graves' disease (TSH receptor antibody-positive) Exposure keratopathy Conjunctival and periorbital oedema Restrictive ocular motility Proptosis Optic neuropathy Parathyroid disease Band keratopathy Corneal calcium deposition Phaeochromocytoma Hypertensive retinopathy Cotton wool spots Flame haemorrhages Optic disc oedema with or without macular oedema Cushing's syndrome Posterior subcapsular cataract Diabetic retinopathy Central serous retinopathy Thyroid carcinoma Horner's syndrome with absent unilateral facial sweating (TSH = thyroid stimulating hormone) Fig. 27.1 The extraocular musculature (right eye). Adapted from Batterbury M, Bowling B, Murphy C. Ophthalmology. An illustrated colour text, 3rd edn. Churchill Livingstone, Elsevier Ltd; 2009. Medial rectus Superior rectus Superior oblique Inferior oblique Orbicularis oculi muscle (palpebral portion) Inferior rectus Lateral rectus (cut) Levator palpebrae superioris 27.4 Ophthalmic features of respiratory disease Condition Ophthalmic findings Chronic obstructive pulmonary disease (p. 573) Optic disc oedema (type 2 respiratory failure) Cystic fibrosis (p. 580) Diabetic retinopathy Tuberculosis (p. 588) Anterior uveitis Choroidal granuloma Serpiginous choroiditis Peripheral retinal arteritis Optic neuropathy, visual loss and disturbance of colour vision (adverse effects of ethambutol and isoniazid) Sarcoidosis (p. 608) Anterior uveitis (granulomatosis) Mutton fat keratitic precipitates Iris nodules Choroidal granuloma Panuveitis Multifocal choroiditis Retinal periphlebitis Sicca syndrome, caused by lacrimal gland infiltration Exposure keratopathy, caused by corneal exposure secondary to facial nerve palsy Optic neuropathy, caused by optic disc oedema secondary to meningeal infiltration Lung cancer (p. 928) Horner's syndrome (p. 1091) Cancer-associated retinopathy • the sclera/cornea, a fibrous outer layer analogous to the meningeal dura • the choroid, ciliary body and iris (together known as the uveal tract), a vascular middle layer analogous to the pia-arachnoid • the retina, an inner layer analogous to white matter. The major structures of the eye are shown in Figure 27.2. During embryogenesis, overlying ectoderm sinks into the neuroectoderm of the optic vesicle to form the lens vesicle, thus inducing the optic vesicle to form the two-layered optic cup. The inner and outer layers form the neurosensory retina and the retinal pigment epithelium, respectively. The intervening space is continuous with the third ventricle of the diencephalon,

 The limbus lies at the junction between the cornea and sclera, and contains stem cells and Schlemm's canal. The stem cells allow continuous regeneration of the corneal epithelium. Schlemm's canal, with its overlying trabecular meshwork, drains aqueous fluid from the anterior chamber into the external veins of the episclera and conjunctiva. The avascular cornea is nourished by diffusion from the anterior chamber, limbal capillaries and oxygen dissolved in the tear film. The cornea, assisted by the lens and the length of the eye, determines the refractive ability of the eye. the cilia of the third ventricle continuing as cilia on the outer neurosensory retina. Laterally, these cilia form the outer segments of the photoreceptors. Initially, the hyaloid artery supplies the lens and vitreous. In its final form, the vitreous develops from the retina and the hyaloid artery regresses, leaving only the central retinal artery and its branches.

Mesenchyme forms the tarsal plates of the eyelid, the stroma and the endothelium of the cornea, the sclera and the choroid. Surface ectoderm, as well as forming the lens, forms the epidermis of the eyelid, the conjunctiva, the epithelium of the cornea and the lacrimal gland. Sclera/cornea The sclera lends shape to the eye and provides attachment for the ocular musculature. It makes up five-sixths of the eyeball, the other sixth being formed by transparent cornea. 27.5 Ophthalmic features of rheumatological/ musculoskeletal disease Rheumatoid arthritis • Keratoconjunctivitis sicca • Peripheral ulcerative keratitis (‘corneal melt’) • Painless episcleritis • Scleritis and scleromalacia Seronegative spondyloarthropathies • Conjunctivitis (chlamydiaassociated reactive arthritis) • Anterior uveitis Connective tissue diseases Dermatomyositis • Periorbital oedema with violaceous eyelid rash Sjögren’s syndrome • Dry eyes Treatment effects • Bull’s eye maculopathy (hydroxychloroquine) • Viral retinitis (immunosuppression) Systemic vasculitides Giant cell arteritis • Central/branch retinal artery occlusion • Ischaemic optic neuropathy Behçet’s disease • Occlusive retinal vasculitis (posterior uveitis) • Anterior uveitis with hypopyon Granulomatosis with polyangiitis (Wegener’s) • Scleritis with involvement of adjacent cornea (sclerokeratitis) • Retro-orbital inflammation (see Fig. 25.49) Polyarteritis nodosa • Peripheral ulcerative keratitis • Scleritis • Retinal arteritis Others/non-specific • Necrotising scleritis/ sclerokeratitis/peripheral ulcerative keratitis • Anterior ischaemic optic neuropathy • Extraocular myositis (painful diplopia) • Retinal arteritis • Pupil-sparing 3rd nerve palsy • 6th nerve palsy • Proptosis • Occipital lobe infarction Diseases of bone Paget’s disease, polyostotic fibrous dysplasia • Optic neuropathy Others/non-specific • Anterior uveitis (adverse effect of bisphosphonates) 27.7 Ophthalmic features of skin disease Rosacea • Posterior blepharitis • Keratitis Acne vulgaris • Dry eye (adverse effect of isotretinoin) • Papilloedema (adverse effect of tetracycline) Psoriasis • Anterior uveitis Eczema • Atopic keratoconjunctivitis Urticaria • Angioedema Bullous diseases • Ocular cicatricial pemphigoid • Stevens–Johnson syndrome Alopecia areata • Eyebrow and eyelash loss Cutaneous melanoma • Melanoma-associated retinopathy Skin tumours • Eyelid tumours (basal cell carcinoma, squamous cell carcinoma, keratoacanthoma, naevus, melanoma) Skin infections • Stye (eyelash folliculitis) • Acute blepharoconjunctivitis (herpes simplex) • Chronic conjunctivitis (molluscum contagiosum) 27.6 Ophthalmic features of gastrointestinal disease Malabsorption • Corneal and conjunctival keratinisation • Rod photoreceptor loss Chronic pancreatitis • Diabetic retinopathy Inflammatory bowel disease • Episcleritis • Non-necrotising scleritis • Anterior uveitis Large bowel tumours • Atypical congenital retinal pigment epithelium hypertrophy (familial adenomatous polyposis) Inherited liver disease • Kayser–Fleischer corneal rings, sunflower cataracts (Wilson’s disease) • Diabetic retinopathy (haemochromatosis)

Histologically, the centre of the retina is termed the macula lutea, its yellowish appearance caused by the presence of the xanthophylls (yellow pigments) lutein and zeaxanthin. At the centre of the macula, the neurosensory retina dips to form the fovea. The single-layered retinal pigment epithelium is highly metabolically active and is essential for the maintenance and survival of the overlying photoreceptors. The neurosensory retina initiates the visual pathway. Its photoreceptors synapse with radially arranged bipolar neurons, which in turn synapse with circumferentially arranged optic nerve ganglion cells. ‘Horizontal’ and amacrine cells within the plexiform layers modulate neuronal activity between bipolar cells, photoreceptors and the ganglion cells. At the fovea, a one-to-one relationship between cones, bipolar neurons and ganglion cells leads to the highest acuity. In the peripheral retina, many rods converge on to a bipolar neuron, and many

bipolar neurons converge on to a ganglion cell, leading to lower acuity. In effect, the peripheral retina conveys black-and-white sentinel vision, alerting the brain to move the higher-acuity colour vision of the fovea into gaze. Photoreceptors are specialised neurons that cause neurotransmitters to be released in response to light ('phototransduction'). There are three types of photoreceptors: namely, rods, cones and ganglion cells, the latter of which independently respond to blue light, influencing circadian rhythms. The sclera is pierced posteriorly by the optic nerve at the lamina cribrosa, a sieve-like conduit. Its outer layer, the episclera, consists of loose connective tissue, separating it from Tenon's capsule, the soft-tissue socket of the eye. Choroid, ciliary body and iris – the uveal tract Posteriorly, the choroid acts as a conduit for branches of the ophthalmic artery and veins. The choriocapillaris, a network of widebore, fenestrated capillaries, abuts the retinal pigment epithelium. The ciliary body forms the junction between the choroid and the iris, and lies just inferior to the limbus. Anteriorly, its ciliary processes produce aqueous (fluid) that circulates through the pupil into the anterior chamber. Posteriorly, it constitutes the pars plana and forms the attachments for the suspensory ligaments of the lens. The ciliary muscle encircles the eye within the ciliary body. Contraction of this muscle relaxes the suspensory ligaments of the lens, bringing near objects into focus. The iris bows gently forwards as it lies against the lens. It is divided into a pupillary zone, containing the circumferential sphincter pupillae muscle, and a ciliary zone, containing the dilator pupillae. Retina The retina consists of the neurosensory retina and the retinal pigment epithelium. The two layers are adherent only adjacent to the optic disc and at the edge of the pars plana. Fig. 27.2 The main structures of the eye. The inset shows the arrangement of the retinal cells. Inset adapted from Douglas G, Nicol F, Robertson C (eds). Macleod's Clinical examination, 13th edn. Churchill Livingstone, Elsevier Ltd; 2013. Limbus Sclera Choroid Retina Fovea Hyaloid canal Retinal vessels Optic nerve Extraocular muscle Optic nerve fibres Ganglion cell Amacrine cell Bipolar cell Horizontal cell Cone Rod Pigment epithelium Cornea Iris Pupil Lens Anterior chamber (aqueous) Ciliary muscle Ciliary body Conjunctiva Vitreous gel Suspensory ligaments

1168 • MEDICAL OPHTHALMOLOGY The tangent screen is a piece of black cloth attached to a wall, in front of which the operator introduces moving targets into the patient's field of view. It retains an important role in the positive identification of functional peripheral field loss (tunnel vision) versus pathological field loss (funnel vision), although the results are somewhat operator-dependent. Goldmann perimetry is a mechanical improvement on tangent screen perimetry, which utilises targets of varying size and illumination. An automated version is available. Automated threshold perimetry Automated visual fields test the threshold of the eye's ability to see at various points within the visual field, forming complex outputs that can be stored digitally. Internal quality assurance mechanisms monitor stability of fixation, false positives due to trigger-happy patients and false negatives due to performance fatigue. Many patients need practice before accurate results are obtained; first-time fields are rarely reliable and often show spurious and misleading findings. Most automated perimetry assesses only central vision. Few neurological disorders start peripherally, the exception being unilateral loss of peripheral field with disease of the anterior pole of the occipital lobe. However, retinal pathology, such as retinal detachment and retinitis pigmentosa, may be missed if reliance is placed on automated perimetry rather than clinical examination. Visual field defects on perimetry that affect the whole of the superior or inferior half of the visual field need to be differentiated by confrontation into arcuate visual field defects, which affect central field only, and altitudinal field defects, which affect both central and peripheral vision. Arcuate visual fields defects localise a lesion to the optic nerve head, whereas a lesion

anywhere along the optic nerve can cause an altitudinal defect. Imaging See Figure 27.4. Photography Digital photography is utilised to document surface anatomy. Colour images are ideal for lesions affecting the skin and cornea. For the retina, however, red-free imaging brings additional benefits, particularly for discriminating red haemorrhages or abnormal new vessels from the red background of the retina. Lens The lens is a transparent flexible structure suspended between the iris and the vitreous. Its flexibility enables objects over a range of distances to be focused on the retina. It has a capsule, a central nucleus and a peripheral cortex. It continues to grow throughout life, becoming less flexible with age. Vitreous The vitreous gel is 99% water and 1% collagen/hyaluronic acid. The outer edge (cortex) of the vitreous condenses to form the anterior and posterior hyaloid membranes. The base of the vitreous strongly adheres to the ora serrata/pars plana and the optic disc rim, where the internal limiting membrane of the retina is thinnest. Lesser degrees of adhesion occur at the parafoveal retina and along the retinal vessels. Blood supply of the orbit/eye The main blood supply of the orbit originates from the intracranial internal carotid artery. The ophthalmic artery, the first branch of the internal carotid artery, traverses the subarachnoid space to enter the optic canal within the dural sheath of the optic nerve. On leaving the optic canal, it emerges from the dural sheath to course briefly along, and then over, the optic nerve and reach the medial wall of the orbit. Several arterial circles are formed. The major arterial circle of the iris is formed within the ciliary body by anterior ciliary arteries anastomosing with the posterior ciliary arteries. The pial branches of the optic nerve and the short ciliary arteries join together, as the circle of Zinn, to supply the intraocular optic nerve. The infraorbital artery, a branch of the maxillary artery, also contributes to the orbital blood supply, in particular the inferior rectus, the inferior oblique and the lacrimal sac. The orbit is drained by the superior and inferior ophthalmic veins, which converge to drain through the superior orbital fissure into the cavernous sinus. Investigation of visual disorders History is the key to diagnosing visual disorders, with examination and investigations used to confirm or refute the expectations formed by the history. Perimetry In the era before modern radiology, manual perimetry was utilised as a non-invasive form of ‘neuroimaging’. Nowadays, perimetry is largely automated and its main role lies in the monitoring of glaucoma; it also has a lesser role in assessing neuro-ophthalmic disorders. All methods of perimetry are subjective and rely on patient cooperation and mental agility. Amsler chart The Amsler chart (Fig. 27.3) is the simplest method of documenting the visual field, and is easy for both patient and clinician to understand and perform. It can be used for all forms of visual field loss but is best suited to follow up the central scotomata of macular disorders, which are often too subtle for other methods of perimetry. Tangent/Goldmann kinetic perimetry Manual perimetry methods, such as tangent screen and Goldmann kinetic perimetry, appeal to the non-specialist, as they produce easily interpretable contoured maps of the visual field. Fig. 27.3 Amsler chart. The Amsler chart is a grid of 0.5 cm squares with a dot in the centre. The subject is asked to fix on the central dot with one eye and any distorted or missing lines are recorded.

Ocular ultrasound The main role of ultrasound is where the retina is obscured: for instance, by cataract or vitreous haemorrhage. It also has an important role in diagnosing choroidal melanoma, based on its distinctive internal reflectivity. Visual electrophysiology Electrophysiology is used to localise disorders to the photoreceptors (electroretinogram), the retinal ganglion cells (pattern electroretinogram) or the optic pathways (visual evoked potential). The site of photoreceptor involvement can be further localised to specific regions of the retina (multifocal electroretinogram)

or the macula itself (pattern electroretinogram). Electrophysiology requires cooperation, correction of refractive errors and the ability to fixate. Voluntary suppression of the electrical responses is possible by simply not focusing on the target. Despite this, it remains the investigation of choice for visual symptoms unexplained by clinical examination. Presenting problems in ophthalmic disease Presenting problems that are ophthalmological manifestations of predominantly neurological disease (e.g. ptosis, diplopia, oscillopsia, nystagmus and pupillary abnormalities) are discussed in Chapter 25. Optical coherence tomography Optical coherence tomography is the optical equivalent of ultrasound, using light rather than sound waves to create its images. It is invaluable, not least for assessing the integrity of the layers of the retina and detecting macular oedema of any cause. Autofluorescence The retinal pigment epithelium contains autofluorescent lipofuscin, which can be excited by blue- and green-coloured light and captured by digital imaging. Increased autofluorescence occurs when there is abnormal accumulation of lipofuscin, as seen with certain inherited retinal dystrophies; excess retinal pigment epithelium metabolic activity, such as at the edge of evolving atrophic macular degeneration; or drug deposition, such as with hydoxychloroquine. Fundus angiography Fluorescein angiography is an invasive technique with risks including local extravasation of dye at the site of intravenous injection and anaphylaxis. Currently, its role is limited to the diagnosis of retinal vasculitis, retinal and choroidal neovascularisation, and capillary occlusion. Non-invasive angiography is now possible using optical coherence tomography, but its applicability is limited by small field of view and inability to demonstrate flow or leakage. Indocyanine angiography directly images the choroidal circulation and is particularly useful in guiding laser treatment for the choroidal polyps of polypoidal choroidal vasculopathy. Fig. 27.4 Ocular imaging. A Colour retinal photograph from a healthy subject. B Red-free retinal photograph from a healthy subject. C Optical coherence tomogram of a normal eye, showing the layers of the retina. In this image, the macula shows normal foveal indentation. D Fundus autofluorescence (FAF) of the right eye in a normal subject. Distribution of FAF intensity shows typical background signal with reduced signal at the optic disc (absence of autofluorescent material) and retinal vessels (absorption). Intensity is markedly decreased over the fovea due to the absorption of the blue light by yellow macular pigment. E Fundal fluorescein angiogram of a normal adult retina. F Ocular ultrasound image showing typical biconvex appearance of a choroidal melanoma. A, B, C and F, Courtesy of Aberdeen Royal Infirmary. D, From Schmitz-Valckenberg S, Fleckenstein M, Hendrik PN, et al. Fundus autofluorescence and progression of age-related macular degeneration. Survey Ophthalmol 2009; 54(1):96–117. E, From Witmer MT, Szilárd K. Wide-field imaging of the retina. Survey Ophthalmol 2013; 58(2):143–154. A B C D E F

 Photophobia may also be a feature of meningitis, usually with accompanying neck stiffness and headache (meningism, p. 1118). Glare is a common early feature of cataract, particularly triggered by oncoming car headlights when driving at night. It is a relatively common indication for surgery. It may also be an issue where there is insufficient melanin in the retinal pigment epithelium, e.g. in atrophic age-related macular degeneration, in ocular albinism or following extensive pan-retinal laser therapy. If surgery is not an option, or while surgery is awaited, the symptom of glare may be reduced by wearing a broad-brimmed hat. Photopsia A flickering light sensation is indicative of photoreceptor activity, either through traction, as in the setting of posterior vitreous detachment, or inflammation, as in the setting of autoimmune or paraneoplastic retinopathy. Rarely, photopsia is a symptom of occipital lobe epilepsy, in which case there is usually an accompanying homonymous hemianopia. Blurred vision Blurred vision describes the situation in which patients are able to see what they are looking at, but

what they are looking at is out of focus. The most common cause of intermittent blurred vision is dry eye; the most common cause of permanent blurred vision is cataract. If blurred vision is worse in the morning and eases as the day progresses, this suggests macular oedema. Loss of vision In visual loss, patients are no longer able to see all or part of what they are looking at. Some symptoms associated with visual loss require urgent ophthalmological assessment (Box 27.8). Watery/dry eye The most common cause of a watery eye is a dry eye triggering reflex lacrimation. Patients with dry eye may complain of a foreign body or gritty sensation in the eye or intermittent visual blurring, triggered by reduced blinking, as occurs when reading or when concentrating on a distant object, such as the television. Pruritus Common causes of itch are an acute allergic response to either airborne allergens or direct contact. A significant proportion of people are allergic to topical chloramphenicol, a first-line treatment for many minor ocular ailments. Pain/headache The key consideration in deciding whether or not ocular pain and/or headache originates from the eye is whether there is a ciliary flush (red eye) or no ciliary flush (white eye). Red eye The presence of a ciliary flush in the region of the limbus is a key finding in intraocular causes of pain. The presence of watering or watery discharge is not a discriminatory feature, and over-reliance on this symptom often results in anterior uveitis being misdiagnosed as viral conjunctivitis. White eye In the absence of a ciliary flush, ocular or periorbital pain is most commonly caused by migraine. Pain on eye movement is a cardinal feature of optic neuritis and scleritis. In optic neuritis the eye is white, whereas in scleritis, except for posterior scleritis, it is red. Posterior scleritis, in which the visible sclera is white, should be diagnosed only in the setting of positive signs such as disc swelling and exudative retinal detachment, or with confirmation by ocular ultrasound. A more common cause of severe ocular/ periocular pain, with associated photophobia and lacrimation, is cluster headache (p. 1096), which is often misdiagnosed as scleritis. Just like scleritis, cluster headache responds to oral glucocorticoids, adding to the diagnostic confusion. Intermittent, subacute angle closure glaucoma can cause headache, but usually accompanying corneal oedema causes haloes (a form of glare with rainbow colours), elicited by looking at lights or blurring of vision. Giant cell arteritis is an uncommon, but usually striking, cause of headache, predominantly seen in the elderly. Rarely, it presents with sudden painless visual loss in the absence of raised inflammatory markers. Diagnosis can be made by demonstrating choroidal shutdown on fluorescein angiography. Photophobia/glare Excessive sensitivity to light, rather than fear of light, usually indicates ciliary muscle spasm due to inflammation in the iris. Common causes are corneal abrasion, acute anterior uveitis and contact lens-related keratitis. Occasionally, photophobia can be a symptom of congenital retinal dystrophies, especially cone photoreceptor deficiency. 27.8 Red flag symptoms in visual loss* Symptom Possible causes Sudden onset Retinal artery occlusion Ischaemic optic neuropathy Headache Giant cell arteritis if age > 55 years Eye pain Angle closure glaucoma Keratitis Scleritis Anterior uveitis Pain on eye movement Optic neuritis Scleritis Distortion Choroidal neovascular membrane: Age-related macular degeneration Pathological myopia Posterior uveitis Idiopathic Macular hole Epiretinal membrane Worse in the morning Macular oedema: Diabetic macular oedema Retinal vein occlusion Uveitis *The presence of any of these symptoms in a patient with visual loss requires emergency referral to an ophthalmologist.

most common cause is thyroid eye disease, when proptosis is termed exophthalmos. Proptosis is a sign of retro-orbital expansion and may be intraconal or extraconal. When expansion is within the

cone of extraocular muscles, then movement forwards will be in line with the visual axis. When outside, the eye is additionally displaced to the side. The primary clinical concern is whether vision is at risk due to optic nerve compression or corneal exposure. In addition, there may be double vision. In thyroid eye disease, diplopia may be absent if the disease is symmetrical. Instead, restricted ocular movements make patients move their head en bloc when looking at objects deviating from the primary position of gaze. To the patient, however, the overarching concern is often the change in appearance. Specialist ophthalmological conditions Ocular inflammation Inflammation can affect any part of the eye. In structures in direct contact with the environment, particularly the cornea and the conjunctiva, inflammation is most likely to be caused by infection. In other structures, such as the uveal tract and sclera, inflammation is more likely to be caused by autoimmune conditions, although it may also be a manifestation of infection or malignancy. Although the latter conditions may present with indicative ocular signs, their presence is often appreciated only retrospectively, after failure to respond to immunosuppression. Most non-infective forms of ocular inflammation are idiopathic; all are more common in the presence of other autoimmune conditions. Some may be directly associated but asynchronous in disease activity, such as the anterior uveitis of ankylosing spondylitis (p. 1028). Others are direct manifestations of an overarching, underlying, inflammatory condition such as the keratoscleritis of granulomatosis with polyangiitis (formerly known as Wegener’s granulomatosis). Sjögren’s syndrome Sjögren’s syndrome is the archetypal autoimmune disease and its secondary form is associated with a large number of other autoimmune conditions (see Box 24.64, p. 1039). The cardinal features are inflammation of the lacrimal gland, its conjunctival accessory glands and the parotid gland, leading to hyposecretion of tears and saliva. Involvement of the lacrimal gland alone causes keratoconjunctivitis sicca, a syndrome of dry eyes and corneal and conjunctival irritation. Keratoconjunctivitis sicca, however, can also be caused by reduced function of the lacrimal glands and/or lacrimal ducts from other causes. Treatment of the ophthalmological manifestations of Sjögren’s syndrome is symptomatic, and consists of supplementing tear production with artificial tears (e.g. hypromellose) and reducing tear loss by humidification and avoidance of dry environments. If these measures are insufficient, tear drainage may be reduced with surgical options such as punctal plugs and punctal occlusion. Peripheral ulcerative keratitis Peripheral ulcerative keratitis (‘corneal melting’) is an autoimmune disorder affecting the corneal limbus, where it may be The most common cause of transient visual loss is the aura of migraine, usually a positive phenomenon with the object of regard seemingly hidden by something in the way, rather than a negative phenomenon in which part or all of what is being looked at is missing. With positive visual phenomena the obstruction is often white or coloured, expanding across the visual field, or in a constant position but shimmering. Negative visual phenomena are a cardinal feature of ocular, usually retinal, ischaemia, with complete absence of vision (blackness) occupying part or all the visual field. Transient ocular ischaemia is usually embolic in nature but is occasionally seen in giant cell arteritis, where it suggests critical optic nerve ischaemia. Permanent monocular negative visual phenomena usually indicate previous optic nerve or retinal infarction. Tiny negative visual phenomena may also be seen in capillary disorders such as diabetic retinopathy, where patchy macular capillary occlusion may, for instance, cause letters to be missing from words on reading. Distortion of vision Distortion is a cardinal symptom of disruption of foveal photoreceptor alignment. The most common cause is choroidal neovascularisation. Less commonly, it can be caused by epiretinal membrane formation, where posterior hyaloid surface scarring causes foveal traction. Usually with distortion, objects are not only misshapen but also smaller (micropsia), due to the photoreceptors being pulled apart. Macropsia, where objects look bigger than normal, is

uncommon. It is sometimes seen in the ‘Alice in Wonderland’ syndrome, a paediatric variant of migraine where there is altered visual perception of body images. Eyelid retraction Eyelid retraction is usually caused by inflammatory thyroid eye disease or thyrotoxicosis (see pp. 631 and 645, and Fig. 18.8). The first muscle to be affected in thyroid eye disease is the inferior rectus. The enlarged muscle tethers the eye and restricts upgaze. Compensatory increased innervation to the superior rectus and the levator palpebrae superioris, as well as direct inflammation, leads to eyelid retraction. In thyrotoxicosis, increased sympathetic nervous activity leads to bilateral eyelid retraction. This, however, resolves with beta-blockade and treatment of thyrotoxicosis. Rarely, bilateral eyelid retraction is a sign of dorsal midbrain pathology (Collier’s sign), where it is accompanied by a supranuclear upgaze palsy and convergence-retraction nystagmus. Optic disc swelling Optic disc swelling can be a developmental variant of normal (pseudopapilloedema) or caused by optic nerve pathology, or reflect more widespread nerve fibre oedema as with retinal vein occlusion. Neurological causes of optic disc swelling are discussed in on page 1090. Proptosis Proptosis, particularly if bilateral and symmetrical, is often first recognised when it is quite advanced. Accompanying eyelid retraction is a typical feature of thyroid eye disease. By far the

 may induce active systemic infection. Furthermore, the most commonly used biologic for uveitis – anti-tumour necrosis factor therapy (e.g. adalimumab, infliximab) – may trigger demyelination. The most common form of uveitis is anterior uveitis, which is usually idiopathic but may be associated with other autoimmune conditions, particularly HLA-B27-related spondyloarthropathies (p. 1027); it is rarely caused directly by infection. Acutely, dilating drops are used to prevent the inflamed iris from sticking to the lens (posterior synechiae) and obstructing the outflow of aqueous fluid, while a tapering dose of topical glucocorticoids, usually over 4–6 weeks, mitigates the local signs and symptoms of the self-resolving inflammation. Inadequate treatment can lead to pupil block glaucoma and cataract. Posterior complications can also develop, predominantly macular oedema, the main cause of visual impairment in all forms of uveitis. With intermediate uveitis, inflammation occurs at the pars plana, with most symptoms, predominantly floaters, being a result of inflammation of the vitreous base. Unlike anterior uveitis, pure intermediate uveitis is not associated with iris inflammation; instead, white blood cells are seen predominantly in the anterior vitreous, with a lesser amount overspilling into the anterior chamber. Treatment is challenging. Topical therapy is ineffective, as it does not penetrate beyond the anterior chamber, but symptoms of floaters are not often sufficient to justify systemic immunosuppression. In some cases, vitritis (vitreous inflammation), or more commonly macular oedema, may cause visual impairment. Occasionally, retinal neovascular proliferation may occur, either as an inflammatory response or as a direct result accompanied by adjacent scleritis. It may be directly associated with inflammatory disorders in which immune complexes are formed, particularly rheumatoid arthritis, systemic lupus erythematosus and granulomatosis with polyangiitis. Pain and redness are helpful indicators but may not always be present. Systemic immunosuppression is always required but topical glucocorticoids should be used cautiously due to the risk of aggravating keratolysis (corneal thinning). Secondary infection should be prevented with topical antibiotics and attention should be paid to corneal hydration, through the use of artificial tears and lubricants. More common causes of peripheral corneal ulceration are blepharitis and acne rosacea, causing ocular irritation rather than frank pain. Hypersensitivity to staphylococcal exotoxin leads to stromal infiltrate adjacent to, but sparing, the limbus (marginal keratitis). Resolution of this self-limiting condition can be assisted by the use of topical chloramphenicol, with or without topical glucocorticoids. Prevention is through management of the underlying condition,

usually with ocular lid hygiene for simple blepharitis and metronidazole gel for rosacea. Scleritis Scleritis is usually accompanied by severe pain, worse on eye movement and often waking the patient through the night. Diagnosis of anterior scleritis is usually straightforward, with the eye showing diffuse or nodular erythema (although it may have to be searched for under the eyelids). Posterior uveitis is often accompanied by reduced vision and oedema of the retina, choroid and extraocular muscles. White patches of necrosis (pallor) within the erythema are an ominous sign, indicative of systemic vasculitis. Non-necrotising scleritis is commonly idiopathic but may be associated with other autoimmune conditions, particularly rheumatoid arthritis and inflammatory bowel disease. It is also common with herpes zoster ophthalmicus, intraocular involvement being indicated by the involvement of the lateral external nose (Hutchison's sign). Necrotising scleritis requires aggressive immunosuppression; non-necrotising scleritis can occasionally be managed by topical glucocorticoids or non-steroidal anti-inflammatory drugs (NSAIDs) but usually requires oral glucocorticoids. Some patients with recurrent episodes of scleritis, or in whom inflammation is gradual and prolonged, may develop scleral thinning (scleromalacia), revealing the underlying blue choroid. Episcleritis Episcleritis is a benign self-limiting condition of uncertain aetiology, occasionally associated with other inflammatory disorders. Sectoral redness of the episclera is usual, although nodules can form. Often confused with scleritis, although usually less symptomatic, the diagnostic topical application of phenylephrine turns the inflamed episclera white but has no effect on the redness of scleritis. Treatment is with cold artificial tears, although occasionally topical NSAIDs or topical glucocorticoids are required. Uveitis Uveitis is an overarching term for inflammation anywhere in the uveal tract, retina or vitreous. It may be classified according to speed of onset, location, specific features, or aetiology (Box 27.9). Syphilis can cause all forms of uveitis. Active tuberculosis may present with an occlusive vasculitis or serpiginous (snake-like) choroiditis emanating from the optic disc. Latent tuberculosis is a particular concern because treatment of the uveitis with biologics 27.9 Aetiology of uveitis Idiopathic • Anterior uveitis often associated with the HLA-B27 haplotype, even in the absence of other manifestations Primary ophthalmic conditions • Trauma, including penetrating injury and ophthalmic surgery • Fuchs' heterochromic cyclitis • Posner–Schlossman syndrome Rheumatological • HLA-B27-associated (seronegative) spondyloarthropathies: ankylosing spondylitis, psoriatic arthritis, reactive arthritis • Juvenile idiopathic arthritis Systemic vasculitides • Behçet's disease • Polyarteritis nodosa • Granulomatosis with polyangiitis (Wegener's) Systemic infections (only the more common causes are listed) • Brucellosis • Herpes virus infections (cytomegalovirus, herpes simplex virus, varicella zoster virus) • Leptospirosis • Lyme borreliosis • Syphilis • Toxoplasmosis • Tuberculosis • Whipple's disease Gastrointestinal conditions • Inflammatory bowel disease (Crohn's disease, ulcerative colitis) Malignancy • Primary central nervous system lymphoma (rare) Systemic conditions of unknown cause • Multiple sclerosis • Sarcoidosis

All layers of the cornea may be involved: the epithelium in the form of dendritic ulceration; the stroma in the form of white infiltrate and occasionally necrosis; and the endothelium in the form of localised oedema and keratitic precipitates. Loss of corneal sensation is common following herpes simplex keratitis, and occasionally neurotrophic keratopathy may result. Epithelial disease is self-limiting but treatment with topical or oral antivirals reduces the risk of stromal involvement and scarring. Stromal and endothelial disease requires additional topical glucocorticoids, but only once any epithelial defect has healed. Herpes simplex keratitis is analogous to herpes labialis;

recurrences are therefore common and, if frequent, may warrant long-term oral antivirals. Corneal grafting may be required but the risk of recurrence remains. Bacteria also cause infectious keratitis, especially following corneal trauma or contact lens misuse. Other risk factors for microbial keratitis include topical glucocorticoids and pre-existing ocular surface disease. Bacterial keratitis has many causes, some of which do not respond to chloramphenicol, so topical quinolones are used as first-line agents. Rarely, the free-living amoeba Acanthamoeba castellanii may be a cause of contact lens-associated keratitis, presenting subacutely and leading to corneal nerve infiltration, keratitis and accompanying scleritis. Fungal keratitis is the most common cause of infectious keratitis in developing countries, particularly if there has been corneal trauma and contact with soil or plant matter. It is usually caused by Fusarium. Fungal keratitis has no particular distinguishing features and delayed diagnosis is common. If it is suspected, cultures should be undertaken and antifungal treatment, which is hampered by poor corneal penetration of antifungals, started promptly. Corneal transplantation is often required. Endophthalmitis Endophthalmitis is infection of the anterior and posterior chambers of the eye. It may be exogenous (e.g. from penetrating trauma or following surgery) or, less commonly, endogenous, caused by haematogenous spread of microorganisms within the blood, which gain entry to the eye via the choroid and ciliary body. The causes of endogenous endophthalmitis are therefore the causes of bacteraemia and fungaemia (p. 225). Gram-positive of capillary occlusion. Intermediate uveitis may be associated with demyelination, sarcoidosis and inflammatory bowel disease. Posterior uveitis tends to present with visual impairment secondary to macular oedema, vitritis or choroiditis. More chronic forms also exist and these tend to present with photopsia, visual field defects or distortion inducing choroidal neovascular membranes. Infectious conditions Conjunctivitis Conjunctivitis is predominantly caused by bacteria or viruses, and is usually self-limiting in 7–10 days. Bacterial conjunctivitis is associated with a purulent discharge and viral conjunctivitis with a watery discharge, the latter often being confused with the photophobia and reflex lacrimation of anterior uveitis. Underlying chlamydial infection should always be considered if there is a persistent thick, mucopurulent discharge (p. 340). Allergic conjunctivitis is also common, either as a component of hay fever (allergic rhinitis, p. 622) or as an allergy to chloramphenicol, which is commonly used to treat conjunctivitis. Rarely, conjunctivitis may be associated with inflammatory systemic mucus membrane disorders, such as ocular mucus membrane (cicatricial) pemphigoid or Stevens–Johnson syndrome (pp. 1254 and 1264). The secondary effects of loss of conjunctival function can be devastating to the cornea. Other causes of conjunctival scarring include trachoma (p. 273), chemical burns and orbital radiotherapy. Infectious keratitis/corneal ulceration Inflammation of the cornea should always raise concern about underlying infection (Box 27.10). Central ulceration is always more serious than peripheral, through involvement of the visual axis. Cultures from corneal scraping or biopsy may be required, although much infectious keratitis is treated empirically on the basis of site, morphology and response to treatment. In the West, the most common cause of infectious keratitis is herpes simplex virus type 1 (occasionally type 2) (Fig. 27.5). 27.10 Common causes of infectious keratitis Organism Features/comments Treatment Viruses Herpes simplex Characteristic ‘dendritic’ ulcer is the most common form, often recurrent Topical/systemic aciclovir (with topical glucocorticoid for stromal keratitis once the epithelium is healed) Varicella zoster Herpes zoster ophthalmicus Systemic aciclovir Bacteria Pseudomonas aeruginosa Staphylococcus aureus Coagulase-negative staphylococci Propionibacterium spp. Coagulase-negative staphylococci and Propionibacterium spp. are members of the skin flora, and must not be dismissed as contaminants Topical fluoroquinolone with Gram-positive and Gramnegative cover (e.g. ofloxacin) Subsequent treatment depends on sensitivity testing results Fungi Fusarium sp. Aspergillus sp. Candida sp. Fusarium and

Aspergillus keratitis are often associated with soil and/or corneal trauma; may also be contact lens-related Candida causes post-keratoplasty keratitis Options include topical natamycin (if available), amphotericin B, voriconazole and other azoles (e.g. econazole), and systemic fluconazole or voriconazole Parasites Acanthamoeba castellanii (free-living amoeba) Associated with poor contact lens hygiene Topical polyhexamethylene biguanide Onchocerca volvulus (nematode) See page 292

 Fig. 27.5 Infective keratitis. A Herpes simplex dendritic ulcer stained with fluorescein. B Fusarium keratitis. An irregularly edged lesion suggests a fungal cause but is not pathognomonic. A, Courtesy of McPherson Optometry, Aberdeen. B, From Macsai MS, Fontes BM. Rapid diagnosis in ophthalmology: anterior segment. Elsevier Inc.; 2008. (Courtesy of the External Eye Disease and Cornea Section, Federal University of São Paulo, Brazil.) A B Fig. 27.6 Focal chorioretinitis in clinically suspected endogenous Candida endophthalmitis. This patient was an intravenous drug user and improved with empirical oral fluconazole. From Ryan SJ (ed). Retina, 5th edn. Saunders, Elsevier Inc.; 2013. (Case courtesy of Jeffrey K. Moore, MD.) Fig. 27.7 Sunflower cataract and Kayser–Fleischer ring (arrow) in Wilson's disease. From Kaiser PK, Friedman NJ (eds). Massachusetts Eye and Ear Infirmary Illustrated manual of ophthalmology, 4th edn. Saunders, Elsevier Inc.; 2014. bacteria are most common, followed by Gram-negative bacteria and then fungi. Clinical presentation is with visual blurring and/or visual loss, which are usually unilateral. Ocular findings range from a few deposits in the retina/choroid (chorioretinitis) to panendophthalmitis, in which there is a severe inflammatory reaction in both the anterior and posterior chambers. A specific appearance of the retina is described for Candida endophthalmitis, which characteristically causes creamy-white retinal or chorioretinal lesions (Fig. 27.6). It is vitally important to sample the vitreous, as this may provide the only opportunity to determine the most appropriate therapy. Treatment is with systemic and/or intravitreal antibiotics or antifungal agents, depending on the cause and severity. Vitrectomy may also be required. Cataract Cataract is permanent opacity of the lens (Fig. 27.7). Globally, untreated cataract is the most common cause of visual impairment, although in countries where surgery is available, age-related macular degeneration is a more common cause. The normal lens thickens and opacifies with age, and cataract can be detected in more than half the population over the age 65 (senile cataract). Many ocular and systemic diseases can predispose to cataract formation, the most common being uveitis and diabetes mellitus. Wilson's disease (hepatolenticular degeneration, p. 896) causes a characteristic 'sunflower' cataract. Excessive exposure to ultraviolet light, ionising radiation and glucocorticoid therapy are also predisposing factors. The characteristic symptoms of cataract are progressive loss of vision and glare. If these become serious enough to require treatment, surgical intervention will be required, usually in the form of ultrasonic phacoemulsification with intraocular lens (IOL) implant. Other common ophthalmological findings in old age are shown in Box 27.11. Diabetic eye disease Diabetic retinopathy Diabetic retinopathy is one of the most common causes of visual impairment in people of working age in developed countries. The prevalence of diabetic retinopathy increases with the duration of diabetes. Almost all individuals with type 1 diabetes, and most of those with type 2 diabetes, will have some degree of

retinopathy after 20 years. Fortunately, most patients develop only mild forms of retinopathy. Pathogenesis The underlying pathogenesis of diabetic retinopathy is local vascular endothelial growth factor production initiated by hyperglycaemia-induced capillary occlusion. This occlusion

stimulates increased production of retinal vascular endothelial growth factor, which not only increases capillary permeability, leading to retinal oedema, but also stimulates angiogenesis, leading to new vessel formation. Clinical features The initial clinical feature of diabetic retinopathy, capillary occlusion, is visible only on retinal angiography. Capillaries adjacent to the occluded capillary form discrete swellings (microaneurysms), which leak fluid and blood, causing oedema and retinal haemorrhages (Fig. 27.8). Clinically, microaneurysms appear as isolated red dots, the capillaries being too small to visualise. At the edge of any leaking fluid, lipids precipitate out to form exudate, like the tidemark of the sea. In turn, capillaries with microaneurysms also occlude, their microaneurysms turning white before disappearing entirely from clinical view. As more and more capillaries occlude, larger patches of retinal ischaemia form, leading to sufficient vascular endothelial growth factor production to induce the growth of new vessels at the border of diseased and undiseased retina. Within patches of retinal ischaemia, diseased remnants of partially perfused capillaries form intraretinal microvascular abnormalities (IRMAs) and retinal veins develop multiple diffuse swellings (venous beading). These signs are best seen on fluorescein angiography. 27.11 Common ophthalmological findings in old age • Small pupils that dilate poorly with mydriatics: common neurodegenerative finding, particularly with diabetes. • Spurious findings on automated perimetry: decreasing manual dexterity and cognitive function often render automated perimetry findings unreliable. • Lens opacities: cataract is ubiquitous but requires treatment only if symptomatic. • Drusen: common from mid-life onwards. Larger (soft) drusen are more likely to herald age-related macular degeneration than smaller (hard) drusen. • Glaucoma: angle closure glaucoma is more common as the increasing size of the lens shallows the anterior chamber. Once it is identified, both eyes are always treated to prevent development/ recurrence. Chronic open angle glaucoma is more common in those with a family history or ocular hypertension (isolated raised intraocular pressure). • Impaired upgaze: common. It is differentiated from progressive supranuclear palsy (p. 1114) by the doll’s head manœuvre, the full range of vertical movement being retained in progressive supranuclear palsy PSP. • Ptosis: mechanical ptosis is common due to degenerative disinsertion of the levator palpebrae superioris aponeurosis. A high skin crease and preserved ability to elevate help differentiate it from other causes (p. 1090). • Late-onset presentation of congenital conditions: adult pseudovitelliform macular ‘degeneration’ is an autosomal dominant retinal dystrophy, which causes mild visual impairment. Oculopharyngeal muscular dystrophy is an autosomal dominant condition characterised by later-onset chronic progressive external ophthalmoparesis and swallowing difficulties. 27.12 Medical ophthalmology in adolescence Inherited conditions • Stargardt’s disease: autosomal recessive macular dystrophy that commonly presents in adolescence/early adulthood, causing significant bilateral impairment of central vision. Developmental anomalies • Pathological myopia: due to elongated ocular axial length rather than refractive index of cornea and lens. Increased risk of retinal detachment and choroidal neovascular membrane formation. • Optic disc drusen: come to prominence during adolescence and usually first detected during routine examination. Often mistaken for papilloedema, particularly in the setting of coincidental daily headache. • Amblyopia: occasionally detected after the age of 7 years, particularly in the absence of pre-school screening, when it is unlikely to respond to patching of the other eye. • Keratoconus: presents with increasing astigmatism (distortion of vision due to abnormal corneal topography). Hard contact lenses are the mainstay of therapy. Further progression may be prevented through ‘cross-linking’ surgery. Deterioration of existing conditions • Diabetic retinopathy: in type 1 diabetes, retinopathy usually first presents at least 5 years after diagnosis, which often coincides with adolescence. Puberty may accelerate progression. Greatest risk is disengagement with diabetes care, including retinal

screening, significantly increasing later presentation with advanced symptomatic retinopathy. • Adult manifestations of retinopathy of prematurity: clinical features depend on the type of treatment used in the neonatal period and include retinal detachment, angle closure glaucoma, severe myopia and cataract. Sexual activity • Chlamydia conjunctivitis: onset of sexual activity may lead to this ocular condition, which is associated with reactive arthritis (p. 1031). Untreated coexistent genital tract infection may cause infertility. Transition to adult services • Neurofibromatosis type 1: see page 1131. • Optic nerve astrocytoma/glioma: often develops in late childhood or early adolescence. Sports medicine • Contact sports: eye protection is important for all, especially if there is only one functional eye, e.g. with amblyopia. 27.13 Visual disorders and pregnancy • Ocular inflammation: pregnancy appears to have a protective effect on many inflammatory disorders, although not systemic lupus erythematosus. Most patients can taper treatment during pregnancy. Mycophenolate mofetil is teratogenic. Glucocorticoids and tacrolimus appear safe. The use of biologics during pregnancy should be based on a balance of risks, and professional guidelines should be consulted. • Diabetic retinopathy: may be accelerated during pregnancy because the placenta is a potent source of angiogenic growth factors. Retinal screening each trimester is recommended. • HELLP/pre-eclampsia/eclampsia (p. 1284): retinal features of accelerated hypertension (p. 514) may be seen, including optic disc oedema, flame haemorrhages and cotton wool spots. Occasionally, exudative retinal detachments occur. Vasogenic oedema (posterior reversible encephalopathy syndrome), affecting the posterior occipital and parietal lobes, may cause cortical visual impairment. All features tend to resolve with delivery or control of blood pressure.

 Fig. 27.8 Diabetic retinopathy. A Colour photograph of severe background diabetic retinopathy: multiple blot haemorrhages indicative of capillary occlusion; dot haemorrhages indistinguishable from microaneurysms or microaneurysmal bleeds; and cotton wool spots indicative of arteriolar occlusion. B Red-free image shows the presence of extensive haemorrhages more clearly; the more haemorrhages, the greater the degree of likely capillary occlusion. C Fluorescein angiogram now reveals extensive entrapment of fluorescein within multiple microaneurysms. D Colour photograph showing three cardinal consequences of capillary occlusion: intra-retinal microvascular anomalies occurring within an area of capillary occlusion (top arrow); venous reduplication (rare finding), with venous beading, extending from the reduplication towards the optic disc, occurring where capillaries are occluded either side of the vein (middle arrow); and new vessel formation occurring at the border between the diseased and health retina (bottom arrow). E Red-free image shows these features, particularly intra-retinal microvascular anomalies, more clearly. Note the relative pallor compared to the right-hand side of the image, which is indicative of widespread capillary occlusion. Absolute pallor never occurs, as it is ‘masked’ by the highly vascularised choroid lying underneath. A–E, Courtesy of Aberdeen Royal Infirmary. A B C D E secondary optic atrophy and night blindness (nyctalopia), which interfered with the ability to drive. Modern application of laser is lighter, more tailored to the sites of underlying capillary ischaemia and relatively free of side-effects, only occasionally resulting in loss of the ability to drive. In the UK there is a requirement to inform the driver licensing authority if retinopathy is (or has been) present in both eyes, irrespective of treatment history. Intravitreal injections of anti-vascular endothelial growth factor (e.g. ranibizumab, aflibercept, bevacizumab) also cause temporary regression of proliferative retinopathy, whereas, after pan-retinal laser therapy, background and proliferative types of retinopathy regress permanently. If both eyes have been treated with laser, patients can be safely discharged to a retinal screening programme.

Management of diabetic macular oedema Traditionally, oedema seen on slit-lamp biomicroscopy was categorised according to three patterns of leakage elucidated from fluorescein angiogram studies: • focal leakage from microaneurysms • diffuse leakage from diseased capillaries • ischaemia (no leakage) from thrombosis of the perifoveal capillaries. Laser was applied, either directly on leaking microaneurysms or empirically by placing a grid of burns on the affected macula, to reduce leakage. The main aim was to treat oedema before the fovea was affected, as laser therapy for oedema affecting the fovea was never particularly effective. New vessels and their glial tissue (like a cabbage leaf) grow from retinal veins, through the overlying internal limiting membrane into the vitreous, triggering local inflammation and contracting scars. The vitreous is strongly adherent to the pars plana. It pulls back on the new vessel, triggering further bleeding, growth, inflammation and scarring. If the scarring is sufficient, then tractional retinal detachment and complete blindness may occur. Other retinal lesions, not unique to capillary occlusion, are also seen in diabetic retinopathy. These include flame haemorrhages and cotton wool spots (soft exudates). Flame haemorrhages are horizontal streaky haemorrhages in the retinal nerve-fibre layer. They are also seen in any severe anaemia, e.g. bacterial endocarditis and leukaemia. Cotton wool spots are also situated in the nerve-fibre layer and are usually most numerous nasal to the optic disc, where the nerve fibres crowd together. They are also seen in accelerated hypertension, after severe hypoglycaemia and occasionally in giant cell arteritis. A cotton wool spot combined with an enclosing flame haemorrhage is termed a Roth spot. Roth spots have traditionally been associated with endocarditis, although they may be seen with any cause of a flame haemorrhage. Management of proliferative diabetic retinopathy If untreated, proliferative retinopathy eventually causes severe visual impairment through recurrent vitreous haemorrhage and retinal detachment. Pan-retinal laser photocoagulation therapy is extremely effective at preserving vision, if applied before complications set in. Historically, laser therapy was used empirically to ablate the retina extensively outside the macula. However, this caused

hypertension, hyperlipidaemia and smoking), all of which are prevalent in people with type 2 diabetes. In diabetes, metabolic changes in the lens (which are not yet fully elaborated) cause premature and/or accelerated cataract formation. A rare type of ‘snowflake’ cataract occurs in young patients with poorly controlled diabetes. This does not usually affect vision but tends to make fundal examination difficult. The indications for cataract surgery in diabetes are similar to those in the non-diabetic population, but an additional indication in diabetes is when adequate assessment of the fundus and/or retinal laser therapy becomes impossible. Retinal vascular occlusion Retinal vein occlusion (thrombosis) Retinal vein occlusion is an important vascular cause of visual impairment, visual loss resulting from macular oedema or occasionally from neovascularisation, both of which are managed in a similar way to diabetic macular oedema or proliferative diabetic retinopathy. Although pathogenesis of retinal vein occlusion is not fully understood, the most common mechanism is believed to be compression of a vein by an adjacent arteriosclerotic artery. Retinal vessels are unusual in that, where the arteries and veins cross over each other, they share a common outer layer (tunica adventitia). This means that arteriosclerotic thickening of an artery leads directly to compression of the adjacent vein (arteriovenous nipping). A less common cause of retinal vein occlusion is inflammation of the retinal vein (periphlebitis), also called retinal vasculitis (unlike systemic vasculitis, the arterial system is not involved). Periphlebitis should be suspected in younger patients and in patients with no obvious risk factors for

arteriosclerosis. Diagnosis is made by fluorescein angiography and treatment is with systemic immunosuppression, with or without adjunctive intravitreal therapy. Retinal vein occlusion is associated with systemic hypertension and may rarely result from hyperviscosity due to a myeloproliferative disorder, multiple myeloma, Waldenström's macroglobulinaemia or leukaemia. Glaucoma is associated with retinal vein occlusion but whether this is a direct cause or merely a comorbidity in the elderly is not known. Clinical presentation is with unilateral painless loss of central vision (central retinal vein thrombosis) or an area of peripheral vision (branch retinal vein thrombosis). Fundoscopic features include flame haemorrhages, cotton wool spots, macular oedema and a swollen optic disc (Fig. 27.9). However, retinal screening programmes have demonstrated that extrafoveal macular oedema often resolves spontaneously, and the introduction of intravitreal injection therapy, which rescues vision in 50% of those treated regardless of the mechanism of oedema, has led to a paradigm shift in management. Now, rather than laser treatment of asymptomatic oedema that does not involve the centre of the fovea, the emphasis has shifted to treating those who are symptomatic from centre-involving foveal oedema (confirmed on optical coherence tomography) with anti-vascular endothelial growth factor injections. Although this method of treatment is more effective, monthly injections may be required indefinitely. Prevention There is a clear relationship between glycaemic control and the incidence of diabetic retinopathy. A combination of good glycaemic and blood pressure control also slows the progression of retinopathy. When blood glucose is rapidly lowered in patients with type 1 diabetes, however, there can be a transient deterioration of retinopathy, predominantly in the form of cotton wool spot formation, but occasionally triggering new vessel formation. The trigger is believed to be increased systemic insulin growth factor release, which is most likely to occur with sudden correction of eating disorders or reinstitution of insulin therapy in those who miss out injections, often to induce weight loss. This often occurs during hospitalisation for other reasons. Although, ideally, any improvement in glycaemic control should be gradual, in many circumstances this is hard to achieve, particularly if the patient suddenly decides to comply with treatment, leading to dramatic improvement in glycaemic control. Screening Systematic screening for asymptomatic proliferative retinopathy has been shown to be cost-effective. It has led to the introduction of population-based screening programmes in the UK and other countries, where health care is funded centrally. There is little evidence that screening asymptomatic patients for macular oedema is cost-effective, although a by-product of screening is that suspected macular oedema has become the most common reason for referral from retinal screening to ophthalmology. Although hand-held ophthalmoscopy has been shown to have poor sensitivity compared to examination by slit-lamp biomicroscopy or retinal photography, any form of screening is better than none where resources are scarce. Currently, optical coherence tomography is being added to the screening pathway to reduce false-negative referrals for macular oedema. Historically, annual screening has been advocated. However, evidence now indicates that patients with repeated normal screens, particularly those with type 2 diabetes, can be safely screened every 2 years. In pregnancy, the placenta is a source of angiogenic growth factors. For this reason, although the risk of developing significant retinopathy during pregnancy remains low, pregnant women should be screened every trimester until the placenta is delivered. Other causes of visual loss in people with diabetes Around 50% of visual loss in people with type 2 diabetes results from causes other than diabetic retinopathy. These include cataract, age-related macular degeneration, retinal vein occlusion, retinal arterial occlusion, non-arteritic ischaemic optic neuropathy and glaucoma. Some of these conditions are to be expected in this group, as they relate to cardiovascular risk factors (e.g. Fig. 27.9 Central retinal vein occlusion (thrombosis), showing flame haemorrhages, cotton wool spots,

macular oedema and a swollen optic disc. Courtesy of Aberdeen Royal Infirmary.

1178 • MEDICAL OPHTHALMOLOGY epithelium (‘drusen’), often followed by the development of focal areas of macular hypo- and hyperpigmentation, where diseased retinal pigment epithelial cells have precipitated their pigment (age-related maculopathy). The atrophic form presents with gradual onset of central visual blurring, accompanied, to a lesser degree, by visual distortion. Large (geographic), central patches of atrophy are seen with areas of adjacent hyperpigmentation. In the neovascular form, sudden onset of central distortion, progressing within weeks, is the predominant symptom. Apart from age the main risk factor appears to be smoking. The advent of anti-vascular endothelial growth factor injectors has led to effective therapy for the neovascular form, in many but not all. Unfortunately, treatment is expensive and requires considerable financial and staff resources to treat in timely fashion; delayed treatment can lead to irreversible visual loss. For whichever type, whether treatable or not, visual rehabilitation, through the use of appropriate magnifiers, alteration in lighting and specialised adaptation of everyday living objects, remains important adjunctive therapy. Further information Websites jrcptb.org.uk/specialties/medical-ophthalmology How to train in medical ophthalmology in the UK. ndrs-wp.scot.nhs.uk Scottish Diabetic Retinopathy Screening Collaborative: aspects of screening for diabetic retinopathy, including rationale, organisation, delivery and an on-line training handbook. rcophth.ac.uk/standards-publications-research/clinical-guidelines Royal College of Ophthalmologists, London: as part of its role in championing excellence, produces a range of pragmatic surgical and medical guidelines. sun.scot.nhs.uk Scottish Uveitis Network: standards of care, treatment guidelines and information leaflets. The management of retinal vein occlusion is twofold: management of the underlying aetiology and management of the consequences of retinal vein occlusion. Where an underlying risk factor for arteriosclerosis is clearly present (p. 484), then secondary prevention measures should be commenced. However, the role of secondary prevention of arteriosclerosis in isolated retinal vein occlusion, although common practice by some, remains controversial. Retinal artery occlusion Retinal artery occlusion is usually an embolic phenomenon. Common predisposing factors are therefore (predominantly carotid) atherosclerosis valvular heart disease, arrhythmias and infective endocarditis. The next most common cause is vasculitis, mainly giant cell arteritis (p. 1042). Retinal artery occlusion presents with painless unilateral visual loss, the extent and location of which depend on whether there is a central occlusion or a branch occlusion (peripheral occlusions may be asymptomatic). Transient occlusion of the internal carotid or ophthalmic artery causes transient visual loss, or amaurosis fugax (p. 1152). The typical fundoscopic finding in a central occlusion is a transiently pale retina with a ‘cherry-red’ spot at the macula, the appearance developing over an hour or so after the occlusion (Fig. 27.10). In branch occlusions there is no cherry-red spot and the retinal pallor is regional. Age-related macular degeneration Age-related macular degeneration is the most common cause of visual impairment in the Western world. There are two basic forms: atrophic (dry) and neovascular (wet). The underlying mechanism is dysfunction of the retinal pigment epithelium, leading to overlying photoreceptor death. Choroidal neovascularisation, growing under and into the overlying retina, may occur, distorting the anatomy of the photoreceptors and ending in scar formation. Both forms are preceded by deposits under the retinal pigment Fig. 27.10 Retinal artery occlusion. A Colour fundus photograph of central retinal artery occlusion, showing a classic cherry-red spot and a superior optic disc haemorrhage. B Superior branch retinal artery occlusion due an embolus at the disc branch retinal artery occlusion, showing a pale segment of retina. A, From Duker JS, Waheed NK, Goldman DR. Handbook of retinal OCT. Saunders, Elsevier Inc.; 2014. B, From Bowling B. Kanski’s Clinical ophthalmology, 8th edn. Elsevier Ltd; 2016. A B

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