NOTES
GLOBE PATHOLOGY

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Disorders affecting eye structures; if untreated → severe visual impairment
- Due to damage to cornea, retina, lens, optic nerve
- Inherited/acquired

COMPLICATIONS

- Impaired vision, blindness

SIGNS & SYMPTOMS

- Early stages often asymptomatic
- Visual changes

DIAGNOSIS

DIAGNOSTIC IMAGING

Direct/indirect fundoscopy

- Visualize retina

OTHER DIAGNOSTICS

- *Clinical presentation:* history; visual acuity, field loss

Slit lamp

- Visualize sclera, conjunctiva, iris, lens, cornea

TREATMENT

MEDICATIONS

- Corneal ulcer
  - Antimicrobial, steroid eye drops; analgesics
- Age-related macular degeneration (ARMD)/ diabetic retinopathy (DR)
  - Intravitreal injections of vascular endothelial growth factor (VEGF) antagonists
- Glaucoma
  - Beta blockers, alpha agonists

SURGERY

- Cataract
  - Small incision; removal of opacified lens
  - *Alternative:* leaving lens capsule intact (extracapsular cataract extraction), eye without lens (aphakic eye)
- DR
  - Laser photocoagulation of peripheral retina, vitrectomy
- Glaucoma
  - Laser surgery, trabeculectomy, peripheral iridotomy

OTHER INTERVENTIONS

- ARMD
  - Vitamin, antioxidant supplements; smoking cessation
- DR
  - Glucose, blood pressure control

AGE-RELATED MACULAR DEGENERATION (ARMD)

osms.it/macular-degeneration

PATHOLOGY & CAUSES

- Acquired degenerative disease of macula → loss of central vision; peripheral vision preserved; most common cause of severe visual impairment in older adults in high-income countries
- Results from damage to photoreceptors of macula
- Unilateral/bilateral; contralateral eye at high risk

TYPES

Nonexudative ARMD

- AKA dry/atrophic; most common
- Drusen: extracellular deposits between Bruch membrane, retinal pigment epithelium (RPE)
  - ↑ size, number of soft drusen → ↑ risk of progression to advanced ARMD
- *RPE changes:* geographic atrophy, detachments, subretinal clumping

Exudative ARMD

- AKA wet/neovascular; less common
- *Neovascularization:* abnormal vessel formation under retina originating from choroidal circulation, penetrating through Bruch membrane beneath RPE → leakage of serous fluid, blood → collections, fibrosis

RISK FACTORS

- ↑ age; > 65 most common
- *Family history:* associated with polymorphisms in complement regulatory genes, esp. complement factor H (CFH)
- More common in individuals who are biologically female, white people of Ashkenazi Jewish descent
- Smoking, intense light exposure, heavy alcohol use, obesity, hypertension, hyperlipidemia

COMPLICATIONS

- *Severe visual impairment:* impacts functional status, quality of life; complete loss of vision rare

SIGNS & SYMPTOMS

- *Early stages:* often asymptomatic; blurred vision; metamorphopsia (straight lines seen curved)
- Loss of central vision; gradual progression in nonexudative, rapid over weeks/months in exudative

DIAGNOSIS

DIAGNOSTIC IMAGING

Fluorescein dye retinal angiography

- Fluorescein leaks from abnormal vessels

Optical coherence tomography

- Retinal edema/subretinal fluid

Amsler grid

- Individual holds grid at 36–41cm/14–16in, looks at center dot
  - Curvy lines, blurry spots, scotomas

Direct/indirect fundoscopy

- Nonexudative ARMD
  - *Drusen:* white-yellowish, round/oval deposits
  - *Retinal atrophy:* round patches of depigmentation
  - *RPE clumping:* increased pigmentation
- Exudative ARMD
  - *Neovascularization:* gray discoloration
  - Subretinal fluid/hemorrhage

OTHER DIAGNOSTICS

- *Clinical presentation:* history; ↓ visual acuity, visual fields (central vision loss)

TREATMENT

MEDICATIONS

- Exudative ARMD
  - Intravitreal injections of VEGF antagonists to reduce neovascularization
  - Alternative: photodynamic therapy; injection of photosensitive dye verteporfin → damages neovascular endothelium; application of photo-activating laser

OTHER INTERVENTIONS

- No curative method; therapy aimed at slowing progression
- Vitamin, antioxidant supplements
- Nonexudative ARMD
  - Smoking cessation

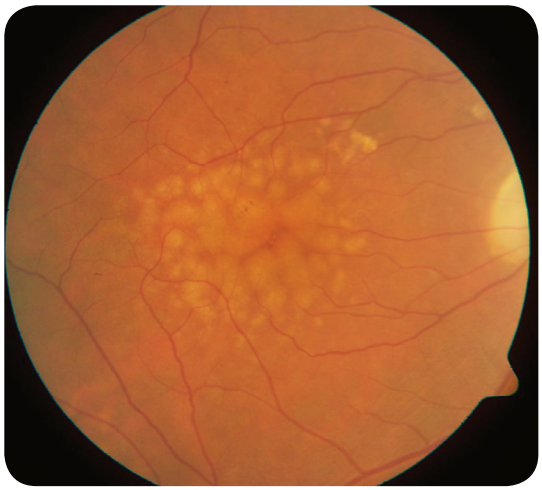

Figure 77.1 Drusen in the macula of individual with age-related macular degeneration.

CATARACT

osms.it/cataract

PATHOLOGY & CAUSES

- Painless, gradual decline in vision due to opacification of lens
- Proteins deposit on lens → reduce transmission of light to retina → decrease in vision
- Often bilateral but asymmetrical; congenital/acquired

TYPES

Nuclear

- Opacification of lens nucleus
- Slow progression of vision loss

Cortical

- Opacification of lens fibers surrounding nucleus (cortex)
- Mild degradation of vision

Posterior subcapsular

- Opacification in posterior cortical layer under lens capsule
- Rapid progression

RISK FACTORS

- Age-related cataract; usually > 60
- Smoking, excessive alcohol use, prolonged drug use (esp. glucocorticoids), exposure to UV light, eye trauma/infections, radiation of intraocular tumor, trisomies (13, 18, 21)
- *Metabolic diseases:* diabetes mellitus, Wilson disease, galactosemia, myotonic dystrophy

COMPLICATIONS

- Blindness (if untreated)
- Secondary posterior subcapsular cataract due to migration of lens epithelium posterior cortical layer

Secondary glaucoma

- Phacolytic
  - Lysed lens proteins clog trabecular meshwork → ↑ pressure
- Phacoanaphylactic
  - Autoimmune reaction to proteins → ↑ pressure
- Phacomorphic
  - Swollen lens → closed angle glaucoma

Surgery

- Residual lens epithelial cells migrate over capsule → opacification, reduction in vision
- Endophthalmitis, bullous keratopathy, intraocular lens dislocation, cystoid macular edema, retinal detachment
- Toxic anterior segment syndrome
  - Inflammation of anterior segment due to noninfectious contaminants of surgical equipment

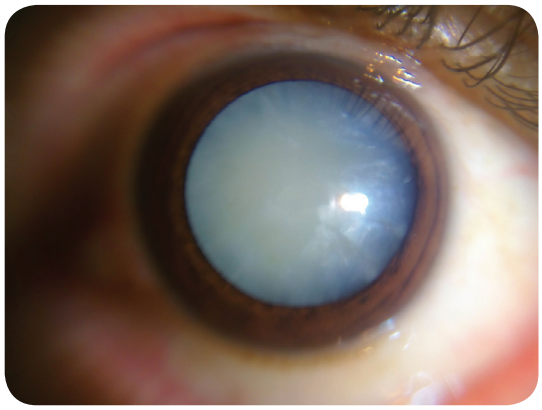

Figure 77.2 The eye of a 50-year-old male with a cataract.

SIGNS & SYMPTOMS

- Painless visual impairment; progresses slowly over many years
- *Myopic shift:* improvement in nearsightedness before decline in vision; lens sclerosis → increase in refractive power
- Blurry vision, poor vision at night, dullness of colors
- Glare, halos around bright lights; predominant in cortical cataract

DIAGNOSIS

DIAGNOSTIC IMAGING

Slit lamp

- Loss of lens transparency

Indirect/direct fundoscopy

- Degree of lens opacity
- Obscuration of fundus details
- Darkening of normal red reflex from fundus

OTHER DIAGNOSTICS

- *Clinical presentation:* history; ↓ visual acuity

TREATMENT

SURGERY

- Small incision
  - Phacoemulsification of lens, implantation of synthetic intraocular lens
- Removal of opacified lens (alternative)
  - Leaving lens capsule intact (extracapsular cataract extraction), eye without lens (aphakic eye)

CORNEAL ULCER

osms.it/corneal-ulcer

PATHOLOGY & CAUSES

- Inflammatory condition of cornea; usually infectious → dissolution of corneal stroma
- Presents as open corneal sore
- AKA ulcerative keratitis
- Exudate, cells leak into anterior chamber → form hypopyon if sufficient quantity

CAUSES

- Bacteria, fungi, viruses (esp. herpes simplex, zoster), protozoa (e.g. *Acanthamoeba*)

RISK FACTORS

- Improper usage of contact lens, corneal abrasions, eye burns, xerophthalmia (i.e. dry eye), eyelid disorders, steroid eye drops, vitamin A deficiency

SIGNS & SYMPTOMS

- Red eye, severe pain, soreness, discharge (tearing, pus), eyelid swelling, blurred vision, vision loss, photophobia

DIAGNOSIS

DIAGNOSTIC IMAGING

- Slit lamp
- Reveals corneal ulcer/hypopyon
- Fluorescein dye
  - Ulcer margins (absorbed by exposed corneal stroma, appears green)
- Herpes simplex ulcers
  - Typical dendritic/geographic pattern

OTHER DIAGNOSTICS

- *Clinical presentation:* history; ↓ visual acuity

TREATMENT

MEDICATIONS

- Antimicrobial eye drops
- Analgesics for pain control
- Steroid eye drops after treatment of infection to reduce swelling, prevent scarring

SURGERY

- Corneal transplantation to replace damaged cornea if scarring decreases vision

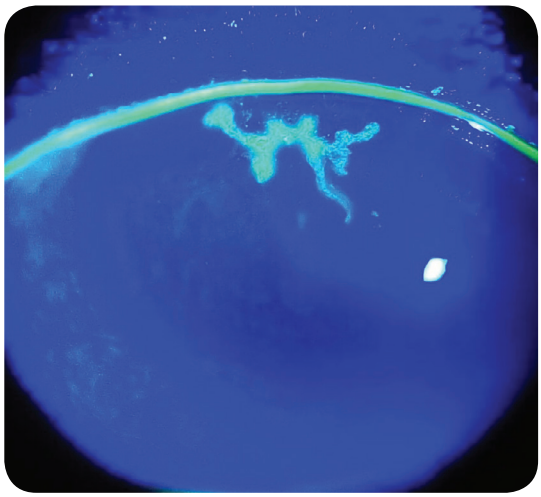

Figure 77.3 A corneal ulcer caused by herpes simplex keratitis viewed with fluorescein under a UV lamp. The ulcer has a classical dendritic pattern.

DIABETIC RETINOPATHY (DR)

osms.it/diabetic-retinopathy

PATHOLOGY & CAUSES

- Type of retinopathy affecting individuals with diabetes mellitus → vision loss
- Long-standing diabetes mellitus/poor glycemic control → chronic hyperglycemia → retinal vascular changes (e.g. abnormal vascular permeability, vascular occlusions) → ischemia → production of VEGF → formation of abnormal blood vessels (neovascularization)

TYPES

Proliferative DR

- Presence of neovascularization

Nonproliferative DR

- Absence of neovascularization; majority of cases; can progress to proliferative; hypertension, fluid retention exacerbate condition

COMPLICATIONS

- Visual loss due to
  - Macular edema (most common); vitreal hemorrhage from neovascularization; retinal detachment; neovascular glaucoma

SIGNS & SYMPTOMS

- Usually asymptomatic until late stages
- Decreased/fluctuating vision; presence of floaters, flashes of lights (photopsias); scotomas

DIAGNOSIS

DIAGNOSTIC IMAGING

Direct/indirect fundoscopy

- Thickening of basement membrane, microaneurysms, microocclusions, exudates, nerve-fiber layer infarcts (cotton wool spots), intraretinal hemorrhage, macular edema

OTHER DIAGNOSTICS

- *Ophthalmologic screening:* annual screening suggested for individuals with diabetes
- *Clinical presentation:* ↓ visual acuity

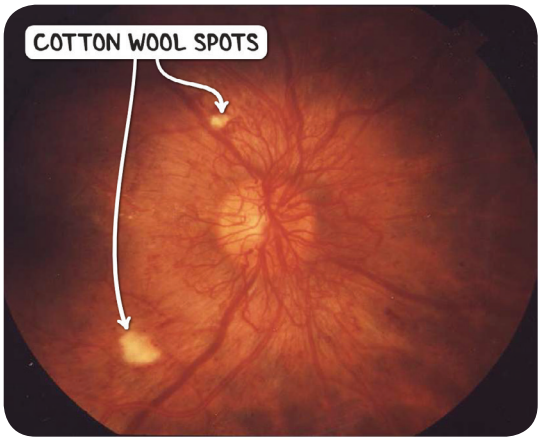

Figure 77.4 A retinal photograph demonstrating proliferative diabetic retinopathy. There are cotton wool spots and as well as neovascularisation of the retina.

TREATMENT

MEDICATIONS

- Intravitreal VEGF inhibitors for proliferative DR, significant macular edema

SURGERY

- Laser photocoagulation of peripheral retina
- Vitrectomy for vitreous hemorrhage/ severe proliferative DR nonresponsive to photocoagulation

OTHER INTERVENTIONS

- Glucose, blood pressure control to reduce progression of nonproliferative DR

GLAUCOMA

osms.it/glaucoma

PATHOLOGY & CAUSES

- Group of eye disorders; intraocular hypertension damages optic nerve → progressive peripheral visual field loss
- Aqueous humour drainage pathway becomes partially/completely blocked → fluid cannot easily drain out → pressure of anterior chamber builds up → intraocular hypertension (pressure > 21mmHg/2.8kPa) → affects eye structures → atrophy of outer rim of optic nerve → peripheral vision loss
- Intraocular pressure increases → continued damage to optic nerve → ganglion cell loss → loss of central vision

TYPES

Open Angle Glaucoma

- Angle between cornea, iris; most common
- Increased aqueous production/decreased outflow
- Secondary to uveitis, vitreous hemorrhage, retinal detachment

Closed Angle Glaucoma

- Narrowing/closure of anterior chamber angle → inadequate drainage of aqueous humor → increased intraocular pressure → optic nerve damage
- *Acute:* rapid buildup of pressure

Normal Tension Glaucoma

- Genetic hypersensitivity to intraocular pressures in normal range

RISK FACTORS

Open angle

- ↑ age, black people of African descent, family history

Closed angle

- ↑ age, family history, biologically-female individuals of Asian descent, hyperopia, medications (e.g. mydriatic eye drops), pseudoexfoliation

COMPLICATIONS

- If untreated, blindness

SIGNS & SYMPTOMS

Open angle

- Asymptomatic

Closed angle

- *Chronic:* often asymptomatic, peripheral vision loss
- *Acute (ophthalmic emergency):* abrupt onset of severe eye pain, redness, blurry vision/vision loss, headache, nausea, halos around lights, fixed mid-dilated pupil, conjunctival redness, corneal edema

DIAGNOSIS

DIAGNOSTIC IMAGING

Tonometry

- ↑ intraocular pressure

Direct/indirect fundoscopy

- Cupping: hollowed-out appearance of optic nerve (thinning of outer rim)
- Increased cup-to-disc ratio; > 0.5 suggestive of glaucoma

Slit lamp

- Special lens to visualize angle (gonioscopy)

OTHER DIAGNOSTICS

- *Clinical presentation:* history, ↓ visual acuity, visual field (peripheral vision loss; central loss at late stages)

TREATMENT

MEDICATIONS

Open angle

- Beta-adrenergic receptor antagonists, carbonic anhydrase inhibitors, alpha adrenergic agonists
  - ↓ production of aqueous humor
- Prostaglandin analogs, alpha adrenergic agonists
  - ↑ outflow of aqueous humor

Acute closed angle

- Eye drops (e.g. beta-blockers, alpha agonists); systemic (e.g. acetazolamide, urea, mannitol, glycerol)

SURGERY

Open angle

- Laser surgery
  - Open trabecular meshwork, increase aqueous outflow (trabeculoplasty); destroy humor producing cells; create new channel for aqueous humour drainage
- Surgical trabeculectomy
  - Create alternate drainage pathway

Acute closed angle

- Peripheral iridotomy with laser
  - Small hole through iris for aqueous humor drainage

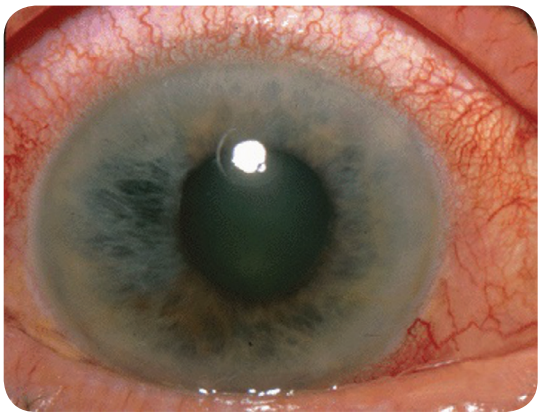

Figure 77.5 A photograph of the eye of an individual with acute angle closure glaucoma. There is ciliary flush and a hazy cornea.

RETINAL DETACHMENT (RD)

osms.it/retinal-detachment

PATHOLOGY & CAUSES

- Separation of retinal photoreceptors from underlying retinal pigment epithelium (RPE), choroid; if untreated leads → vision loss
- Detachment of neurosensory retinal layer from underlying layers → ischemia, progressive degeneration of photoreceptors → vision loss

TYPES

Rhegmatogenous

- Most common
- Full thickness retinal break → vitreous fluid passes into subretinal space → retinal detachment
- Causes
  - *Posterior vitreous detachment:* most common, age 50–75, separation of

posterior vitreous membrane from retina due to natural age-related liquefaction of vitreous → retinal breaks can occur in areas of strong vitreoretinal attachment
    - Ocular trauma

Nonrhegmatogenous

- Vitreous traction
    - Abnormally strong vitreoretinal adhesion → contraction → detachment; proliferative diabetic retinopathy, retinopathy of prematurity
- Exudative
    - Fluid accumulation between layers; inflammatory conditions, choroidal neoplasms

RISK FACTORS

Rhegmatogenous

- High myopia; lattice degeneration (thinning of retinal periphery); family history; history of retinal detachment; ocular trauma; previous intraocular surgery (e.g. cataract surgery)

COMPLICATIONS

- Vision loss, proliferative retinopathy

SIGNS & SYMPTOMS

- *Sudden onset:* floaters/flashes of light; if preceded by posterior vitreous detachment
- *Monocular vision loss:* curtain drawn over vision field

DIAGNOSIS

DIAGNOSTIC IMAGING

- ↓ visual acuity

Ocular ultrasound

- E.g. choroidal masses
- Traction, exudative RD; find underlying cause

Direct/indirect fundoscopy

- *Rhegmatogenous:* wavy appearance, changes with eye movements, changes in vessel direction
- *Tractional:* smooth concave retinal surface; minimal shifting with eye movements
- *Exudative:* smooth retinal surface, shifting fluid

LAB RESULTS

- *Diabetes:* traction, exudative RD; find underlying cause

OTHER DIAGNOSTICS

- Clinical history, physical examination

TREATMENT

SURGERY

- *Laser photocoagulation/cryoretinopexy:* seal retinal breaks, prevent retinal detachment
- Rhegmatogenous RD
    - *Pneumatic retinopexy:* intraocular injection of gas to tamponade retinal break (along with laser or cryoretinopexy)
    - *Scleral buckles:* silicone bands placed are sewed to sclera under rectus muscles (along with laser or cryoretinopexy)
    - *Vitrectomy:* removal of vitreous body to reduce the effect of vitreous traction to retina
- Tractional RD
    - Vitrectomy with scleral buckling

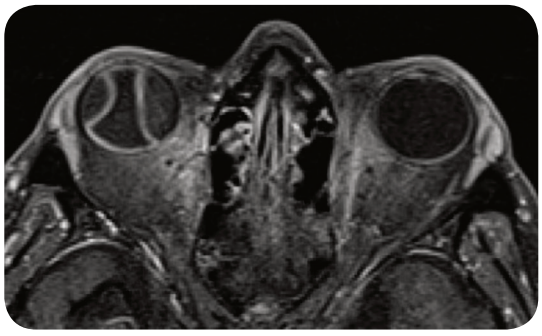

Figure 77.6 An MRI scan of the head in the axial plane demonstrating detachment of the right retina.

RETINOBLASTOMA

osms.it/retinoblastoma

PATHOLOGY & CAUSES

- Intraocular malignant tumor; affects children; presents as leukocoria
- Most common primary intraocular malignancy of childhood; usually < two years
- Associated with intracranial tumor
  - Pinealoblastoma (trilateral retinoblastoma)
- Mutational inactivation of both alleles of retinoblastoma (*RB1*) gene located in chromosome 13

TYPES

Heritable (40%)

- *Germline mutations:* inherited/de novo
- Presents at early age; bilateral/multifocal; 50% risk of passing to offspring

Nonheritable (60%)

- Somatic mutations in both alleles; negative family history
- Presents later in life; unilateral

RISK FACTORS

- Family history
- 13q14 deletion syndrome
  - Microdeletions in region 1 band 4 located in large arm (q) of chromosome 13

COMPLICATIONS

- Fatal if untreated; with prompt treatment, survival > 95%
- Spreads via
  - Choroid → sclera, orbit → destruction of globe → vision loss
  - Optic nerve → brain
  - Subarachnoid space → contralateral optic nerve, brain
  - Blood → lungs, bones, liver
  - Lymphatic vessels → conjunctiva, eyelids, extraocular tissue
- Heritable retinoblastoma
  - Secondary malignancy (e.g. bone, soft tissue sarcomas)

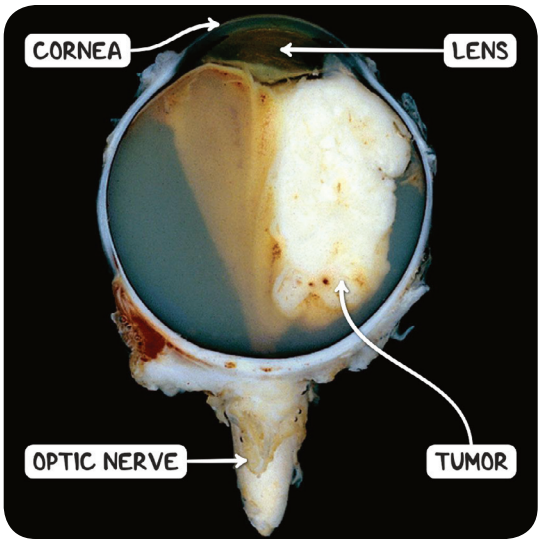

Figure 77.7 The gross pathological appearance of a retinoblastoma.

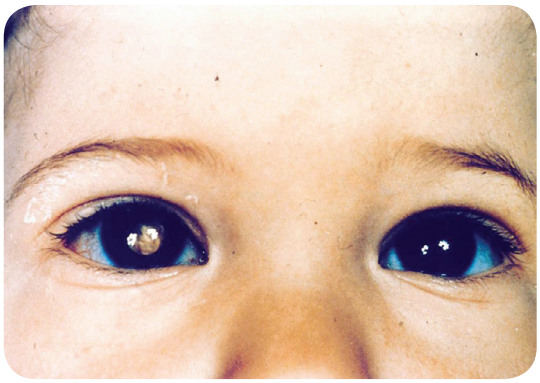

Figure 77.8 A child with retinblastoma causing whitening of the right pupil known as leukocoria.

SIGNS & SYMPTOMS

- Leukocoria (abnormal white reflexion from retina)
- Strabismus, nystagmus, red eye

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI (brain, orbits)

- *T1-weighted:* bright
- *T2-weighted:* dark compared to vitreous
- Detect optic nerve involvement, associated intracranial tumor

Direct/indirect fundoscopy

- Well-circumscribed, translucent, white intraretinal mass

Ocular ultrasound

- Normal globe size, calcification

LAB RESULTS

- Genetic testing
  - Estimate risk in family members, future offspring

OTHER DIAGNOSTICS

- Metastasis evaluation (e.g. bone marrow aspiration, lumbar puncture)

TREATMENT

MEDICATIONS

- Local/systemic chemotherapy
  - Preserve vision, optimize survival

SURGERY

- Cryopexy, laser photoablation, enucleation
  - Preserve vision, optimize survival

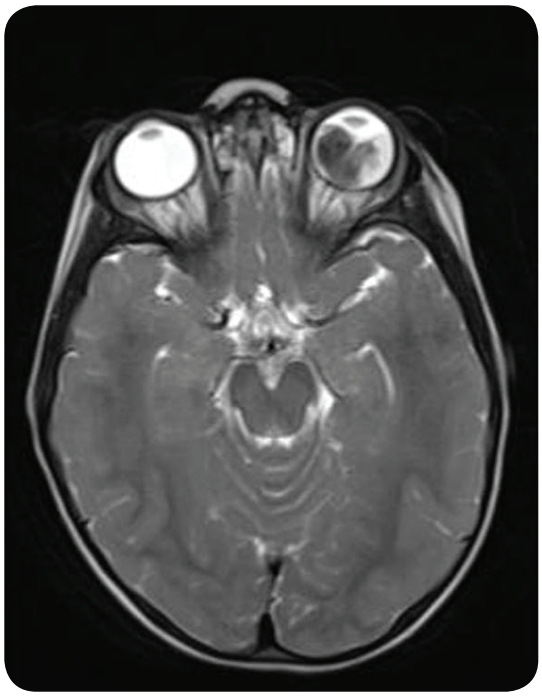

Figure 77.9 An MRI scan of the head in the axial plane demonstrating a retinoblastoma of the left globe.

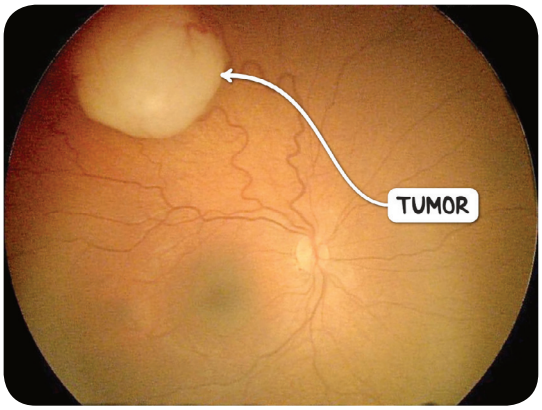

Figure 77.10 A retinoblastoma as seen on fundoscopy.

RETINOPATHY OF PREMATURITY

osms.it/retinopathy-of-prematurity

PATHOLOGY & CAUSES

- AKA retrolental fibroplasia
- Proliferative retinopathy, occurs in preterm infants; if untreated → vision loss
- Common cause of childhood blindness
- Premature birth interrupts development → ↑ risk of vascular insult
- Supplemental oxygen administration → disruption of normal angiogenesis → abnormal growth of blood vessels, fibrous tissue affecting temporal part of retinal periphery
- Regress spontaneously in most cases

RISK FACTORS

- Gestational age < 30 weeks; birth weight ≤ 1.5kg/3.3lbs; excessive oxygen therapy; supplemental oxygen

COMPLICATIONS

- Retinal bleeding, scarring
- Contraction of fibrovascular tissue → retinal detachment → blindness
- *Refractive errors:* myopia, anisometropia
- Squint/strabismus
- Glaucoma

SIGNS & SYMPTOMS

- Blindness due to retinal detachment, if untreated

DIAGNOSIS

DIAGNOSTIC IMAGING

Fundoscopy

- Direct/indirect following pupil dilation
  - Disorganized growth of vessels, fibrous tissue
- Classification
  - *Location:* three concentric zones from optic disc to periphery
  - *Extent:* retina divided in 12 parts (hours of a clock)
  - *Stage I:* thin white demarcation line separating vascularized from avascular retina
  - *Stage II:* ridge of fibrous tissue into vitreous between vascularized, avascular retina
  - *Stage III:* abnormal growth of fibrovascular tissue on ridge; extension into vitreous
  - *Stage IV:* partial retinal detachment
  - *Stage V:* total retinal detachment
  - *Plus disease:* increased venous dilation, tortuosity of posterior retinal vessels, vitreous haze

OTHER DIAGNOSTICS

- Screening of preterm infants

TREATMENT

MEDICATIONS

- Intravitreal injection of VEGF antagonists

SURGERY

- Ablation of retina with laser photocoagulation

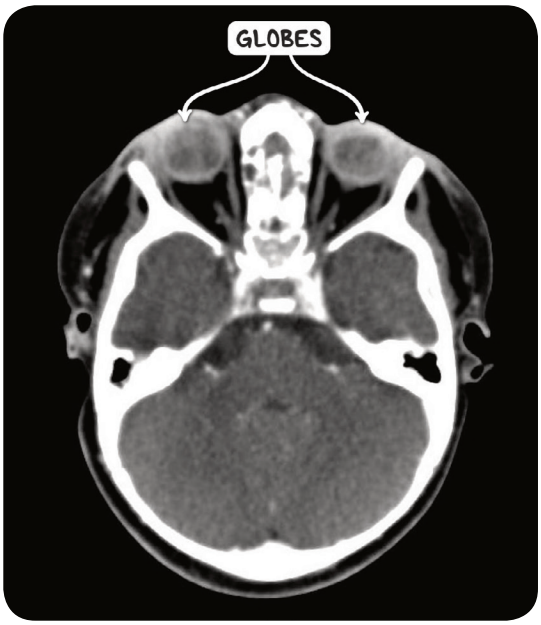

Figure 77.11 A CT scan of the head in the axial plane demonstrating increased density and asymmetry of the globes in a one year old biologically-female individual. The increase in density is caused by retinal detachment and subsequent fibrous reorganisation of the vitreous.