Patient Management in Clinical Practice

3

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3.1 Non-Proliferative Diabetic Retinopathy (NPDR) (Fig. 3.1)

3.1.1 Other Diagnoses to Consider

- Retinal vein occlusion
- Hypertensive retinopathy
- Ocular ischaemic syndrome
- Radiation retinopathy

3.1.2 Risk Factors for Diabetic Retinopathy (DR)

The Royal College of Ophthalmologists (RCOphth) Diabetic Retinopathy Guidelines 2012

- Non-modifiable
  - Genetic factors
  - Gender
  - Duration of diabetes
- Modifiable
  - Glycaemia
  - BP
  - Lipid levels
- Other
  - Carotid arterial disease
  - Pregnancy
  - Renal impairment
  - Smoking

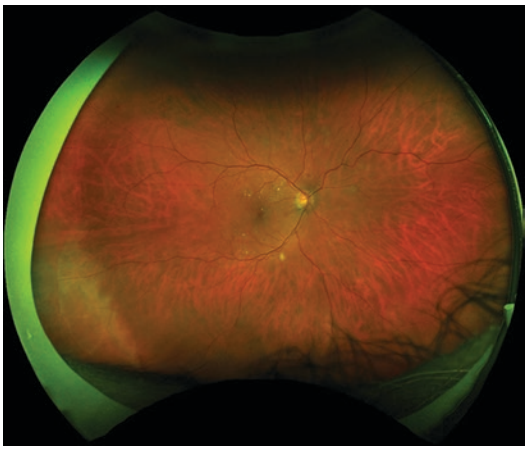

Fig. 3.1 Optos pseudocolour fundus image (right eye) of a diabetic patient with mild NPDR

3.1.3 Classification

- Proposed International Clinical Diabetic Retinopathy Severity Scale 2003
  - Mild NPDR:

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Microaneurysms (MAs) only
  - Moderate NPDR:
    More than just MA' but less than severe NPDR
  - Severe NPDR (4-2-1 rule) — one or more of the following features are present:
    More than 20 intraretinal haemorrhages in each of 4 quadrants
    Definite venous beading in 2 or more quadrants
    Prominent intraretinal microvascular abnormalities (IRMA) in 1 or more quadrants
  - Very severe NPDR:
    Two or more features of severe NPDR are present
- Public Health England NHS Diabetic Eye Screening Programme Grading Definitions 2017
  - R0: No retinopathy
  - R1 (Background DR/mild NPDR):
    Venous loop
    Microaneurysms
    Retinal haemorrhage
    Any exudate or cotton wool spot in presence of other non-referable DR features
  - R2 (pre-proliferative DR/moderate NPDR):
    Venous beading
    Venous reduplication
    Multiple blot haemorrhages (if uncertain, refer only in the presence of IRMA that are definitely seen)
    - Blot haemorrhages (located in OPL and INL) are larger than the width of the smallest of the four branches of the central retinal vein as it crosses the edge of the disc

    IRMA (check that they can still be seen on the colour image as well as the red-free image that has not been enlarged)

3.1.4 Examination

- Microaneurysms (MAs): small red dots
- Intraretinal haemorrhages: dot and blot haemorrhages, flame haemorrhages
- Hard exudates: sharply demarcated yellow-white deposits within the retina
- Cotton wool spots (CWS — patches of relative ischaemia affecting the NFL of the retina): small white patches with wispy borders situated in the inner retina
- Venous beading: localised areas of change in vessel calibre with alternating regions of relative dilation and constriction
- Venous loops
- Intraretinal microvascular abnormalities (IRMA): segments of dilated and tortuous retinal vasculature without crossing both arterioles or veins in the underlying retina
- Subretinal fibrosis

3.1.5 Investigations

- Blood test for diagnosis of diabetes mellitus:
  - Venous fasting glucose ≥7.0 mmol/L and/or
  - Oral glucose tolerance test (75 g anhydrous glucose) with a 2-h value ≥11.1 mmol/L and/or
  - Random venous glucose ≥11.1 mmol/L
- FFA:
  - MAs appear as hyperfluorescent dots visible during the arteriovenous transit phase
  - Intraretinal haemorrhages appear hypofluorescent blocking normal fluorescence from the underlying choroid
  - Exudates appear hypofluorescent
  - CWS appear hypofluorescent
  - IRMA appear hyperfluorescent during the arteriovenous transit phase and are often situated at the borders of areas of capillary non-perfusion

3.1.6 Treatment

- Modification of life-style:
  - Smoking cessation
  - Weight loss
  - Exercise
- Modification of systemic risk factors:
  - Hyperglycaemia control:
    DCCT (The Diabetes Control and Complications Trial Research Group

1995): Type 1 DM — tight control of HbA1C at mean of 7.2% was associated with 76% reduction in onset of retinopathy and slowed progression of DR by 54%, 60% reduction in onset of neuropathy, and 54% reduction in onset of nephropathy at 6.5 years

UKPDS (UK Prospective Diabetes Study Group 1998): Type 2 DM — tight control of HbA1C at mean of 7% was associated with a 25% reduction in the onset of microvascular disease

ACCORD (The ACCORD Study Group and ACCORD Eye Study Group 2010): Type 2 DM — intensive control of HbA1C reduced progression of DR by 42% and reduced development of PDR from 10.2% to 6.5%: avoid Pioglitazone in the presence of macular oedema, personalized HbA1C target should be set, usually between 48–58 mmol/mol (6.5–7.5%)

– BP control:

UKPDS (UK Prospective Diabetes Study Group 1998): Type 2 DM — tight control of BP at mean of 144/82 was associated with a 37% reduction in the onset of microvascular disease and 32% reduction in diabetes related deaths

– Lipid control:

ACCORD (The ACCORD Study Group and ACCORD Eye Study Group 2010): Type 2 DM — 40% reduction in the odds of having progression of DR over 4 years in patients allocated to fenofibrate in combination with a statin, compared to simvastatin alone): consider adding fenofibrate to a statin for NPDR in type 2 DM, avoid statins in pregnancy

3.1.7 Follow-Up

- Mild NPDR: discharge to community for DRSS screening or 12 months follow up if seen in hospital eye service
- Moderate NPDR: 3–6 months
- Severe NPDR: less than 3 months

3.1.8 Prognosis

- In the Diabetic Retinopathy Study (DRS) (The Diabetic Retinopathy Study Research Group 1981), 50% of untreated severe DR will develop proliferative diabetic retinopathy (PDR) within 15 months
- In the Early Treatment Diabetic Retinopathy Study (ETDRS) (Early Treatment Diabetic Retinopathy Study Research Group. ETDRS report number 12. 1991b):
  – 6.2% risk of progression to PDR at 1 year for mild NPDR
  – 11.3% risk of progression to PDR at 1 year for moderate NPDR
  – 20.7% risk of progression to PDR at 1 year for severe NPDR

3.2 Diabetic Macular Oedema (DMO) (Fig. 3.2)

3.2.1 Other Causes of Macular Oedema to Consider

- Inflammatory disorders: post-operative (cataract, VR, corneal), post-laser (PI, PRP), post-cryotherapy, uveitis
- Retinal vascular diseases: DR, RVO, OIS, hypertensive retinopathy, radiation retinopathy, MacTel

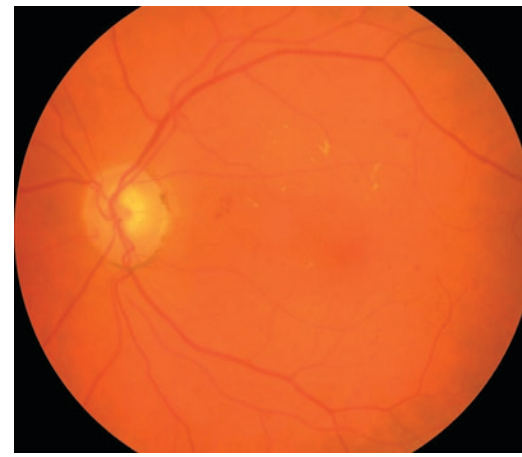

Fig. 3.2 Colour fundus image of a patient with DMO

- Choroidal vascular disease: CNV
- Drugs: latanoprost, topical adrenaline, glitazones, niacin, chemotherapy agents (e.g. paclitaxel)
- Inherited retinal dystrophies: RP, autosomal dominantly inherited CMO
- Disorders of vitreoretinal interface: VMT, ERM
- Optic nerve head abnormalities: optic disc pit, optic disc coloboma
- Tumours of the choroid/retina

3.2.2 Classification

- Proposed International Clinical Diabetic Macular Edema Severity Scale, 2003
  - Mild DME:
    Some retinal thickening or exudates in the posterior pole, distant from the center of the macula
  - Moderate DME:
    Retinal thickening or exudates near the center of the macula but not involving the center
  - Severe DME:
    Retinal thickening or exudates involving the center of the macula
- Public Health England NHS Diabetic Eye Screening Programme Grading Definitions 2017
  - M0: No maculopathy
  - M1:
    Exudate within 1 DD of the centre of the fovea
    Circinate or group of exudates within the macula:
    - A group of exudates is an area of exudates that is greater than or equal to half the disc area and this area is all within the macular area
    - To work out the area, the outer points of the exudates are joined and compared to half the area of the optic disc
    - Any MA or haemorrhage within 1 DD of the centre of the fovea only if associated with a best VA of 6/12 or worse

3.2.3 Examination

- Exudates within the macular
- MAs or retinal haemorrhages within the macular
- Clinically significant macular oedema — CSMO (Early Treatment Diabetic Retinopathy Study Research Group. ETDRS report number 9. 1991a):
  - Retinal thickening at or within 500 μm of the centre of the macula and/or
  - Exudates at or within 500 μm of the centre of the macula, if associated with thickening of the adjacent retina and/or
  - Zone or zones of retinal thickening 1-disc area or larger, any part of which is within 1 DD of the center of the macula

3.2.4 Investigations

- OCT
  - Exudates appear as hyperreflective foci within the retina
  - Macular oedema
  - Traction from ERM or VMT causing underlying macular oedema in the absence of retinal vascular leakage demonstrable by FFA
- FFA
  - Petaloid pattern of leakage from macular oedema
  - Enlarged foveal avascular zone from ischaemic diabetic maculopathy

3.2.5 Treatment

- Focal/grid laser
  - **ETDRS** (Early Treatment Diabetic Retinopathy Study Research Group. ETDRS report number 9. 1991a): focal/grid laser reduced the risk of moderate vision loss (loss of ≥15 letters from baseline) by 50% at 3 years in eyes with mild or moderate NPDR with CSMO

  - Indicated if CMT <400 μm and CSMO is not center involving (RCOphth Diabetic Retinopathy Guidelines 2012)
- Anti-VEGF therapy
  - Aflibercept (Eylea)
    NICE Guidance [TA346]: option for treatment of DMO if CMT ≥400 μm at the start of treatment
    Regimen: a single injection every month for 5 consecutive months, followed by one injection every 2 months with no requirement for monitoring between visits for the first 12 months
    Clinical trials:
    - **VISTA** study (Brown et al. 2015)
    - **VIVID** study (Brown et al. 2015)
  - Ranibizumab (Lucentis)
    NICE Guidance [TA274]: option for treatment of DMO if CMT ≥400 μm at the start of treatment
    Regimen: given monthly and continued until maximum VA is reached — VA stable for 3 consecutive months:
    Clinical trials:
    - **RISE** study (Nguyen et al. 2012; Brown et al. 2013)
    - **RIDE** study (Nguyen et al. 2012; Brown et al. 2013)
    - **RESTORE** study (Mitchell et al. 2011)
- Dexamethasone implant (Ozurdex)
  - NICE Guidance [TA349]: option for treatment of DMO if eye is pseudophakic and CSMO does not respond to non-corticosteroid treatment or such treatment is unsuitable
  - Regimen: A single implant is injected into the vitreous and remains in the vitreous for up to 270 days before fully dissolving
  - Clinical trials:
    MEAD study (Boyer et al. 2014)
    BEVORDEX study (Gillies et al. 2014)
    PLACID study (Callanan et al. 2013)
- Fluocinolone implant (Iluvien)
  - NICE Guidance [TA301]: option for the treatment of chronic CSMO that is insufficiently responsive to available therapies if an eye is pseudophakic
  - Regimen: A single 190 μm of Fluocinolone Acetonide implant is injected with daily release of 0.2 μg/day for 36 months
  - Clinical trials:
    FAME study (Cunha-Vaz et al. 2014)

3.2.6 Follow-Up

- Center involved DMO: 1–3 months
- Non-center involved DMO: 3–6 months
- Stable treated DMO: 3–6 months

3.2.7 Focal and Grid Laser Techniques

Diabetic Retinopathy Clinical Research Network (DRCR.net) laser techniques (Writing Committee for the Diabetic Retinopathy Clinical Research Network et al. 2007)

- Focal treatment
  - Topical anaesthetic
  - Spot size: 50 μm
  - Burn duration: 0.05–0.1 s
  - Burn intensity: mild grey-white burn evident beneath all MAs
  - Directly treat all leaking MA's in areas of retinal thickening between 500 and 3000 μm from the center of the macula
  - Follow up: 3–4 months
- Grid treatment
  - Topical anaesthetic
  - Spot size: 50 μm
  - Burn duration: 0.05–0.1 s
  - Burn intensity: light grey burn
  - Burn separation: two visible burn widths apart
  - Apply to all areas with oedema not associated with MA's: 500–3000 μm superiorly, nasally and inferiorly from center of macula; 500–3500 μm temporally from macular center; no burns placed within 500 μm of optic disc
  - Follow up: 3–4 months

– Complications: pain, worsened VA, choroidal detachment or RD, CNV membrane, vitreous haemorrhage

3.3 Proliferative Diabetic Retinopathy (PDR) (Fig. 3.3)

3.3.1 Other Causes of Neovascularisation to Consider

- Retinal vein occlusion
- Ocular ischaemic syndrome
- Radiation retinopathy
- Occlusive retinal vasculitis — MS, sarcoid, Behcet's disease

3.3.2 High-Risk PDR

- Defined by the Diabetic Retinopathy Study (The Diabetic Retinopathy Study Research Group 1981) with patients at higher risk of visual loss and requires prompt PRP treatment
  - Neovascularisation of the disc (NVD — new vessels on or within 1 DD of the optic disc): NVD ≥1/4 disc area or any size NVD with vitreous and/or pre-retinal haemorrhage
  - Neovascularisation elsewhere in the retina (NVE): NVE ≥1/2 disc area with vitreous and/or pre-retinal haemorrhage

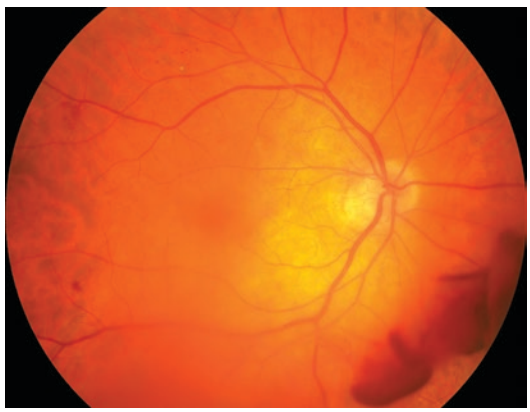

Fig. 3.3 Colour fundus image of a patient with PDR with an active NVE and a vitreous haemorrhage

3.3.3 PDR in Pregnancy

3.3.3.1 NICE Guidance [NG3]

- Diabetic patients planning pregnancy should be informed on the need for assessment of DR before and during pregnancy
- Statins and drugs blocking the renin-angiotensin system should be discontinued before conception and always at first antenatal booking if still being taken
- Ideally, all patients with PDR should be identified and treated prior to conception
- Rapid optimisation of poor glycaemic control should be deferred at least until after retinal assessment
- Retinal assessment during and after pregnancy:
  - Newly pregnant women with pre-existing DM should be offered retinal assessment by digital imaging following their first antenatal clinic (i.e. first trimester, typically 8–12 weeks) appointment (unless they have had a retinal assessment in the last 3 months) and again at 28 weeks (third trimester) if the first assessment is normal. If any DR is present, an additional retinal assessment should be performed at 16–20 weeks (second trimester)
  - At term, DR should not be considered a contraindication to vaginal birth
  - Women who have NPDR diagnosed during pregnancy should have ophthalmological follow up for at least 6 months following the birth of the baby
  - Tropicamide alone should be used if mydriasis is required during pregnancy
- Women with gestational DM are not at increased risk for the development of DR and do not need such monitoring.

3.3.4 Treatment

- Modification of life-style (see Sect. 3.1.6)
- Modification of systemic risk factors (see Sect. 3.1.6)
- Pan-retinal photocoagulation (PRP)

  - Indications (The Royal College of Ophthalmologists Diabetic Retinopathy Guideline 2012): presence of NVD/NVE/NVI/NVA — PRP performed on same day or within 2 weeks of diagnosis, consider PRP for severe/very severe NPDR in older patients with type 2 DM, where retinal view is difficult, prior to cataract surgery, in only eye where first eye lost to PDR, where regular clinic attendance is likely to be poor, difficult to examine patient for other reasons
  - Prognosis (The Diabetic Retinopathy Study Research Group 1981): PRP reduces severe vision loss (<5/200 at two consecutive visits) from high risk PDR by 50% at 2 years
- Vitrectomy
  - Indications (The Royal College of Ophthalmologists Diabetic Retinopathy Guideline 2012): non-clearing (within 3 months for type 2 diabetic and 1 month for a type 1 diabetic) severe vitreous haemorrhage (confirmation of attached retina not possible with ophthalmoscopic examination), significant recurrent vitreous haemorrhage despite maximal PRP, tractional RD involving or threatening the fovea, combined tractional rhegmatogenous RD which involves or threatens to involve the fovea, diffuse CSMO associated with posterior hyaloidal traction
  - Prognosis (The Diabetic Retinopathy Vitrectomy Study Research Group 1988): early vitrectomy (for those with severe vitreous haemorrhage with VA 5/200 or worse) increased chance of 20/40 vision from 12% to 36% in type 1 diabetics

3.3.5 Prognosis

- 25% with type 1 DM and 16% with type 2 DM will develop PDR after 15 years of DM (Klein et al. 1984)

3.3.6 PRP Laser Technique

3.3.6.1 RCOphth Diabetic Retinopathy Guideline 2012

- Topical anaesthetic
- Spot size: 400 μm spot size (if 200 μm is preselected on laser interface, a Mainster 165 PRP lens with a spot magnification factor of 1.96 will produce a theoretical retinal spot size of 392 μm. If other fundus lens is selected, it is expected that appropriate adjustments will be made to spot size selection)
- Burn duration: 20 ms
- Burn intensity: barely visible grey-white burn (titrate power down by up to 50 mW in the periphery)
- Burn separation: 1 visible burn width apart for early or moderate PDR, 0.5 burn width apart for severe PDR
- Retinal surface coverage: burns applied as far peripheral as possible up to the ora serrata, no closer than 3000 μm temporal to fovea, no closer than 500 μm nasal to the optic disc, no further posterior than one burn within the temporal arcades
- No. of sessions to complete full primary PRP: 1–2 sessions within 2 weeks for mild (NVD or NVE <1/3 disc area and flat) and moderate (NVD or NVE >1/3 disc area) PDR, 2–3 sessions in 3–4 weeks for severe (NVD or NVE with tractional RD) PDR, 3–4 sessions within 4 weeks for young patients with type 1 diabetes with PDR (increased risk of developing macular oedema post PRP)
- Follow up: 4 months for early PDR, 3 months for moderate PDR, 2 weeks for PDR in pregnancy. Regression of new vessels is characterised by blunting of the NV growing tips or replacement with fibrosis
- Complications:
  - Related to damage to posterior ocular structures:
    Retinal tear
    Choroidal haemorrhage
    Choroidal neovascularisation

Vitreous, pre-retinal or subhyaloid haemorrhage
Inadvertent optic disc or foveal damage
- Related to loss of visual function:
  Diminished or loss of peripheral visual field — implications for driving
  Diminished colour vision and contrast sensitivity
  Reduced or loss of dark adaptation — effect on night vision
- Related to the destructive nature of the procedure:
  Pain during and shortly after treatment
  Corneal epithelial defects and recurrent erosions
  Mydriasis
  Iris burns and damage/lenticular burns or opacification
- Related to contraction of fibrovascular tissue:
  Progressive traction RD
- Related to break down of blood-retinal barrier breakdown:
  Exudative RD/choroidal detachment/choroidal effusion
  Macular oedema

3.4 Branch Retinal Vein Occlusion (BRVO) (Fig. 3.4)

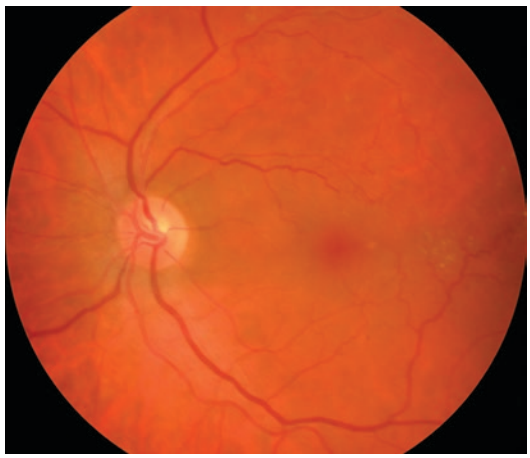

Fig. 3.4 Colour fundus image of a patient with a chronic non-ischaemic BRVO

3.4.1 Other Diagnoses to Consider

- Macular telangiectasia
- Diabetic retinopathy
- Radiation retinopathy
- Susac syndrome: small BRAO (may be multiple) and capillary occlusions, sensorineural hearing loss, subacute encephalopathy, hyperintense lesions in the corpus callosum on T2 MRI
- Behcet's disease
- Sarcoidosis

3.4.2 Risk Factors

- Arteriosclerosis: HTN, DM, smoking, hyperlipidaemia (including secondary to hypothyroidism)
- Glaucoma
- Ocular inflammatory disease: Behcet's disease, PAN, sarcoidosis, SLE
- Haematological: Protein C, protein S or antithrombin deficiency, activated protein C resistance, factor V Leiden, myeloma, Waldenstrom's macroglobulinaemia, antiphospholipid syndrome

3.4.3 Examination

- Acute BRVO: wedge shaped segmental distribution of intraretinal haemorrhage in a quadrant of the fundus, narrowed branch retinal vein passing under a retinal artery, dilated and tortuous retinal vein, cotton wool spots
- Chronic BRVO: telangiectatic vessels (dilation of capillaries) forming collaterals that cross the horizontal raphe, microaneurysms, exudates, sclerosed retinal vein ±NVE > NVD > NVI
- Check for RAPD
- Check the IOP
- Look for NVI on anterior segment examination
- Perform gonioscopy for NVA

3.4.4 Investigations

3.4.4.1 RCOphth Retinal Vein Occlusion (RVO) Guidelines 2015

- BP
- Bloods: FBC, ESR, glucose
- OCT: CMO
- FFA (if uncertain diagnosis): delayed filling of the occluded retinal vein, capillary non-perfusion — >5 DD is defined as an ischaemic BRVO (The Branch Vein Occlusion Study Group 1984, 1986), macular ischaemia, telangiectatic vessels forming collaterals that cross the horizontal raphe

3.4.5 Treatment

- Control of cardiovascular risk factors: HTN, hyperlipidaemia, smoking, DM
- Neovascularisation: sectoral PRP — branch vein occlusion study — BVOS (The Branch Vein Occlusion Study Group 1984, 1986) recommended that laser photocoagulation be applied only after NV is observed, which reduces the likelihood of vitreous haemorrhage from about 60% to 30%
- Macular oedema:
  - Laser photocoagulation
    BVOS (The Branch Vein Occlusion Study Group 1984, 1986):
    - An RCT that aimed to answer three questions: (1) can laser photocoagulation improve VA compared to observation in eyes with macular oedema from BRVO that reduces the vision to 6/12 or worse; (2) can sectoral PRP prevent the development of NV; (3) can sectoral PRP prevent vitreous haemorrhage
    - Wait for at least 3 months if VA 6/12 or worse before considering laser therapy to allow clearing of intraretinal haemorrhages to permit FFA and evaluation of macular oedema and macular ischaemia
    - If perfused macular oedema accounts for the visual loss, and vision continues to be 6/12 or worse without spontaneous improvement, consider grid macular photocoagulation (0.1 s duration, 100 μm spot size, power titrated to produce a "medium" white burn) to the leaking area demonstrated by FFA
    - After 3 years of follow-up, 65% of treated eyes gained two or more lines of vision compared to 37% of untreated eyes
  - Dexamethasone implant (Ozurdex)
    NICE Guidance [TA229]: recommend as an option for treatment of macular oedema due to a BRVO when treatment with laser photocoagulation has not been beneficial or treatment with laser photocoagulation is not considered suitable because of the extent of retinal haemorrhages
    GENEVA study (Haller et al. 2010): A RCT that evaluated the effects of a single dexamethasone implant compared to sham injection for the treatment of macular oedema secondary to BRVO and CRVO. Increase in BCVA of ≥15 ETDRS letters was achieved in 30% of the Ozurdex 0.7 mg group, 26% of the Ozurdex 0.35 mg group, and 13% of the sham group 60 days after injection (peak response) and was maintained through day 90 in BRVO patients. There was no difference between either Ozurdex groups and the sham group at day 180.
  - Ranibizumab (Lucentis)
    NICE Guidance [TA283]: recommend as an option for treatment of macular oedema due to a BRVO when treatment with laser photocoagulation has not been beneficial or treatment with laser photocoagulation is not considered suitable because of the extent of retinal haemorrhages
    BRAVO study (Campochiaro et al. 2010): A RCT to evaluate the efficacy and safety of Lucentis in the treatment of macular oedema from BRVO. Patients were randomised into three groups: (1) sham injection; (2) 0.3 mg Lucentis; and (3) 0.5 mg Lucentis. In the first 6 months, injections were given monthly. At 6 months, both Lucentis groups

gained +16.6 and +18.3 ETDRS letters (0.3 and 0.5 mg groups, respectively) compared with a gain of +7.3 letters in the control group. At 6 months, 55.2% and 61.1% of patients receiving Lucentis 0.3 and 0.5 mg gained ≥3 ETDRS lines compared to 28.8% in the sham injection group

– Aflibercept (Eylea)
  NICE Guidance [TA305]: recommend as an option for treatment of visual impairment caused by macular oedema following BRVO
  VIBRANT study (Campochiaro et al. 2015): A RCT that evaluated the efficacy and safety of Eylea compared to macular grid laser in the treatment of macular oedema from BRVO or HRVO. After 6 months of treatment, 26.7% of the laser group gained ≥3 ETDRS lines compared to 52.7% in the Eylea group. Mean change in letters from baseline was +6.9 letters in the laser group compared to +17.0 letters in the Eylea group.

3.4.6 RCOphth RVO Guidelines 2015 Treatment Algorithm

3.4.6.1 Non-ischaemic BRVO

- Baseline
  – If VA better than 6/12, it is reasonable to regularly observe progress for 3 months
  – If VA is 6/12 or worse with macular oedema and haemorrhages that are not masking fovea:
    FFA is recommended to assess foveal integrity
    If no macular ischaemia is identified, regularly observe for 3 months if macular oedema is mild and in opinion of clinician likely to spontaneously improve (30% chance)
    If mild to moderate macular ischaemia is present consider treatment with ranibizumab or dexamethasone implant (Ozurdex) if spontaneous improvement is unlikely
    If severe macular ischaemia is present — no treatment is recommended and regularly observe for NV formation
  – If VA is 6/12 or worse with macular oedema and haemorrhages that are masking fovea:
    Monthly ranibizumab or baseline dexamethasone implant (Ozurdex) for 3 months
    Perform FFA at 3 months to assess foveal integrity
    If severe macular ischaemia is found to be present at 3 months, no treatment will likely be beneficial and further therapy should be carefully considered
- At 3 months follow up
  – Consider modified grid laser photocoagulation if persistent macular oedema, no or minimal macular ischaemia and other treatments unsuccessful or unavailable
  – If VA 6/9 or better or no macular oedema detected, continue to observe if initially observed. If on anti-VEGF or dexamethasone implant (Ozurdex) therapy, continue as suggested in macular oedema due to CRVO
- Further follow up:
  – If under observation only, follow up 3 monthly intervals for 18 months
  – In case of recurrence or new macular oedema, consider re-initiating intravitreal ranibizumab or dexamethasone implant (Ozurdex) therapy

3.4.6.2 Ischaemic BRVO

- Watch carefully for NV
- If NVE: consider sector laser PRP applied to all ischaemic quadrants ± off license bevacizumab (Avastin)
- Follow up at 3 monthly intervals for up to 24 months

3.4.7 Prognosis

- BVOS (The Branch Vein Occlusion Study Group 1984, 1986):
  – Only eyes with ischaemic BRVO (>5 DD of retinal capillary non-perfusion) are at risk of developing NV — 40% of these eyes develop NV, and of these 40%, 60% will experience periodic vitreous haemorrhage

- Retinal or disc NV, or both, may develop at any time within the first 3 years after an occlusion but are most likely to appear within the first 6–12 months after the occlusion
- Up to 10% of patients with BRVO in one eye will develop any type of RVO in the fellow eye

3.5 Central Retinal Vein Occlusion (CRVO) (Fig. 3.5)

3.5.1 Other Diagnoses to Consider

- Diabetic retinopathy
- Ocular ischaemic syndrome
- Radiation retinopathy
- Hypertensive retinopathy

3.5.2 Risk Factors

- Arteriosclerosis: HTN, DM, smoking, hyperlipidaemia (including secondary to hypothyroidism)
- Glaucoma
- Ocular inflammatory disease: Behcet's disease, PAN, sarcoidosis, SLE

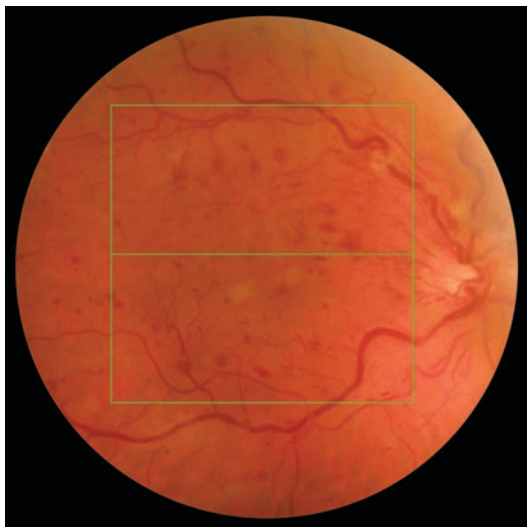

Fig. 3.5 Colour fundus image of a patient with an acute non-ischaemic CRVO

- Haematological: Protein C, protein S or antithrombin deficiency, activated protein C resistance, factor V Leiden, multiple myeloma, Waldenstrom's macroglobulinaemia, antiphospholipid syndrome
- Pharmacological: oral contraceptive pill
- Eye disease case-control study group (Risk factors for central retinal vein occlusion, The Eye Disease Case-Control Study Group 1996): HTN, DM (ischaemic CRVO), glaucoma, cardiovascular disease (ischaemic CRVO)

3.5.3 Examination

- Acute CRVO: retinal haemorrhages (flame shaped and deep blot type) in all 4 quadrants of the fundus with a dilated tortuous retinal venous system, cotton wool spots, optic disc swelling, CMO
- Chronic CRVO: optociliary shunt vessels (collateral vessels connecting the choroidal and the retinal vasculature — do not leak on FFA), telangiectatic capillary bed, persistent dilatation and tortuosity, perivenous sheathing, NVI > NVD > NVE, CMO, glaucomatous optic neuropathy
- Check for an RAPD
- Check the IOP
- Look for NVI on anterior segment examination
- Perform gonioscopy for NVA

3.5.4 Investigations

3.5.4.1 RCOphth RVO Guidelines 2015

- BP
- Bloods: FBC (leukaemia), ESR (myeloma), glucose
- OCT: CMO
- FFA (if uncertain diagnosis): delayed filling of the occluded retinal vein, capillary non-perfusion, macular ischaemia, telangiectatic vessels forming collaterals that cross the horizontal raphe

3.5.5 Treatment

- Control of cardiovascular risk factors: HTN, hyperlipidaemia, smoking cessation, DM
- Neovascularisation:
  - Full scatter PRP: central vein occlusion study — **CVOS** (The Central Vein Occlusion Study Group 1997) recommended that laser photocoagulation be applied only after NV is observed, with greater resolution of NVI/NVA by 1 month after PRP in 56% of no early treatment eyes (no NVI or NVA present) compared with 22% of early treatment eyes (NVI or NVA present)
- Macular oedema:
  - Dexamethasone implant (Ozurdex)
    NICE Guidance [TA229]: recommend as an option for the treatment of macular oedema following CRVO
    GENEVA study (Haller et al. 2010): A RCT that evaluated the effects of a single dexamethasone implant compared to sham injection for the treatment of macular oedema secondary to BRVO and CRVO. Increase in BCVA of ≥15 ETDRS letters was achieved in 29% of the Ozurdex 0.7 mg group and 9% of the sham group 60 days after injection but not at 90 or 180 days.
  - Ranibizumab (Lucentis)
    NICE Guidance [TA283]: recommend as an option for treatment of visual impairment caused by macular oedema following CRVO
    CRUISE study (Brown et al. 2010): A RCT to evaluate the efficacy and safety of Lucentis in the treatment of macular oedema from CRVO. Patients were randomised into three groups: (1) sham injection; (2) 0.3 mg Lucentis; and (3) 0.5 mg Lucentis. In the first 6 months, injections were given monthly. At 6 months, both Lucentis groups gained +12.7 and +14.9 ETDRS letters (0.3 and 0.5 mg groups, respectively) compared with a gain of +0.8 letters in the control group. At 6 months, 46.2% and 47.7% of patients receiving Lucentis 0.3 and 0.5 mg gained ≥3 ETDRS lines compared to 16.9% in the sham injection group
  - Aflibercept (Eylea)
    NICE Guidance [TA305]: recommend as an option for treatment of visual impairment caused by macular oedema following CRVO
    CORPERNICUS study (Boyer et al. 2012): comparison of Eylea and sham injection — the proportion of patients who gained ≥15 letters from baseline in the Eylea and sham groups was 56.1% and 12.3% at week 24, respectively
    GALILEO study (Holz et al. 2013): comparison of Eylea and sham injection — the proportion of patients who gained ≥15 letters from baseline in the Eylea and sham groups was 60.2% and 22.1% at week 24, respectively
- Delay in initiating treatment up to 6 months results in fewer visual gains compared to immediate initiation of treatment. Therefore, treatment should be initiated as soon as the diagnosis is established (RCOphth RVO Guidelines 2015)
- Careful consideration should be given to further therapy in such eyes that do not improve in terms of Snellen VA or OCT central subfield thickness after three loading injections at monthly intervals and treatment with anti-VEGF is not recommended if no response occurs after six injections (RCOphth RVO Guidelines 2015)
- No robust data on outcomes of switching steroid to an anti-VEGF agent or switching between anti-VEGF agents or combining steroids with anti-VEGF agents for macular oedema due to CRVO (RCOphth RVO Guidelines 2015).

3.5.6 Follow Up

- Non-ischaemic CRVO (may resolve completely without any complications): initial follow up every 3 months for 6 months, follow up for at least 2 years but the development of disc

collaterals and the resolution of macular oedema for at least 6 months should allow the discharge of the patient from clinical supervision (RCOphth RVO Guidelines 2015)
- Ischaemic CRVO: follow up after 6 months should be every 3 months for 1 year (RCOphth RVO Guidelines 2015)
- RCOphth RVO Guidelines 2015 recommends that oestrogen containing HRT and OCP should not be commenced in women with history of RVO. However, the continued use in a patient who develops RVO does not appear to be associated with a higher rate of recurrence.

3.5.7 RCOphth RVO Guidelines 2015 Treatment Algorithm

3.5.7.1 Non-ischaemic CRVO

- Baseline:
  - Measurements: VA, colour fundus photography, FFA, OCT, IOP, gonioscopy
  - If VA is 6/96 or better — commence on either anti-VEGF therapy or dexamethasone implant (Ozurdex)
  - If VA less than 6/96 — offer treatment, high risk of NV
  - If VA better than 6/12 — reasonable to observe for spontaneous resolution
- Choice of agent: anti-VEGF preferred in eyes with previous hx of glaucoma and younger patients who are phakic, dexamethasone implant (Ozurdex) may be better choice in patients with recent cardiovascular events and in those who do not favour monthly injections
- Re-treatment: monthly intravitreal anti-VEGF injections are continued until maximum VA is achieved (defined as stable VA for 3 consecutive monthly assessments), once maximum VA is achieved monitor and resume treatment if VA loss occurs due to macular oedema (or treat and extend)
- Stopping treatment: consider stopping anti-VEGF therapy if after 3 consecutive monthly treatments, VA has not improved by at least five letters and CMT has not reduced from baseline/recommend stopping anti-VEGF therapy is recommended after 6 consecutive monthly treatments, VA has not improved by at least five letters and CMT has not reduced from baseline
- Switching agents: no RCT that provides evidence that switching to another anti-VEGF agent or intravitreal steroids may be effective. Consider switching from anti-VEGF to steroids or vice versa if response is poor or suboptimal.

3.5.7.2 Ischaemic CRVO

- Features suggestive of an ischaemic CRVO (RCOphth RVO Guidelines 2015)
  - Poor VA
  - RAPD
  - Presence of multiple dark deep intraretinal haemorrhages
  - Presence of multiple cotton wool spots
  - Degree of venous dilation and tortuosity
  - FFA showing greater than ten-disc areas of capillary non-perfusion on seven field FFA
  - ERG: reduced b wave amplitude, reduced b:a ratio (negative ERG) and prolonged b-wave implicit time
- If NV occurs and AC angle is open: urgent PRP, review 2 weeks post PRP (RCOphth RVO Guidelines 2015)
- If NV occurs and AC angle is closed ± raised IOP: urgent PRP with cyclodiode/GDI (RCOphth RVO Guidelines 2015)
- Consider prophylactic PRP in ischaemic CRVO without NV if limited follow up is likely and FFA shows >30-disc areas of capillary non-perfusion (RCOphth RVO Guidelines 2015).

3.5.8 Prognosis

- At 3 years, there was a 45% chance of developing neovascular glaucoma after onset of ischaemic CRVO — highest risk if VA <6/60 or >10 DD of non-perfusion on FFA (The Central Vein Occlusion Study Group 1997)

- Overall, 34% of initially perfused eyes converted to non-perfused status after 3 years (The Central Vein Occlusion Study Group 1997)
- Risk of CRVO in contralateral eye is 5% by 1y (RCOphth RVO Guidelines 2015).

3.6 Cilioretinal Artery Occlusion (CLRAO) in a Young Patient (Fig. 3.6)

3.6.1 Causes

- Embolic: cardiac valvular disease, arrhythmias, cardiac septal defects, cardiac myxoma, intravenous drug use (talc)
- Coagulopathies: antiphospholipid syndrome, protein C and S deficiency, lupus anticoagulant, anti-thrombin III deficiency, activated protein C resistance, factor V Leiden, leukaemia, lymphoma
- Collagen vascular diseases: SLE, PAN, Wegener's granulomatosis
- Pharmacological: cocaine, OCP
- Infective: syphilis, toxoplasmosis, mucormycosis, lyme disease
- Retinal migraines (vasospasm): ≥2 attacks of a fully reversible monocular positive and/or negative visual phenomena with migraine without aura begins during the visual symptoms or follows them within 60 minutes

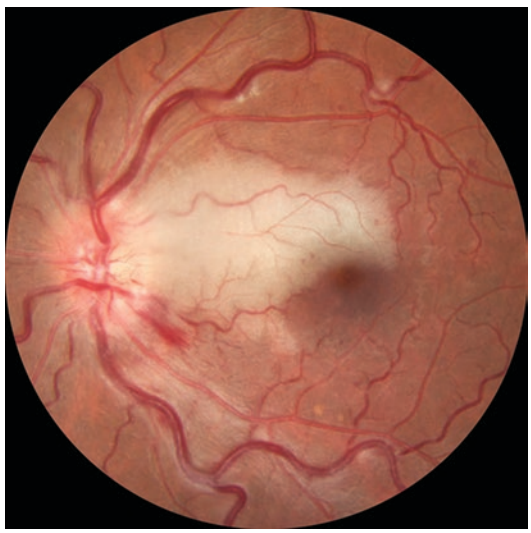

Fig. 3.6 Colour fundus image of a patient with a cilioretinal artery occlusion

3.6.2 Examination

- Retinal whitening secondary to inner retinal oedema extending from the temporal disc into the macula in the distribution of cilioretinal artery perfusion

3.6.3 Investigations

- Hypercoagulability evaluation for young patients with a suggestive history (e.g. FHx, prior history, miscarriage): factor V Leiden mutation, protein C/S and anti-thrombin deficiencies, homocysteine levels, antiphospholipid antibodies
- Syphilis serology: VDRL
- Vasculitis screen: ANA, ANCA
- Transthoracic/trans-oesophageal echocardiography
- ECG
- Carotid doppler US
- OCT: inner retinal oedema (acute) and inner retinal atrophy (chronic)
- FFA: look for filling of the cilioretinal artery during the choroidal phase

3.6.4 Treatment

- No proven treatments for CLRAO exist
- Refer to stroke (TIA) clinic for carotid doppler ± echocardiography if embolus identified
- Treat neovascularisation with PRP

3.6.5 Prognosis

- Isolated CLRAO: 90% of eyes achieve 6/12 or better vision
- CLRAO associated with CRVO: 70% of eyes achieve 6/12 or better vision
- CLRAO in conjunction with AION: 0% of eyes achieve 6/12 or better vision

3.7 Usher Syndrome (Fig. 3.7 and Table 3.1)

3.7.1 Other Diagnoses to Consider

- RP
- CSNB
- Vitamin A deficiency
- Choroideremia
- Gyrate atrophy
- MAR
- CAR

3.7.2 History

- Night blindness
- Positive FHx

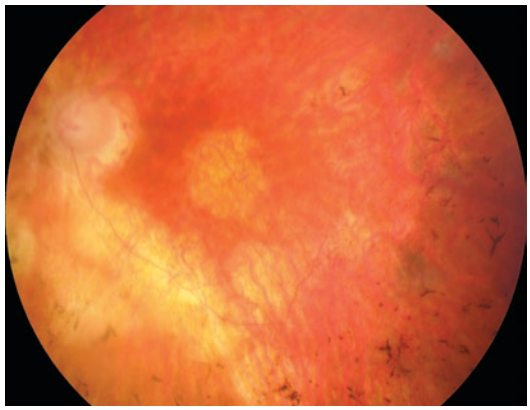

Fig. 3.7 Colour fundus image of a patient with Ushers syndrome showing RP changes

Table 3.1 Useful facts about Ushers syndrome

- AR condition that results in RP with associated congenital hearing loss
- Occurs in 1 of every 10 deaf children (5% of all cases of congenital deafness)
- Subdivided into three groups:
  - Type 1: most severe form, associated with delayed sitting and walking due to abnormal vestibular function
  - Type 2: normal vestibular function
  - Type 3: sensorineural hearing loss is postlingual (as opposed to the prelingual loss in USH1 and USH2) with patients acquiring normal speech

3.7.3 Examination

- Peripheral retinal atrophy with bone spicule like pigmentation
- Retinal arteriolar attenuation
- Waxy pallor of the optic disc

3.7.4 Investigations

- VF: constricted (ring scotoma)
- EDTs: abnormal ERG
- Audiogram: sensorineural hearing loss

3.7.5 Treatment

- Cochlear implantation for sensorineural deafness
- Visual impairment registration and referral to low vision aids service
- Sensory visual impairment service (specialist schools)
- Sense Usher service
- Royal National Institute of Blind people (RNIB) website/telephone helpline

3.8 Rhegmatogenous Retinal Detachment (RD) (Fig. 3.8 and Table 3.2)

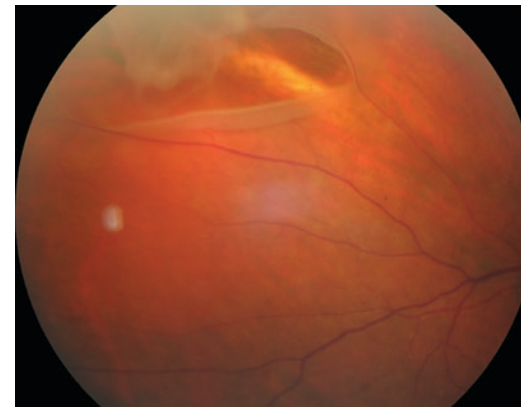

Fig. 3.8 Colour fundus image of a patient with an acute rhegmatogenous retinal detachment secondary to a large horse-shoe retinal tear

Table 3.2 Useful facts about rhegmatogenous RD

- Incidence of RD is approximately 10 in 100,000 (Saidkasimova et al. 2009)
- Approximately 90% of patients with acute symptoms of PVD have a retinal tear at the time of initial examination. Approximately 10% of retinal tears are not seen at initial presentation or develop later (Sharma et al. 2004)

3.8.1 Risk Factors

- Hereditary/congenital/developmental/degenerative
  - Myopia
  - Retinal breaks
  - Male gender
  - Hereditary vitreoretinopathies, e.g. Sticklers syndrome
  - Lattice degeneration
  - Cystic retinal tuft
  - Degenerative retinoschisis
- Prior ocular surgery
  - Aphakia/pseudophakia
  - Nd:YAG posterior capsulotomy
  - Other surgery involving vitreous gel
- Prior ocular trauma
- Inflammatory
  - CMV retinitis
  - ARN
- Other
  - Fellow eye non-traumatic RD, e.g. giant retinal tear (GRT)

3.8.2 Retinal Tears

- 15% of eyes with a symptomatic PVD develop retinal tears (full thickness defects in the retina) of various types
- 60% of retinal tears occur in the superotemporal quadrant
- Tears with persistent vitreoretinal traction
  - Symptomatic horseshoe-shaped retinal tears: treatment required
  - Symptomatic operculated retinal tear with vitreoretinal traction on a nearby retinal vessel: treatment required
- Tears without persistent vitreoretinal traction
  - Symptomatic operculated retinal tears without vitreoretinal traction on a nearby retinal vessel: no treatment required unless the possibility of vitreoretinal traction cannot be excluded
- Retinal holes
  - Asymptomatic atrophic retinal holes within areas of lattice degeneration or in the outer layers of degenerative retinoschisis: no treatment required
- Retinal dialysis
  - Tear of the retina from its insertion at the ora serrata
  - Vitreous adherent to the posterior retina (no tendency for posterior flap to fold over)
  - Most secondary to trauma and are most commonly found in the inferotemporal quadrant
  - Treatment: observation if signs of chronicity (e.g. tidemarks and retinal cysts) present, laser demarcation if limited RD, segmental scleral buckles if extensive RD
- Giant retinal tear (GRT)
  - A retinal tear of more than 3 clock hours of circumferential extent
  - Posterior vitreous is detached (hence posterior flap has a tendency to fold over) and the vitreous gel is adherent to the anterior flap
  - Associated with high myopia, Marfan syndrome, Stickler syndrome, trauma
  - Treatment: vitrectomy, endolaser and silicone oil for affected eye ± prophylactic 360° laser or cryopexy for fellow eye.

3.8.3 Lincoff Rules

- Describes how the location of a retinal break determines the distribution of subretinal fluid (Lincoff and Gieser 1971)
  - For superotemporal or superonasal RDs, the primary break lies within 1.5 clock hours of the highest border of the RD
  - For total or superior RDs that cross the 12 o'clock position, the primary break is at 12 o'clock or in a triangle with the apex at the ora serrata at 12 o'clock and sides extend 1.5 clock hours to either side
  - For inferior RDs, the higher side of the RD indicates on which side of the optic disc the primary break is located
  - For inferior bullous RDs, the primary break is located superiorly.

3.8.4 History

- Symptoms (flashes/floaters) and signs (Weiss ring: detachment at optic disc) of PVD
- Visual field defect for RD that has progressed sufficiently posteriorly.

3.8.5 Examination

- Pigmented cells ("tobacco dust") in the vitreous — sign associated with a high chance of associated retinal tear
- Dilated fundus exam with 360° indentation with indirect ophthalmoscopy (for patients who present acutely with flashes and floaters) to exclude the presence of tractional retinal tears (RCOphth Guidelines - see Sect. 3.8.8)
- Subclinical RD: SRF extending more than 1 DD from the break but not posterior to the equator
- Signs of chronicity (see Fig. 3.9): tidemarks (present from 3 months: imply stability of the extent of the detachment), intraretinal cysts (present from 1 year), PVR.

3.8.6 Investigations

- B-scan: if poor fundal view present (Fig. 3.10)

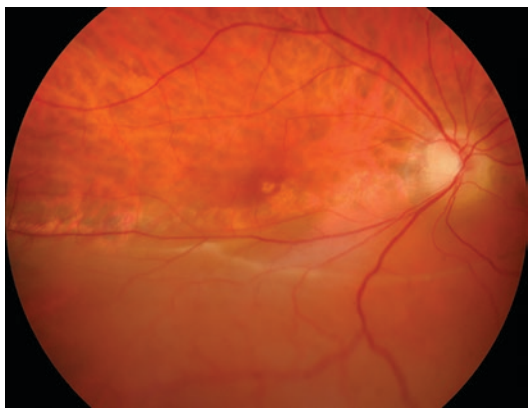

Fig. 3.9 Colour fundus image of a patient with a chronic rhegmatogenous RD with progression of subretinal fluid beyond a tide mark

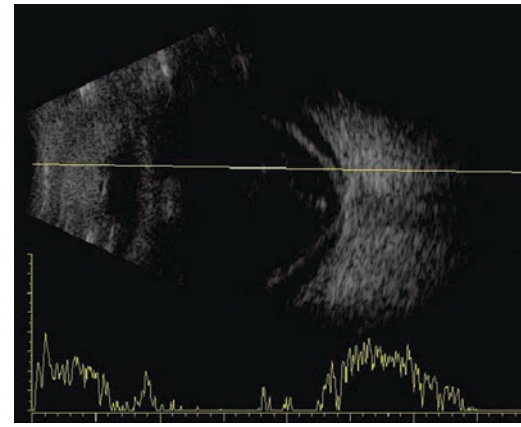

Fig. 3.10 B-scan of a patient with a total rhegmatogenous RD

3.8.7 Treatment

- Round hole RD
  - Laser demarcation:
    For asymptomatic RD's or those with minimal symptoms
  - Segmental scleral buckling
- Detachment due to retinal dialysis
  - Laser demarcation
  - Segmental scleral buckling
- Detachment secondary to U (horseshoe) tears
  - Laser demarcation:
    Small asymptomatic peripheral detachment
    Although laser photocoagulation creates an instant adhesion this is not up to full strength for up to 14 days — rapidly progressing fluid may extend through the area of demarcation before a strong enough adhesion develops
  - Pneumatic retinopexy
    Detachments with breaks limited to one quadrant, usually superior
  - Scleral buckling
    Young patients
    Anteriorly located small holes with localised RD in phakic patients
  - Vitrectomy
    Older patients with a liquefied vitreous
    Wide and bullous RD
    Presence of breaks in multiple quadrants
    Presence of RD with marked traction with different anterior posterior depth of breaks

Absence of an apparent retinal break in a pseudophakic patient
GRT RD
Macular hole RD

- Prophylactic therapy for asymptomatic retinal tears in phakic non-fellow eyes is usually not recommended except for an inferior retinal dialysis and for a non-traumatic GRT that occurred in the first eye
- Maximum strength of chorioretinal adhesion following laser photocoagulation is achieved between 3 and 14 days later (stronger adhesion than normal appears within 24 h of the application of treatment).

3.8.8 The RCOphth Ophthalmic Services Guidance for the Management of Acute Retinal Detachment 2010

- Retinal tears
  - Tractional (horseshoe) retinal tears should be treated urgently with laser photocoagulation or cryotherapy
  - Asymptomatic retinal breaks and atrophic round holes do not require any treatment
  - Asymptomatic retinal breaks and atrophic round holes with localised subretinal fluid may require treatment (localised RD is often asymptomatic, progresses very gradually if at all) but does not need to be treated as an emergency — non urgent referral is recommended to a local retinal specialist or department to determine what management is best tailored to the patient needs
- Reduce progression of RD
  - Bed rest
  - Dependent posturing: posture with tear at the lowest location
- RD surgery
  - Urgent surgery required if RD is reaching within 1 DD of the fovea, particularly with a superior bullous detachment
  - Where there is imminent danger of foveal detachment and expertise and facilities to operate urgently are unavailable locally, a transfer should be agreed to a suitably equipped and staffed unit with an available VR surgeon.

3.9 Macular Hole (MH) (Fig. 3.11 and Table 3.3)

3.9.1 Differential Diagnosis

- Lamellar hole
  - Absence of a contractile ERM
  - Defects in the inner fovea with cleft between the inner and outer retina
  - Bi- or tri-lobulated red central circular defect on biomicroscopy
  - Negative Watzke-Allen test (thin beam of light projected over hole — broken or thinned centrally in MH)
- Pseudohole
  - Presence of a contracted ERM with thickening of the macula
  - U or V shape of the fovea

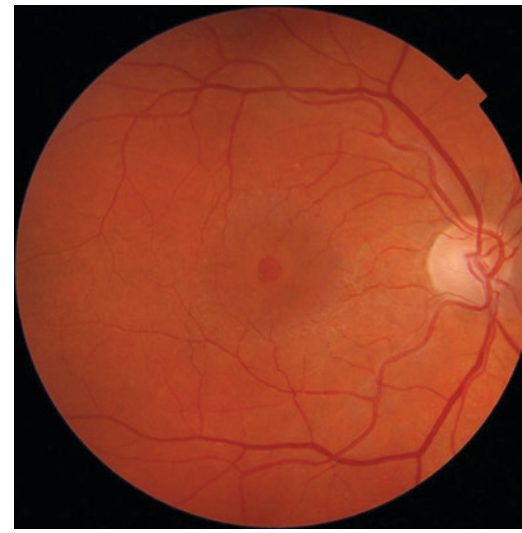

Fig. 3.11 Colour fundus image of a patient with a full thickness macular hole

Table 3.3 Key facts about macular holes

• Round opening in the foveal center
• Occurs in middle-aged or elderly patients
• More common in females
• Incidence is approximately 7.8 per 100,000 population (McCannel et al. 2009)
• Prevalence of 1/3300 (McDonnell et al. 1982)

3.9.2 Risk Factors

- Age ≥65 years old
- Female sex

3.9.3 Causes

- Idiopathic: due to abnormal vitreofoveal traction
- Secondary
  - Trauma: sudden axial compression of the eye resulting in equatorial expansion and retinal rupture of the fovea
  - Pathological myopia
  - VMT/ERM
  - Chronic CMO.

3.9.4 Classification

- Biomicroscopy (Gass Classification)
  - Stage 1a (impending MH): focal central yellow spot, loss of foveal depression
  - Stage 1b (occult MH): yellow foveolar ring
  - Stage 2 (full thickness MH): central round <400 μm diameter retinal defect
  - Stage 3 (full thickness MH): central round ≥400 μm diameter retinal defect, no Weiss ring
  - Stage 4 (full thickness MH): stage 3 with Weiss ring (PVD)
- OCT (see Fig. 3.12)
  - Stage 1a: inner foveal cyst
  - Stage 1b: inner foveal cyst completed by disruption of the outer retina up to the RPE, posterior hyaloid still attached to the intact roof of the cyst
  - Stage 2: disruption in roof of the cyst with a partially detached operculum from hole edge
  - Stage 3: complete absence of the roof with vitreous completely detached form the retinal surface over the posterior pole and is not connected to the hole edge
  - Stage 4: OCT unable to diagnose stage 4 MH, stage 4 MH remains a diagnosis from biomicroscopy with the presence of a Weiss ring

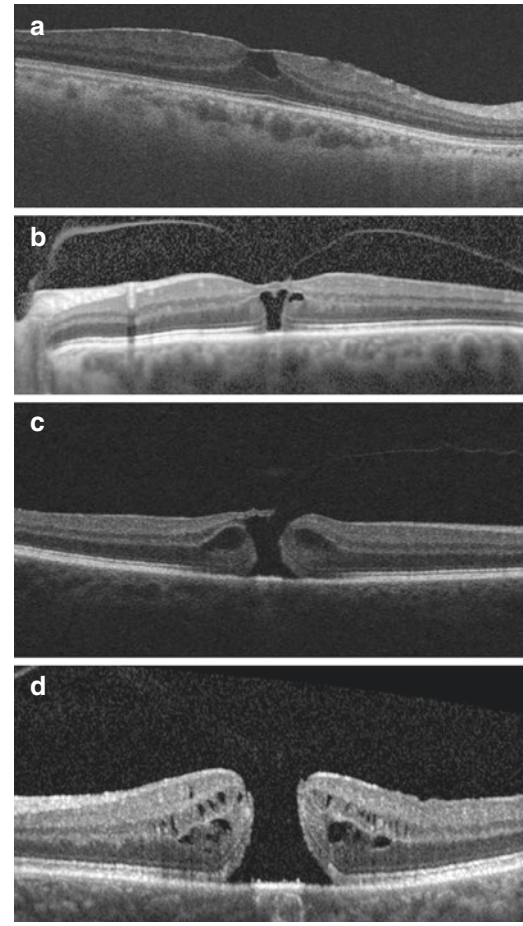

Fig. 3.12 OCT staging of macular holes (**a**) Stage 1a, (**b**) Stage 1b, (**c**) Stage II and (**d**) Stage III

- The International Vitreomacular Traction Study Classification System (Duker et al. 2013)
  - Vitreomacular adhesion (VMA): vitreous adhesion to central macula with no demonstrable retinal morphologic changes
  - Vitreomacular traction (VMT): vitreous adhesion to central macula with demonstrable changes by OCT but no full thickness tissue dehiscence; may include the following: cystoid changes in macula, elevation of fovea above RPE, tissue cavitation, loss of foveal contour
  - Small full thickness MH: hole ≤250 μm, may be round or have a flap adherent to vitreous; operculum may or may not be present

- Medium full thickness MH: hole >250 μm but ≤400 μm; may be round or have a flap adherent to vitreous; operculum may or may not be present
- Large full thickness MH: hole >400 μm; vitreous more likely to be fully separated from macula
- Impending MH: term used when a full thickness MH is observed in one eye and VMA or VMT is observed on OCT in the fellow eye
- Lamellar MH: partial thickness foveal defect that typically appears on biomicroscopically as a round or oval, well-circumscribed, reddish lesion. Anatomic OCT-based features of lamellar MH include the following: (1) a defect in the inner fovea (may not have actual loss of tissue); (2) maintenance of an intact photoreceptor layer (lamellar MH can be distinguished from full thickness MH on OCT by the presence of intact photoreceptors at the base); (3) an irregular foveal contour; (4) intraretinal splitting (schisis), typically between the outer plexiform and outer nuclear layers
- Macular pseudohole: Anatomic OCT-based features of macular pseudohole include the following: (1) invaginated or heaped foveal edges; (2) steep macular contour to the central fovea with near-normal central foveal thickness; (3) concomitant ERM with central opening; (4) no loss of retinal tissue

3.9.5 Examination

- Yellow spot (stage 1a)
- Yellow foveal ring (stage 1b)
- Central red round area at the fovea (stage 2–4)
- Positive Watzke-Allen test: shine a vertical thin beam of light using the slitlamp over the macular hole — narrowing or gap in the beam of light is seen in macular holes (Tanner and and Williamson 2000).

3.9.6 Investigations

- OCT: measurements in MH include base diameter (BD — linear dimension of MH at the level of the RPE layer) and minimum linear diameter (MLD — minimum horizontal diameter in the scan in an area excluding the operculum)

3.9.7 Treatment

- Idiopathic MH
  - Observation:

    For stage 1 MH: high rate of spontaneous resolution. Surgery has shown no benefit (Smiddy et al. 1988; de Bustros 1994)
  - Medical

    NICE Guidance [TA297] — Ocriplasmin is an option for treating VMT in adults only if:
    - An ERM is not present and
    - They have a stage 2 FTMH with a diameter of ≤400 μm and/or
    - They have severe symptoms
  - Surgical

    Vitrectomy + ILM peeling + gas tamponade for holes without VMA
- Traumatic MH
  - High spontaneous closure rate (50%). Recommended to wait 4 months from the trauma before surgical intervention (Yamashita et al. 2002).

3.9.8 Prognostic Factors for Treatment of Idiopathic MH

- Preoperative VA: eyes with better preoperative VA achieve higher rates of anatomical closure and visual gain
- Preoperative BD and MLD measurement: smaller preoperative MLD and BD measurements are associated with better visual outcomes and anatomical closure
- Duration of symptoms: anatomical closure and visual outcomes were higher in patients with a shorter duration of symptoms.

3.9.9 Face Down Posturing for Idiopathic MH

- Cochrane review (Solebo et al. 2011) of three RCT's that directly compared face-down posturing following idiopathic MH surgery with no face-down posturing:
  - For MH ≤400 μm, face down posturing had no significant effect on successful hole closure
  - Two of the RCT's found that there was a significant benefit of face-down posturing for successful closure when the diameter was >400 μm
  - Face down posturing for at least 5 days postoperatively should be recommended for patients with MH >400 μm in size and holes >1 year in duration.

3.9.10 Development of Idiopathic MH in Fellow Eyes

- A fellow eye with PVD has a <1% risk of progressing to a MH (Ezra 2001)
- A fellow eye without a PVD has a 15.6% risk of progressing to a MH over 5 years (Ezra et al. 1998).

3.9.11 Success Rates for Idiopathic MH Closure

- 88% success rate for stage 2 macular holes (Ruby et al. 1994)
- 69% success rate for stage 3 and 4 macular holes (Freeman et al. 1997)
- Holes <400 μm have a 94% chance of closure compared with 56% for those 400 μm or more (Ip et al. 2002).

3.9.12 Post-Operative Complications of Surgery

- Retinal tears during surgery: 12.7% with PVD induction and 3.1% without PVD induction (Chung et al. 2009)
- Retinal detachment: 6.6–14% (Guillaubey et al. 2007)
- Re-opening of the hole: 11% (Bhatnagar et al. 2007) especially in those who have postoperative cataract extraction
- Cataract
- Endophthalmitis

3.10 Toxoplasmosis (Fig. 3.13)

3.10.1 Other Diagnoses to Consider

- Infectious: TB, syphilis, rubella, CMV retinitis, herpes simplex, toxocariasis
- Non-infectious: sarcoidosis

3.10.2 History

- Symptoms: asymptomatic, floaters, reduced vision
- Immunocompromised: post organ transplantation, HIV positive, therapeutic immunosuppression for systemic disease (e.g. SLE, RA, GPA).

3.10.3 Examination

- Acute lesions: intensely white focal lesions with overlying vitreous inflammatory haze adjacent ("headlight in the fog") to old hyper-

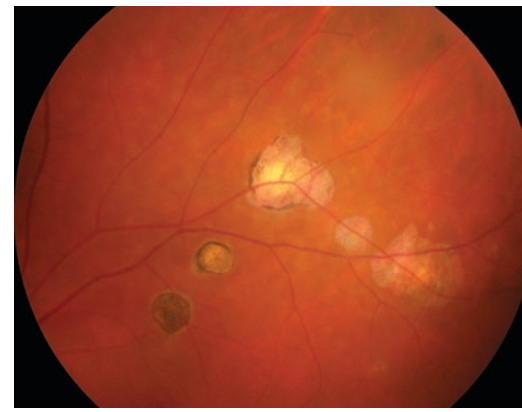

Fig. 3.13 Colour fundus image of a patient with a chronic toxoplasmosis scar

pigmented scars (satellite lesions), periphlebitis
- Chronic lesions: hyperpigmented scars with an atrophic centre devoid of all retinal and choroidal elements — the underlying sclera gives the lesion its white centre
- Check the IOP
- Perform an anterior segment examination to look for any visually significant cataract.

3.10.4 Investigations

- VDRL: rule out syphilis
- ACE, CXR: rule out sarcoidosis
- HIV serology: rule out HIV
- Pregnancy test
- Anti-toxoplasma IgM and IgG antibodies:
  - Negative IgG and negative IgM antibodies implies infection has not occurred
  - Positive IgG and negative IgM antibodies implies an infection that was in the distant past
  - Positive IgM antibodies may suggest a recently acquired infection.

3.10.5 Treatment

- Inflammation
  - In immunocompetent patients, the disease is self-limiting and does not require treatment unless sight threatening
  - Indications for treatment:
    Lesions involving the disc, macula, or papillomacular bundle
    Lesions threatening a major vessel
    Marked vitritis
    Any lesion in an immunocompromised patient
  - No corticosteroids if patient is immuno-compromised
  - Triple therapy: pyrimethamine, sulfadiazine, folinic acid, corticosteroids
  - Co-trimoxazole (trimethoprim + sulfamethoxazole) + corticosteroids
  - Intravitreal dexamethasone + clindamycin
  - Oral clindamycin
  - Spiramycin or atovaquone if maternal infection acquired during pregnancy (15% in the first trimester and 60% in the third trimester risk of fetal transmission if acquired during pregnancy)
- Cataract extraction once uveitis is inactive for ≥3 months.

3.11 Vogt-Koyanagi-Harada (VKH) Syndrome (Fig. 3.14 and Table 3.4)

3.11.1 Other Diagnoses to Consider

- Sympathetic ophthalmia: history of penetrating eye injury
- Sarcoidosis
- Posterior scleritis: T-sign on B-scan
- Uveal effusion syndrome: lacks intraocular inflammation
- Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)

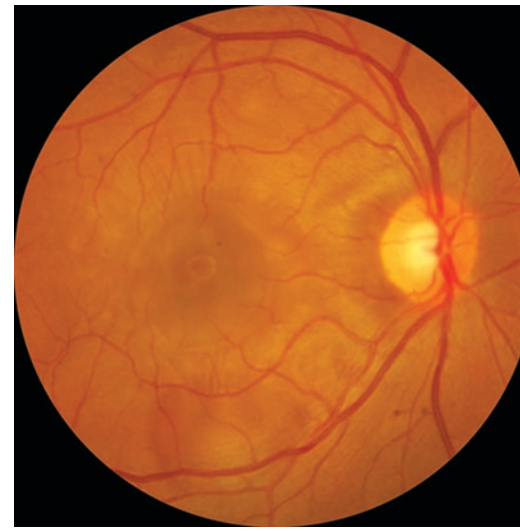

Fig. 3.14 Colour fundus image of a patient with VKH syndrome showing multiple serous RDs

Table 3.4 Key facts about VKH syndrome

• VKH syndrome is a bilateral granulomatous inflammatory panuveitis often associated with exudative RD and with extraocular manifestations
• No history of penetrating ocular trauma or surgery preceding initial onset of uveitis

3.11.2 Examination

- Systemic features
  - Cutaneous not preceding ocular/CNS disease:
    - Vitiligo
    - Poliosis
    - Alopecia
  - Neurological
    - Sterile meningism: headaches, neck stiffness, photophobia
    - Encephalitis
    - CN palsies
  - Auditory
    - Tinnitus
    - Deafness
    - Vertigo
- Ocular features
  - Prodromal stage:
    - Non-specific viral like illness
    - Meningism
  - Acute uveitic stage:
    - Bilateral panuveitis: anterior uveitis, multifocal choroiditis
    - Multiple serous RD's
    - Optic disc swelling
  - Chronic uveitic stage (convalescent phase):
    - Vitiligo
    - Perilimbal vitiligo — Sugiura's sign
    - Poliosis
    - Choroidal depigmentation: pale optic disc with bright red-orange choroid (sunset glow fundus)
    - Small yellow well circumscribed areas of chorioretinal atrophy
  - Chronic recurrent stage:
    - Acute episodic exacerbations of granulomatous anterior uveitis
    - Subretinal choroidal neovascular membrane
    - Cataracts (posterior subcapsular)/glaucoma

3.11.3 Investigations

- B-scan: choroidal thickening
- OCT: serous RD
- FFA: multifocal areas of pinpoint leakage, focal areas of delay in choroidal perfusion, large placoid areas of hyperfluorescence
- LP: CSF pleocytosis

3.11.4 Treatment

- Inflammation: high dose systemic corticosteroids ± immunosuppresants
- CNV membrane: anti-VEGF agents (avastin)
- Cataracts: cataract extraction if VA reduced and uveitis absent for a minimum of 3 months
- Glaucoma: drops, surgery

3.12 Malattia Leventinese/Doyne Honeycomb Retinal Dystrophy (Fig. 3.15)

3.12.1 Other Diagnoses to Consider

- AMD
- Fundus flavimaculatus: flecks do not hyperfluoresce on FFA, subnormal EOG, ERG and dark adaptation normal
- Sorsby macular dystrophy
- Pattern dystrophies
- Best disease (in its later stages)

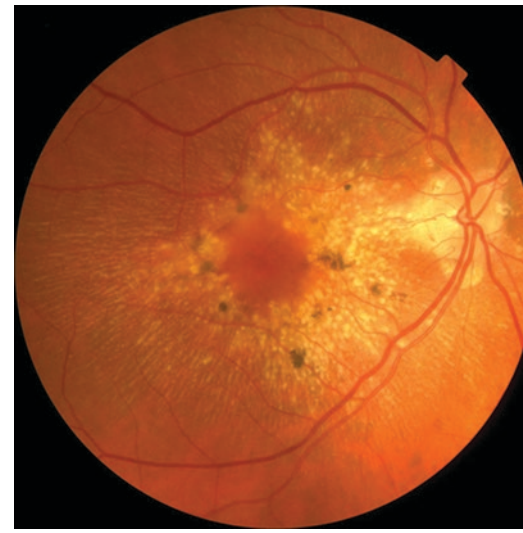

Fig. 3.15 Colour fundus photo of the right eye of a patient with malattia leventinese

3.12.2 Examination

- Presence of multiple elongated yellow-white deposits between the RPE and inner collagenous zone of Bruch's membrane in a radiating pattern throughout the macula that is present early in life (often by the second decade).
- These elongated drusen may also be found outside the arcades, especially nasal to the disc, which is unusual in other types of macular degeneration.
- These drusen may also be found in some patients in a peripapillary pattern or on the margin of the disc itself.
- Coalescence of drusen may simulate a vitelliform lesion
- RPE atrophic changes ± chorioretinal atrophy

3.12.3 Investigations

- OCT: hyperreflective thickening of the RPE-Bruch membrane complex, associated with localised dome-shaped elevations (see Fig. 3.16)
- FFA: during the arterial phase, multiple, round, sharply defined fluorescent spots corresponding to the lesions observed at ophthalmoscopy, no leakage of fluorescein is seen
- EDTs: ERG, EOG, dark adaptation normal in the initial stages
- Genetic testing: single mutation in the fibulin-3 gene

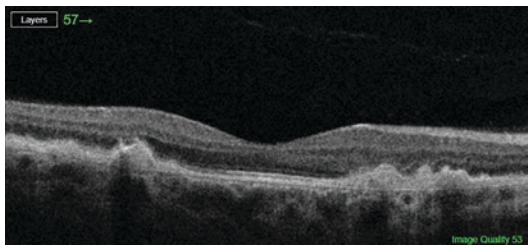

Fig. 3.16 OCT image of the same eye of the same patient as shown in Fig. 3.15 showing areas of hyperreflective thickening of the RPE-Bruch membrane complex, associated with localised dome-shaped elevations

3.12.4 Treatment

- Genetic counselling and discussion with patient
- CNV: anti-VEGF agents

3.13 Approach to the Adult Watering Eye

3.13.1 History

- "Do the tears flow down your cheek or do they stay in your eye?": watery eye (no spilling of tears onto the cheek) vs tearing eye (tears overflow onto the cheek)
- "Do the tears flow down your cheek inside when you are resting or mainly when you are outside in cold or wind?": partial obstruction (if tearing only present in the wind and cold) vs complete obstruction
- "Is the problem unilateral or bilateral?": tearing eye (i.e. obstruction in lacrimal drainage system) usually unilateral, watery eye usually bilateral
- Ask about findings suggestive of obstruction of the lacrimal system: unilateral symptoms, epiphora, history of dacryocystitis, onset after conjunctivitis (obstruction of puncta or canaliculi), facial fracture (damage to NLD), or nasal surgery (history of nasal surgery — damage to NLD)
- Ask about any pro-secretory drugs, e.g. oral pilocarpine for Sjogren Syndrome

3.13.2 Differential Diagnosis of a Watery Eye in an Adult

- Poor tear film: blepharitis/MGD
- Reflex tearing: entropion, trichiasis, reduced or incomplete blinking from parkinsonism, incomplete eyelid closure from CN VII palsy
- Inadequate lacrimal pump: ectropion, CN VII palsy (reduced strength of eyelid closure), lid laxity

3.13.3 Differential Diagnosis of a Tearing Eye in an Adult

- Result of canalicular or NLD obstruction
  - Children: congenital NLDO
  - Young adults: trauma (canalicular laceration or facial trauma), canalicular obstruction (post viral conjunctivitis with scarring of each canaliculus)
  - Middle-aged adult: dacryolith (episodes of recurrent epiphora which resolves spontaneously ± signs of acute dacryoadenitis)
  - Older adults: primary NLDO (PANDO): scarring in distal portion of NLD, symptoms include: epiphora, chronic mucopurulent discharge (chronic dacryocystitis) and acute cellulitis of the lacrimal sac (acute dacryocystitis)

3.13.4 Examination

- Examine for possible causes of a watery eye
  - Eyelid problems:
    Ectropion and entropion
    Lacrimal pump problems — CN VII palsy, lid laxity — lid distraction test (manually pulling lower eyelid away from eyeball: more than 6 mm off eyeball implies lid laxity) and snap test (measure horizontal lid laxity by pulling the lower eyelid inferiorly toward the inferior orbital rim. Eyelid with no laxity will spring back into position without a blink. Can be quantified by counting no. of blinks before eyelid returns to normal position)
    Punctal problems — eversion of punctum, canaliculitis (swelling and erythema of the canalicular portion of the eyelid, pouting punctum with dilated punctum, pressure on canaliculus expresses pus), congenital punctal atresia (one or more punta are absent), stenosis of punctum (antiglaucoma drops, phospholine iodide, following eyelid eversion such as with an ectropion — stenosis resolves once lid position restored)
  - Eyelash problems — trichiasis secondary to marginal entropion, blepharitis/MGD (keratin plugging, posterior lid telangiectasia, hyperaemia of eyelid margin)
  - Tear film abnormalities — meniscus high/low, faster TBUT (<10 s), Schirmer's test
- Examine for possible causes of a tearing eye
  - Lacrimal examination:
    Rule out dacryocystitis first: diagnosis of NLDO is made if signs of acute dacryocystitis (erythema, swelling, and tenderness in the medial canthus) are present, you can express pus/mucoid from lacrimal sac, or a mucocele is present (palpable cystic mass present in medial canthus caused by obstruction at both the NLD below and common internal punctum above causing lacrimal sac to fill with mucus)
    Evaluate tear lake with slit lamp: enlarged if obstruction present — mucoid/pus in tear lake if NLD obstructed, no debris in tear lake if punctum or canaliculi obstructed
    Evaluate cornea — rule out any pathologic changes, watch patient blink spontaneously to see how much cornea is covered with a blink
    Evaluate lid margins for signs of blepharitis or marginal entropion
    Evaluate position of punctum — normal punctum not easily visible without slight manual eversion of the eyelid
    Check lacrimal system vital signs:
    - Dye disappearance test: 2% fluorescein into each fornix. After 5 min, check to see how much dye is retained in eye. Normal result documented as spontaneous symmetric dye disappearance. An abnormal result is recorded as dye retained in right or left eye,
    - Lacrimal probing to demonstrate patency of upper and lower canaliculi using a lacrimal probe: probe should be placed vertically in the punctum for 1–2 mm. Lid pulled temporally and probe directed towards the can-

thal angle. Probe should pass easily to lacrimal sac where a hard stop (lacrimal bone) is felt. A soft stop indicates canalicular obstruction.

- Lacrimal irrigation: using a lacrimal irrigation cannula in the lower canaliculus, not the sac, you should be able to irrigate saline easily into the nose without any reflux around the cannula or out the upper canaliculus (normal NLD). If you cannot irrigate with pressure on syringe then the duct is closed (anatomic obstruction — regurgitation through same canaliculus irrigated through if obstruction in upper or lower canaliculus, regurgitation through opposite canaliculus than the one irrigating through if common canaliculus obstruction). If you can irrigate with pressure on syringe then duct is partially obstructed (functional obstruction)

Perform a nasal examination — nasal endoscopy if possible, to rule out intranasal tumours or mucosal abnormalities

3.13.5 Investigations

- Dacryoscintigraphy (DSG): indicated for functional NLDO (patient gives hx typical of PANDO but you cannot demonstrate an obstruction) and gives an estimate of the physiologic drainage of tears. If any delay is noted (delayed filling of NLD), a DCR is recommended (DCR not recommended if no filling of NLD seen)
- Dacryocystogram (DCG): useful if previous trauma, destructive disease (inflammatory) or suspected tumour
- Jones testing — considered in cases of partial obstruction to determine level of block:
  - Jones I — physiological without syringing — 2% fluorescein into lower fornix, after 5 min, assess dye recovery with a cotton bud placed at NLD opening at inferior meatus, positive if dye recovered and implies normal patency, negative if no dye recovered and implies partial obstruction or lacrimal pump failure
  - Jones II — non-physiological after syringing — wash out fluorescein from fornix, insert lacrimal cannula into the lower canaliculus and irrigate, assess dye recovery from nose as before, positive if dye recovered and implies partial obstruction of NLD, negative if no dye recovered and implies partial obstruction above the lacrimal sac (punctal or canalicular obstruction)

3.13.6 Treatment

- In all cases, eyelid and eyelash problems should be treated before lacrimal surgery
- Poor tear film: lid hygiene, lubricants, punctal plugs, punctal cautery
- Reflex tearing: treat entropion, lubricants
- Lacrimal pump problems: ectropion/laxity of lower eyelid — LTS, CN VII palsy — lubricants, LTS, gold weight placement in upper eyelid
- Punctal stenosis: discontinue treatment with any known offending eye drop, two- (vertical cut of punctum and horizontal cut of canaliculus) or three-snip (excision of a small triangle of the posterior wall of the vertical and horizontal portion of the canaliculus) punctoplasty
- Punctal eversion: if no lid laxity present — medial spindle procedure (combination of a posterior lamella shortening procedure and a mechanical inversion of the lid margin) only, if lid laxity present — LTS ± medial spindle procedure (LTS alone may return punctum to normal position — check at slit-lamp to assess for this)
- Canaliculitis: curette the canaliculus through a dilated punctum ± punctoplasty (keep curetting until you do not retrieve any more sulfur granules or "stones") — topical antibiotic drops post-operatively
- Canalicular obstruction: canalicular reconstruction over stents (lacerations or localised obstructions following trauma), DCR with Lester-Jones tube placement (Pyrex tube that carries the tears from the conjunctival cul-de-sac through a DCR ostium into the nose,

Table 3.5 Key facts about a Lester-Jones tube

Anatomy
- The proximal end of the tube lies at the medial commissure and the distal end lies within the middle meatus of the nose

Indications
- Symptomatic epiphora secondary to extensive scarring of both upper and lower canaliculi
- Congenital atresia or complete absence of the canaliculi with epiphora
- Symptomatic epiphora secondary to lacrimal pump failure, e.g. chronic facial palsy
- Failed re-do DCR
- Chronic epiphora due to eyelid malpositions which eyelid surgery has failed to or is unable to control, e.g. ichthyosis, severe chronic eczema

Complications
- Tube displacement — scleritis from local scleral indentation and irritation
- Tube obstruction
- Lacrimal sac infection

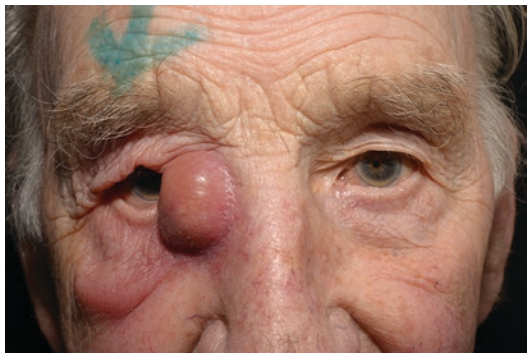

Fig. 3.17 Facial photo of a patient with a lacrimal sac abscess

bypassing the obstructed canaliculi — see Table 3.5)
- Acute dacryocystitis: do not probe or irrigate, oral or IV antibiotics, if lacrimal sac abscess (see Fig. 3.17) is present — incision and drainage of the lacrimal sac through an external incision will speed recovery but risks formation of a fistula, DCR (external/endonasal) delayed until inflammation has settled
- Chronic dacryocystitis (mucopurulent discharge but with no signs of cellulitis): topical antibiotics and DCR (external/endonasal), do not probe or irrigate
- Suspected dacryolith: if more than two episodes occur within a year, a DCR (external/endonasal) is a reasonable therapeutic option.
- Functional NLDO (anatomically the NLD is open on irrigation but the tears do not seem to pass into the nose spontaneously under normal conditions): DCR or silicone stent intubation of the NLD (remove stents at 6 months post op — success about 75%)

3.13.7 Dacryocystorhinostomy (DCR)

- Treatment for congenital (when blockage sufficient to prevent passage of a probe) and acquired NLD obstruction
- External DCR (gold standard): the obstructed NLD is by-passed by forming an anastomosis of the lacrimal sac and nasal mucosa through a nasal ostium created by an external skin incision.
- Endonasal DCR: the ostium and anastomosis are made from the inside of the nose, using an endoscope

3.14 Approach to the Paediatric Watering Eye

3.14.1 History

- Onset: soon after birth or if it is more recent
- Photophobia: suggests congenital glaucoma, uveitis, corneal disease (e.g. cystinosis), FB in conjunctival sac
- Eye rubbing or poking: suggests a retinal dystrophy such as LCA
- Watery nose on same side as the watery eye: suggests excessive lacrimation rather than blocked tear drainage

3.14.2 Examination

- External examination
  - Tearing, red macerated skin, stickiness may be seen
  - In NLDO, tear lake is thickened, brimming the lower lid margin — measures 2 mm or more with fluorescein staining of the tear film (normally <1 mm)
  - Secondary bacterial conjunctivitis with generalised conjunctival redness
  - Perilimbal conjunctival injection more specific for keratitis or uveitis
  - Generalised corneal haze with secondary corneal epithelial oedema may be a sign of glaucoma — estimate horizontal corneal diameter using a ruler held close to the lid
  - Congenital swelling over the nasolacrimal sac is probably a dacryocystocele
- Slit lamp examination
  - Puncti: presence or absence, ectropion
  - Lid: epiblepharon with inturned eyelashes, blepharitis
  - Conjunctiva: inspect inferior conjunctival fornix looking for diffuse redness and swelling of the conjunctiva — suggesting chlamydia conjunctivitis
  - Cornea: crystals, abrasions, FB, ulcers, KP's, Haab striae and corneal oedema
  - AC: hypopyon,
  - Iris: posterior synechiae
  - Lens: cataract
- Fluorescein testing
  - Staining with abrasions or epithelial oedema
  - Dye disappearance test
- IOP
- Fundus examination
  - Disc cupping in glaucoma
  - Posterior segment pathology, e.g. retinoblastoma (can present as a red watery eye with a pseudo-hypopyon)
- Cycloplegic refraction, fundus examination
  - Unilateral myopia in a child with unilateral glaucoma

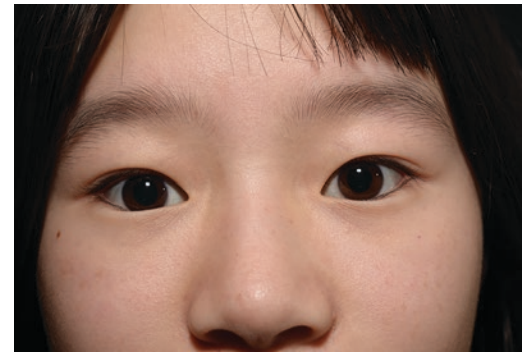

Fig. 3.18 Facial photo of a patient with an epiblepharon

3.14.3 Differential Diagnosis

- Reflex tearing (lacrimation)
  - Lids:
    Blepharitis
    Epiblepharon (see Fig. 3.18): irritation from inturned eyelashes
  - Conjunctiva:
    Conjunctivitis: infective (viral, bacterial), allergic, chemical
    Conjunctival sac or subtarsal FB
  - Cornea:
    Corneal FB
    Corneal abrasion
    Keratitis
    Cystinosis
  - Congenital glaucoma (see Sect. 9.4): horizontal corneal enlargement, Haab striae, buphthalmos, increased CDR, raised IOP
  - Anterior uveitis
- Decreased lacrimal drainage
  - NLDO
  - Lid malposition
  - Punctal malposition
  - Punctal occlusion (punctal atresia)
  - Anomalous drainage system (blocked or absent) with craniofacial abnormalities

Fig. 3.19 Facial photo of a patient with a congenital NLDO showing a positive 'fluorescein dye disappearance test'

Table 3.6 Key facts about CNLDO

- Caused by a persistent membranous obstruction at the valve of Hasner — in more than 90% of patients, this membrane will spontaneously rupture within the first year of life
- Diagnosis is made on a history of a watery eye that has been present from the first few weeks of birth — usually unilateral but may be asymmetrically bilateral

3.14.4 Congenital Nasolacrimal Duct Obstruction (CNLDO) (Fig. 3.19 and Table 3.6)

3.14.4.1 Examination

- Child is well with no evidence of irritation or photophobia
- Periocular skin may become red and excoriated
- Stickiness or crusting of the lashes
- Eye remains white without evidence of active infection, although conjunctivitis may complicate the condition
- Increased tear meniscus
- Mucocele may develop — contents can be expressed into the conjunctival sac

3.14.4.2 Investigations

- Dye disappearance test:
  - Fluorescein 1% is instilled into each lower conjunctival fornix and cobalt blue light from the slitlamp illuminates the eyes
  - Tear meniscus evaluated at 5 min
  - Normally fluorescein disappears from tear meniscus by 5 min but remains present in children with obstruction
  - Grading (MacEwan and Young 1991):
    0 = no fluorescein
    1 = thin fluorescing marginal tear strip
    2 = more fluorescein persists, higher tear film
    3 = wide, brightly fluorescing tear strip, spillage

3.14.4.3 Treatment

- Conservative (for the first year of life as high rate of spontaneous resolution):
  - Crigler massage: must push index finger posterior to the anterior lacrimal crest to empty the sac, idea is to massage as often as necessary to empty the sac — massage may build up enough pressure in the sac so that the membrane is broken
  - Antibiotics if conjunctivitis present (avoid antibiotics in watery white eyes)
- Syringing and probing (performed when spontaneous resolution of the tearing and mattering does not occur by 1 year of age) — 90% success rate:
  - Procedure performed under GA in an outpatient setting
  - Patient preparation — spray a vasoconstricting agent in the nose
  - Dilation of the punctum using a Nettleship dilator
  - Passage of probe into the sac until a "hard" stop is felt
  - Rotation of the probe 90° and passage of the probe into the NLD about 15 mm aiming slightly posteriorly and laterally
  - Fluorescein-stained saline irrigation using a disposable cannula
  - Confirmation that probe is in the nose (suction fluorescein tinged saline irrigation fluid — suction is in nose whilst canaliculus is irrigated with fluorescein stained saline)
  - Apply topical antibiotic ointment
- NLD intubation with silicone stents (performed when probing fails):
  - The upper and lower canalicular stents are tied so that the knot lies underneath the inferior turbinate

  - Leave stents in place for 6 months
  - A small amount of tearing will often remain with the stents in place, especially when child has a cold (no discharge should be seen however)
  - Remind parents that tears do not flow through the stents and that any residual tearing usually resolves when the stents are removed
  - If prolapse of stents occur — stents cannot be repositioned because the knot is up in the duct so just tape the loop to the cheek
- DCR (indicated with persistent epiphora despite probing and intubation).

3.15 Approach to the Patient with Proptosis

3.15.1 History

- Pain: caused by inflammation, infection, acute pressure changes (haemorrhage), and a highly malignant tumour growing into bone or nerves (neoplasms in general do not cause pain until a complication related to the neoplasm arises)
- Progression: rapid (hours to days — suggest inflammation or infection), intermediate (weeks to months — suggests more chronic types of inflammatory processes such as thyroid disease), slow (months to years — suggests a benign neoplasm or lymphoma)
- Past medical history: any previous neoplasm elsewhere such as lymphoma or breast carcinoma, any past trauma of the face (caused facial asymmetry that may accentuate or diminish the appearance of a proptotic eye), any history of thyroid disease

3.15.2 Examination

- Orbital examination: start by evaluating the change in the position of the eye in terms of axial and non-axial displacement, next palpate the orbital rims and soft tissues to see if any abnormality is present, then you will check briefly for any pulsations, last you will search for other clues in the periocular area that may give you information to develop a differential diagnosis
- Proptosis: axial displacement in anterior direction (thyroid orbitopathy with enlargement of the EOM, optic nerve tumours or a benign cavernous haemangioma). Measure axial displacement with Hertel exophthalmometer.
  - Inferior displacement (problems arising in the area of the lacrimal gland, defects in the orbital roof due to trauma, encephalocele, or frontal sinus mucocele formation)
  - Lateral displacement (problem in the ethmoid sinus — subperiosteal abscess — an acute process — arising in the ethmoid sinus and extending into the subperiosteal space, sinus carcinomas — slowly progressive process, mucocele — very slowly progressive process)
  - Upward displacement (lymphoid lesion, maxillary sinus tumours)
  - Medial displacement (enlarged lacrimal gland).

    Measure non-axial displacement with a Ruler or McCoy Tri-Square
- Palpation: start with palpation of the orbital rims and then move toward the eye, palpating the superior and inferior fornix for any anterior masses — if present determine size, shape and position, determine if there is any tenderness in the area of the lesion (infectious or inflammatory disorders will often cause the skin to be erythematous and warm to touch)
- Pulsation: pulsations of the eye suggests either an arterial vascular malformation in the orbit (if high flow you may be able to hear a bruit or feel a thrill) or the absence of orbital bone that allows the normal pulsations of the brain to push on the eye (e.g. absence of sphenoid wing in NF-1), venous lesions do not pulsate but they will usually show enlargement with the Valsalva manoeuvre (orbital or conjunctival varix) or with the head in a dependent position
- Periocular changes: temporal flare of the lateral position of the upper lid and lid lag seen

on downgaze (thyroid orbitopathy), conjunctival salmon patch (orbital lymphoma), fullness of the temple (sphenoid wing meningioma), periocular skin malignancy (intraorbital spread of cutaneous carcinoma)

3.15.3 Investigations

- Orbital imaging serves two purposes — providing diagnostic information (what the mass is) and providing information used to plan orbitotomy (want to know the best surgical approach to biopsy the mass)
- CT for bony orbital trauma
- MRI for imaging of the orbital apex, chiasm, optic nerve tumours, FLAIR sequence for optic neuritis due to demyelinating disease, STIR sequence for thyroid orbitopathy

3.15.4 Orbital Disease Occurring in Adults

3.15.4.1 Differential Diagnosis

- Axial displacement:
  - Enlarged EOMs — thyroid orbitopathy, orbital pseudotumour
  - Intraconal mass — cavernous haemangioma
  - Optic nerve tumour — optic nerve meningioma
- Nonaxial displacement:
  - Inferior displacement — lacrimal gland (benign mixed or lymphoid tumour), frontal sinus (mucocele), orbital roof (sphenoid wing meningioma)
  - Lateral displacement — ethmoid sinus (abscess or mucocele)
  - Superior displacement — maxillary sinus (carcinoma), orbital fat (lymphoid tumour)
  - Medial displacement (rare) — benign mixed tumour of lacrimal gland
- Enophthalmos:
  - Scirrhous carcinoma of the breast — infiltrative sclerosing tumour

3.15.4.2 Thyroid Eye Disease (Fig. 3.20 and Table 3.7)

Other Diagnoses to Consider

- Allergic conjunctivitis — acute in onset from a new exposure, causes itching, papillary conjunctival reaction, not associated with eyelid retraction or proptosis
- Myasthenia gravis — diplopia worsens throughout the day and improves after rest (not variable in TED), may present with ptosis (not associated with TED)
- Orbital myositis — causes enlargement and inflammation of the muscle body and tendon insertion (muscle body only in TED), not associated with eyelid retraction, usually unilateral (bilateral presentation unlikely for orbital myositis, TED can present unilaterally or bilaterally)
- Orbital tumours — typically unilateral in presentation causing proptosis and ocular motility disturbances, unlikely to cause eyelid retraction or lid lag
- Carotid-cavernous fistula — patient may hear pulse-synchronous tinnitus, presentation may include pulsatile proptosis, dilated conjuncti-

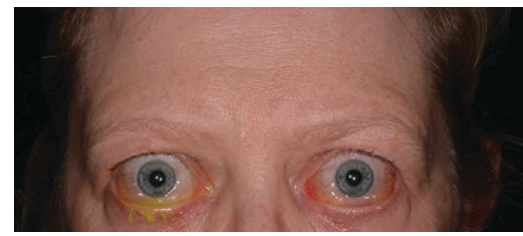

Fig. 3.20 Facial photo of a patient with TED showing superior and inferior lid retraction, proptosis, chemosis, caruncular oedema and upper lid oedema

Table 3.7 Key facts about TED

• Most common cause of unilateral or bilateral proptosis • Affects women five to six times more often than men • Onset most common in the early 40s and mid-60s • TED is most commonly associated with Graves disease (90%) but may occur in 3% of Hashimoto's thyroiditis, 6% euthyroid, and 1% primary hypothyroidism

val and episcleral vessels, elevated IOP, enlarged EOM, would not cause eyelid retraction or temporal flare
- CPEO — slowly progresses over 5–15 years with most patients presenting with ptosis, all cardinal directions of gaze are affected, with downgaze most likely spared (TED conversely typically affects downgaze and nasal gaze)
- Inflammatory orbitopathy (e.g. GPA) — GPA typically presents with a mix of upper and lower respiratory tract and renal pathologies. Patients may have conjunctivitis, episcleritis, scleritis, and/or uveitis (other than conjunctivitis, these findings are uncommon in TED patients)
- IgG4-related orbitopathy — painless swelling of the EOM's, lacrimal glands, and infraorbital nerves in combination with paranasal sinus disease, multi-organ fibrosis and sclerosis (pancreas, liver, salivary glands, retroperitoneum) may co-exist

History

- Any pain and rate of progression: gradual onset, slow progression without pain. No pain is associated, but discomfort, more like pressure or orbital fullness, is often present
- Any diplopia (restrictive strabismus) or blurred vision (optic nerve compromise)
- Ask about symptoms of hyper- or hypo-thyroidism
- Past medical history often reveals systemic thyroid disease
- A family history is common
- Ask about risk factors for TED: smoking, history of thyroid disease (hyper- or hypo-thyroidism), poor control of thyroid function is a risk factor for reactivating TED

Examination

- Check lids
  - Measure the eyelid position and function (PA, MRD1, LF)
  - Look for lid swelling and erythema
  - Look for upper and lower lid retraction
  - Look for temporal flare of the upper eyelid — lid just keeps getting higher toward the lateral canthus (peak of normal eyelid is just nasal to the pupil)
  - Look for lid lag in downgaze.
  - Look for lagophthalmos
- Check proptosis
  - Measure the degree of proptosis using an exophthalmometer
  - Axial, usually bilateral, but can be quite asymmetric
- Check optic nerve function for compressive optic neuropathy
  - VA
  - RAPD
  - Colour vision: first sign of early optic nerve compression is reduced colour vision
  - 24-2 HVF
  - Serial visual evoked potentials (VEP — provides objective assessment of optic nerve function — important to know that patient is euthyroid before evaluating the result, as hypothyroid patients without optic nerve compression can show a delay in the P100 component of the VEP)
- Slit lamp examination
  - Check corneal sensation
  - Look for conjunctival and caruncular injection and/or chemosis
  - Look for signs of corneal exposure, superior limbic keratoconjunctivitis
  - Check IOP in primary position and upgaze (more than 5 mmHg difference)
  - Perform a dilated fundus exam to look for optic disc swelling or pallor and choroidal folds
- Check extraocular muscle involvement
  - Mechanical restriction of ocular movement ± pain on looking in the direction of limited movement
  - Retraction of the globe occurs when movement away from the site of the restriction is attempted (commonly seen on upgaze)
  - In order of decreasing frequency, the muscles involved are: IR muscle (restricted up gaze), MR muscle (restricted abduction), SR muscle (restricted downgaze), LR muscle (restricted adduction although LR is usually spared even when enlargement is evident on CT scan)
  - Common ocular posture is hypotropia of the more affected eye, sometimes with associated ET

  - An abnormal head posture, commonly chin elevation, is often adopted, ± face turn: purpose is to avoid an uncomfortable position of gaze, to centralise a field of binocular single vision
  - Enlarged vertical fusion amplitude
- Systemic examination
  - Examine for goitre, palmar erythema, atrial fibrillation, and pretibial myxedema
  - Look for signs of hyperthyroidism (warm peripheries, tachycardia, atrial fibrillation, hair loss) or hypothyroidism (bradycardia, dry thin hair, dry coarse skin)

Investigations

- Thyroid functions tests (TSH, T4 — most patients will have a high T4 and a low TSH level, although in 5–10% of patients, thyroid orbitopathy will be associated with a euthyroid condition) and thyroid autoantibodies (anti-TSH receptor, anti-thyroid peroxidase, anti-thyroglobulin antibodies)
- In some patients, the diagnosis is so obvious that no imaging is necessary
- CT scan with axial and coronal cuts (see Fig. 2.46): enlarged extraocular muscles, proptosis (>1/3 of eye in front of imaginary line from medial to lateral canthus), CT is preferred imaging modality for planning orbital decompression
- MRI (T2 STIR): better soft tissue resolution and used for grading disease activity, enlarged muscle bellies with sparing of the tendons
- Orthoptic review: Hess/Lees chart, field of binocular single vision, field of uniocular fixation
- Serial visual evoked potentials (VEP — provides objective assessment of optic nerve function — important to know that patient is euthyroid before evaluating the result, as hypothyroid patients without optic nerve compression can show a delay in the P100 component of the VEP)
- Forced duction test: confirm presence and extent of mechanical restrictions

Disease Stratification

- If TED is suspected, determine disease activity and disease severity in order to assess the urgency of treatment
- Disease activity — grade disease activity using the Clinical Activity Score — CAS (Mourits et al. 1997) — at initial visit, patients are given a CAS score of 1–7, 1 point for each sign or symptom (ocular pain at rest in the last 4 weeks, ocular pain on eye movement in the last 4 weeks, eyelid swelling that is considered to be due to active TED, eyelid erythema, conjunctival injection considered to be due to active TED, chemosis, inflammation of caruncle or plica semilunaris); At follow-up visits, add the three following criteria (increase of at least 2 mm proptosis during a period of one to three months, decrease in uniocular motility in any one direction of at least 5° during a period of one to three months, decrease in VA equivalent to 1 Snellen line during a period of one to three months) for a potential CAS score of 10 (1 point for each sign or symptom)
- TED is considered "active" if the CAS is 3 or more at the initial visit or 4 or more at the follow up visits
- Disease severity:
  - EUGOGO classification scheme (Bartalena et al. 2008):
    Mild TED: lid retraction less than 2 mm, exophthalmos less than 3 mm above normal, mild soft tissue involvement, transient or no diplopia, corneal exposure responsive to lubricants — insufficient to justify immunosuppressive/surgical treatment
    Moderate-severe TED: lid retraction at least 2 mm, exophthalmos at least 3 mm above normal, moderate to severe soft tissue involvement, constant diplopia — sufficient impact on QOL to justify immunosuppression if active or surgical intervention if inactive
    Sight threatening TED: optic nerve neuropathy and/or corneal breakdown — warrant immediate intervention
  - NOSPECS:
    No signs or symptoms
    Only signs no symptoms
    Soft tissue involvement
    Proptosis
    EOM involvement
    Cornea involvement
    Sight loss

Rundle's Curve

- Depicts schematically the typical course of disease severity with time
- Characterised by an active phase of increasing severity, a regression phase of decreasing severity, and an inactive plateau phase

Treatment

- Achieve a euthyroid state without post-treatment hypothyroidism — seek consultation with an endocrinologist if the patient is not seeing one. Treatment of hyperthyroidism — carbimazole or propylthiouracil, radioactive iodine — short course of prophylactic oral steroid to prevent new onset or progression of TED, thyroidectomy. Treatment of hypothyroidism — levothyroxine
- Promotion of smoking cessation
- Before initiating treatment, determine where the patient's condition falls in the natural history of the disease. Try to determine whether patient is in the "active" stage (swelling or redness of the orbital, lid, and conjunctival tissues — eyelids look "wet" as though you could squeeze oedema fluid out, eyelid swelling and any diplopia are much worse in the mornings) or "chronic" stage (morning eyelid swelling and diplopia are gone, signs of acute inflammation are no longer present, any remaining proptosis and lid retraction probably will not change) of the disease
- Mild TED/CAS <3 — most patients will require only medical management during the active stage — monitor patients for corneal exposure and treat irritation with lubricating drops and ointment, elevate head of the bed to reduce morning swelling or diplopia, sunglasses to decrease photophobia and feelings of dryness, prisms for diplopia
- Moderate-severe TED/CAS ≥3 — consider immunosuppression (systemic corticosteroids — IV methylprednisolone or oral prednisolone, rituximab, etanercept, AZT) or orbital radiotherapy (2000 rad — for patients with restrictive myopathy but not for acute optic nerve compression — contraindications include history of skin cancer, age less than 35 years old)
- Sight threatening TED — admit patient, IV methylprednisolone 1 g every day for 3 days (maximum total dose of 8 g — if dose exceeds measure LFT's as small risk of acute liver damage). Surgical decompression (fat and/or bony decompression) if the steroid therapy fails and if systemic steroid therapy is contraindicated or has intolerable side effects.
- Surgical (decompression then strabismus surgery then lid surgery) — when you have confirmed that there has been no change over 3–6 months, the patient may want to consider procedures to improve the remaining proptosis, lid retraction, and strabismus (to correct diplopia: conservative — prisms, botulinum injection, and Bangerter foils, surgical —indicated when there is diplopia in primary gaze and downgaze and stable inactive TED with stable myopathy for at least 6 months)

Prognosis

- Poor prognostic factors: smoker, male, older age at onset, diabetes, reduced vision, rapid progression at onset, longer duration of active disease

3.15.4.3 Orbital Pseudotumour (Table 3.8)

Other Diagnoses to Consider

- Bacterial orbital cellulitis — patient usually sick (febrile, weak, etc.), onset usually takes place over a few days, pain usually less than with orbital pseudotumour
- Orbital haemorrhage — onset usually more sudden, with progression occurring over a few minutes, rather than hours

History

- Any pain and rate of progression — acute/abrupt onset of pain with rapid progression occurring over hours to a day or at most two
- Past medical history is only helpful for children in whom a viral syndrome may precede the onset

Table 3.8 Key facts about orbital pseudotumour

• Any of the orbital tissues may become infiltrated with inflammatory cells (dacryoadenitis or myositis)
• Both young and old people are affected

Examination

- Look for proptosis
- Look for periocular signs of acute inflammation predominate — lid swelling, chemosis
- Look for limited motility
- With palpation, the tissues are tense and warm, but no distinct mass will be present. The inflamed areas are tender to touch. There are no pulsations.

Investigations

- FBC, CRP: normal
- CT scan (see Fig. 2.47): poorly circumscribed (poorly defined margins) mass may be present in any orbital space, dacryoadenitis, myositis (diagnosis can usually be made clinically if the onset and pain are typical)

Management

- Rapid response to oral prednisolone (80 mg/day) is characteristic. Treatment should be continued for 6–8/52 with a tapering schedule.

3.15.4.4 Cavernous Haemangioma (Table 3.9)

History

- Any pain and rate of progression — painless and slow progression

Examination

- Vision: not affected unless the mass pushes directly on the eye causing a hyperopic shift
- Look for proptosis: unilateral, axial
- The typical cavernous hamangioma is too far posterior to be palpable
- There are no associated periocular signs
- Although lesion is vascular, there is low flow so no pulsations are seen

Investigations

- CT scan (see Fig. 2.48): well circumscribed oval or round mass, usually in the muscle cone (intraconal)

Table 3.9 Key facts about cavernous haemangioma

• Most common benign orbital tumour in adults • Most common around age 40

Management

- Observation: repeat CT scan at three to four months or sooner if any visual loss, pain or change in proptosis occurs
- Removal via orbitotomy: if diagnosis is uncertain, vision loss is present, or the patient does not want observation, excisional biopsy (removal) is recommended.

3.15.4.5 Optic Nerve Meningioma (Table 3.10)

History

- Any pain and rate of progression — no pain, rate of progression is very slow over months to years
- Any vision loss — patient's usually note vision loss from compression of the nerve before tumour is large enough to cause proptosis

Examination

- Look for proptosis — usually minimal at the time of presentation — if present, the proptosis is axial
- No external signs of disease are present
- Palpation of the orbit is normal
- No abnormal pulsations of the eye are seen
- Look for optic disc swelling — may be present
- Look for optociliary shunt vessels — compression of the CRA can occur so that blood flow is shunted to the retina via the ciliary vessels

Investigations

- CT scan: enlargement of the optic nerve, calcification of the arachnoid (parallel radiodense lines on the sides of the nerve — tram tracking)
- MRI scan (see Fig. 2.55): to determine extent of the tumour into the orbital apex and chiasm — will be able to see posterior extent of the tumour without the artefact of the bones in the apex obscuring the soft tissue detail as on a CT scan

Table 3.10 Key facts about optic nerve meningioma

• Most often seen in middle-aged adults • Benign tumour originates in the arachnoid villi of the meningeal sheath of the optic nerve

- Incisional biopsy: if diagnosis cannot be made clinically

Treatment

- Observation: recommended if VA is good
- Excision: debulking of an optic nerve meningioma cannot be done without damage to the vision, so no attempt to excise is usually done until useful vision is lost (blind eye) or the tumour is extending toward the optic canal as seen on serial MRI examination
- Meningioma's in patients younger than 35 behave more aggressively, suggesting that earlier excision should be considered

3.15.5 Orbital Diseases Occurring in Childhood

- Malignancy is a less common cause of proptosis
- Congenital abnormalities are more common causes — choristoma (normal tissue in an abnormal anatomic location, e.g. dermoid cyst), and hamartoma (normal tissue in abnormal quantity, e.g. haemangioma or glioma)
- Thyroid orbitopathy is a rare cause of proptosis in children
- Infection is a common cause of proptosis in children
- Rhabdomyosarcoma must be considered in any child with rapidly progressive proptosis

3.15.5.1 Differential Diagnosis

- Dermoid cyst
- Capillary haemangioma
- Orbital cellulitis
- Lymphangioma
- Rhabdomyosarcoma
- Optic nerve glioma

3.15.5.2 Dermoid Cyst (Fig. 3.21 and Table 3.11)

Other Diagnoses to Consider

- Lateral anterior dermoid: lacrimal gland mass, lipodermoid, teratoma, plexiform neurofibroma

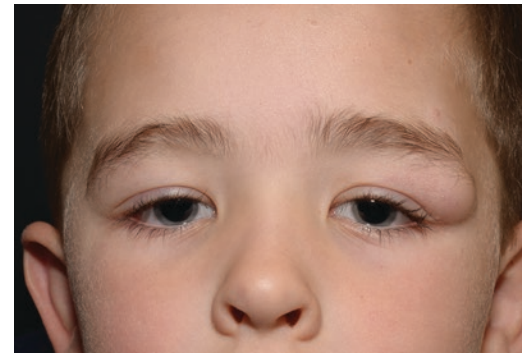

Fig. 3.21 Facial photo of a patient with a left dermoid cyst

Table 3.11 Key facts about dermoid cysts

- A choristoma containing skin and skin appendages such as hair and oil glands
- In utero, a bit of skin is "pinched" in a suture line where the tissue gradually forms a cyst. The lining of the cyst is normal skin. The contents of the cyst include keratin, oil and hair
- If the cyst wall does not contain skin appendages, it is called an epidermal cyst

- Medial anterior dermoid: mucocele, haemangioma, encephalocele
- Cyst with spontaneous rupture: orbital cellulitis, orbital pseudotumour
- Deep dermoid with mass effect: primary cranial nerve palsy

History

- Onset — first few months of life, deep orbital dermoid cysts, such as those originating from the sphenozygomatic suture, present later, usually in young adults
- Pain — painless
- Progression — mass increases in size very slowly
- Diplopia — mass effect of a deep dermoid cyst

Examination

- Location of cyst (forms differentials): cyst can occur at any suture line, but it is most commonly seen at the frontozygomatic suture line (frontonasal suture next most common)
- Palpate cyst: smooth to palpation, can be either freely moveable or attached firmly to the bone. No mass palpable for a deep orbital dermoid cyst

- Displacement of globe/proptosis: mass effect of a deep orbital dermoid cyst
- Ocular motility: deficits caused by a deep orbital dermoid cyst

Investigations

- Imaging of the typical frontozygomatic dermoid cyst in an infant is *not* required if you can feel around the equator of the mass, suggesting that the entire mass is outside of the orbital cavity
- If the mass is firmly fixed to the bone or you cannot feel around the mass, there may be a component of the cyst extending into the bone or in the orbit itself. Imaging is not absolutely necessary, but it may help you to plan your operation because some bone removal may be required in rare patients.
- If mass is nasal (differentials — haemangioma, encephalocele), order a scan if you are not absolutely sure that the mass is a dermoid cyst
- CT scan: well circumscribed round mass adjacent to the bone, contents of the cyst may have the density of water or oil; occasionally one can see an interface between the oil and water layers (dermoid cyst); deep orbital dermoid cyst usually diagnosed on CT (large well circumscribed mass within an area of bone moulding to accommodate the slow growth of the cyst), as there may be no characteristics in the history or examination to make a definitive diagnosis.

Treatment

- Excision of cyst: rupture during removal may lead tio recurrence

3.15.5.3 Capillary Haemangioma (Fig. 3.22 and Table 3.12)

History

- Onset and pain — not present at birth but appears in the first few months of life, painless

Examination

- Look for a blush of red or blue to skin with little elevation (cutaneous haemangioma) and/or bluish elevation with no surface vascularisation (subcutaneous haemangioma) on the lid/forehead

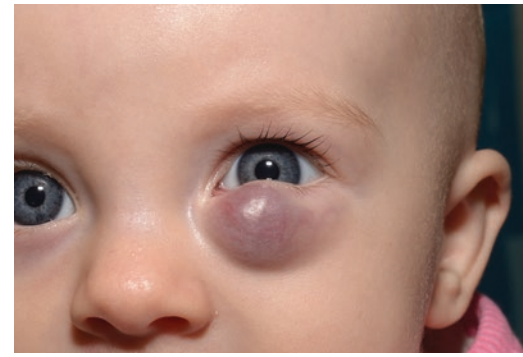

Fig. 3.22 Facial photo of a patient with a lower eyelid capillary haemangioma

Table 3.12 Key facts about capillary haemangiomas

- The most common orbital hamartoma.
- Haemangiomas, if untreated, have three phases: initial growth phase (ends before 6 months of age), stable phase, spontaneous involution phase (begins at 1 year of age up until age 8)

- Look for proptosis: subcutaneous portion of haemangioma may extend into the orbit causing displacement of the eye inferiorly or proptosis
- Look for ptosis: any large eyelid lesion can cause ptosis
- Cycloplegic refraction: during the growth phase look for astigmatism and amblyopia
- Slight changes in size occur with crying, probably as a result of vascular engorgement (low flow lesion so no pulsations are present)

Treatment

- Indications — amblyopia, astigmatism, or bony orbital asymmetry develops
- Intralesional steroid injection (Triamcinolone [Kenalog, Squibb] 40 mg/mL + betamethasone 6 mg/mL) — helpful if an upper eyelid mass causes amblyopia — follow up 6 weeks post injection
- Oral prednisolone — 1–2 mg/kg/day — if a mass is in the orbit causing proptosis or if the haemangioma is very large — include paediatrician in this treatment
- Systemic propranolol (Leaute-Labreze et al. 2015) — 3 mg/kg/day for 6 months
- Surgical excision with subsequent reconstruction of the resultant skin defect

Table 3.13 Key facts about orbital cellulitis

- Infection of the ethmoid sinus (sinusitis) spilling into the orbit is the usual cause
- Other causes: dacryocystitis, dental abscess, penetrating orbital trauma (septal perforation), surgical (strabismus and retinal surgery)
- Preseptal cellulitis — in younger children, in whom the orbital septum is not fully developed there is a high risk of progression and so should be treated similarly to orbital cellulitis. Unless there is an obvious cause for the preseptal cellulitis, such as an insect bite, you should consider the possibility of an ethmoid infection causing the eyelid swelling. Preseptal inflammation without evidence of a skin wound should be considered sinus in origin until proven otherwise. Order a CT scan to find out

3.15.5.4 **Orbital Cellulitis** (Table 3.13)

Differential Diagnosis of Inflammatory Proptosis

- Inflammation:
  - Orbital inflammatory disease: onset over days or weeks, afebrile, children are more likely to have anterior/posterior uveitis, normal FBC
  - Sarcoidosis: anterior/posterior uveitis, arthropathy, skin rash
  - Wegener's granulomatosis: bilateral, globe displacement with orbital mass, nasal blockage/discharge/bleeds, hearing loss, pain over paranasal sinuses
  - Ruptured dermoid cyst: globe displacement
- Penetrating orbital trauma
- Neoplasia:
  - Benign orbital tumours — lymphangioma, haemangioma
  - Malignant orbital tumours — rhabdomyosarcoma, leukaemia, metastatic disease
- Endocrine:
  - TED: lid retraction

Classification

- Chandler classification of orbital complications of sinusitis (Chandler et al. 1970):
  - Class I: Inflammatory oedema (preseptal cellulitis)
  - Class II: Orbital cellulitis
  - Class III: Subperiosteal abscess (SPA)
  - Class IV: Orbital cellulitis
  - Class V: Cavernous sinus thrombosis

History

- Any pain and rate of progression — proptosis develops over a few days with associated pain
- Recent history of URTI
- History of sinus disease
- History of any dental abscess
- History of dacryocysitis
- History of trauma — septal perforation
- History of surgery — lacrimal procedure, orbitotomy, lid operation, strabismus operation
- History of diabetes or immunocompromised (more for adults) — fungal orbital cellulitis

Examination

- Child looks sick (unlike with orbital pseudotumour) — weak, tired, and febrile (check temperature)
- Mild to advanced signs of orbital inflammation (similar to orbital pseudotumour) — proptosis, swollen, red, tender and warm lids, chemosis, limited extraocular movements (mechanical limitation)
- Look for optic nerve compromise — VA, RAPD, Colour vision
- Look for dacryocystitis
- Look for an insect bite/FB from trauma

Investigations

- FBC (raised WCC), CRP, Blood cultures
- CT orbits and sinus (see Fig. 3.23) — sinus disease, abscess formation in the orbit (subperiosteal/intraorbital abscess) ± intracranial, cavernous sinus thrombosis

Treatment

- Consult with ENT (sinus drainage) and paediatricians
- Broad-spectrum IV antibiotics and nasal decongestants (ephedrine) ± IV fluid: improvement should occur within 24–48 h. Daily review.
- Any Intraconal/orbital abscess should be drained
- Indications for early drainage of a SPA (Garcia and Harris 2000): age more than 9, presence of frontal sinusitis, non-medial location of SPA, large SPA, suspicious of anaerobic infection (e.g. presence of gas in abscess on CT), recur-

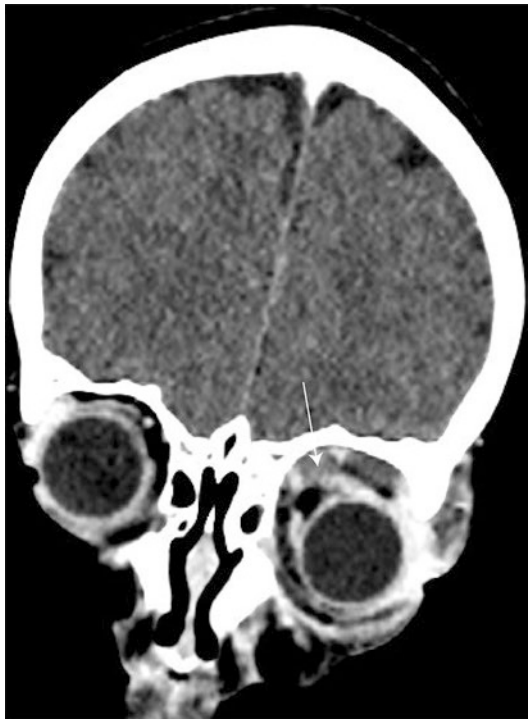

Fig. 3.23 Coronal CT scan image of a patient with an orbital cellulitis showing a superior subperiosteal abscess (white arrow)

rence of SPA after prior drainage, evidence of chronic sinusitis (e.g. nasal polyps), acute optic nerve compromise, infection of dental origin

Complications

- Subperiosteal and orbital abscess
- Cavernous sinus thrombosis: CN III, IV, V_1, VI CN palsies, retinal venous dilatation + optic disc swelling
- Meningitis
- Septicemia
- Brain abscess
- Optic neuropathy
- CRAO

3.15.5.5 Optic Nerve Glioma (Table 3.14)

History

- Pain and rate of progression: slowly progressive, no pain
- History of NF-1/Family history of NF-1 (first degree relative)

Table 3.14 Key facts about optic nerve glioma

• Occurs primarily in children in the first decade of life. Most tumours are unilateral
• Gliomas originate within the optic nerve tissue itself

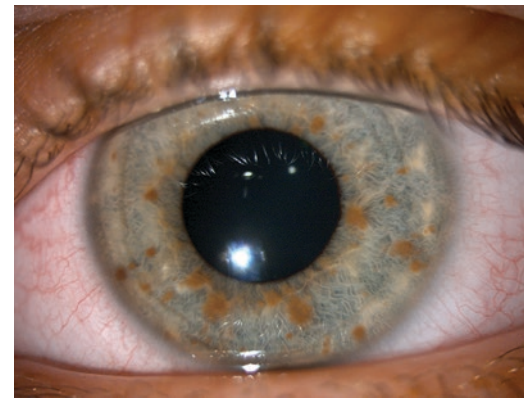

Fig. 3.24 Anterior segment image of a patient with NF-1 showing lisch iris nodules

Examination

- Look for axial proptosis: suggests an Intraconal mass
- Check optic nerve function: VA, RAPD, Colour vision — optic nerve compromise
- Look for signs of NF-1: café-au-lait spots, plexiform neurofibroma, lisch iris nodules (see Fig. 3.24), axillary/inguinal freckling
- Look for optic disc swelling

Investigation

- CT scan (see Figs. 2.54 and 2.56): enlarged nerve, often fusiform in shape, mass causes eccentric enlargement of the nerve, no calcification
- MRI scan: to delineate posterior extent of tumour — optic nerve tumour is characteristically bright on a T2-weighted scan — chiasm can be involved in up to 50% of cases of optic nerve glioma
- Incisional biopsy: only if diagnosis is in question

Treatment

- Observation with serial MRI scans performed every 6 months or so — majority of optic nerve gliomas are benign (hamartomas) and little or no growth posteriorly along the nerve will be seen over time

- Excision: only recommended for blind eyes with disfiguring proptosis or posterior spread threatening the chiasm, usually performed through a transcranial orbitotomy, removing the entire nerve
- Chemothetrapy/radiotherapy: for chiasmal or midbrain involvement

3.15.5.6 Rhabdomyosarcoma

History

- Pain and rate of progression: rapidly progressive painless proptosis over a period of several days to a few weeks. 70% occur in the first decade of life

Examination

- Look for proptosis: typically non-axial with the superonasal quadrant being involved most commonly, typically proptosis is relatively advanced somewhat out of scale to the short duration of symptoms
- Look for periocular ecchymosis (differential: neuroblastoma metastatic to orbit — bilateral periocular ecchymoses are typical)
- Look for enlarged preauricular or cervical lymph nodes
- Palpate for smooth mass in the anterior orbit, sometimes fixed to bone. No abnormal pulsations.
- Tumour may involve facial structures outside the orbit so look for masses elsewhere, including in the nose

Investigations

- CT scan: well circumscribed orbital mass with associated bone destruction, if mass extends outside orbit — you will see extensive soft tissue involvement and bone destruction
- MRI scan: if any of the cranial bones are involved, an MRI scan will be necessary to determine the extent of intracranial involvement
- Incisional biopsy

Treatment

- Early oncology consultation for systemic work up
- Combination of chemotherapy and radiotherapy

3.16 Approach to the Patient with Ptosis

3.16.1 Classification of Ptosis

- Simple congenital ptosis (see Fig. 3.25)
  - Eyelid is ptotic because of a dystrophy of the levator muscle itself (muscle is fibrotic and infiltrated with fat) — "simple" implies that the only problem causing the ptosis is the dystrophic levator muscle
  - Almost always bilateral, often asymmetric
  - Ranges from mild to severe
  - Reduced levator function
  - Weak or absent skin crease
  - Lid hang up on downgaze
- Involutional ptosis (aponeurotic ptosis)
  - Ptosis is caused by the aponeurosis separating from the tarsal plate
  - The term "disinsertion" is used, implying a slippage of aponeurosis off the tarsal plate or thinning of the aponeurosis ("dehiscence") itself
  - Associated with normal, or near normal, levator function (muscle is normal)
  - A high skin crease is the result of the levator fibers to the skin being dragged upward with the disinserted aponeurosis
  - Lid margin remains low throughout downgaze: lid drop on downgaze

Fig. 3.25 Facial photo of a patient with a simple congenital ptosis

  - Ranges from mild to severe
  - May be bilateral or unilateral
- "Unusual" types of ptosis
  - "Unusual" types of ptosis are usually associated with reduced levator function, but levator function also can be normal
  - Congenital causes:

    Superior rectus weakness:
    - Congenital ptosis associated with SR weakness in 5% of cases but has little clinical implication

    Marcus Gunn jaw winking (see Fig. 9.29):
    - Miswiring of CN V (pterygoid muscles) to CN III causing the drooping upper eyelid to elevate with movements of the mouth

    Blepharophimosis syndrome (see Fig. 3.26):
    - Ptosis (bilateral, symmetric, poor levator function),
    - Epicanthus inversus (medial canthal fold of skin extending from lower eyelid to upper eyelid)
    - Telecanthus
    - Blepharophimosis of the eyelids (horizontal aperture of eyelid narrowed laterally and medially)
  - Acquired causes:

    Neurogenic (abnormal innervation and normal muscle):
    - Myasthenia Gravis (see Figs. 9.30 and 9.31):
      - Reduced Ach receptors at neuromuscular junction
      - Diplopia
      - Variable ptosis: change in lid position from minute to minute or changes occurring throughout the day
      - Test fatigability: ask patient to look up for 30–60 s and eyelid will fatigue and slowly drop
      - Investigate with edrophonium testing: IV injection of Tensilon results in temporary elevation of the ptotic eyelid
      - Investigate with ice pack test: cooling of eyelid allows eyelid to elevate temporarily
      - Treatment with systemic oral pyridostigmine, thymectomy, immunosuppression, surgical ptosis correction if medical treatment unsuccessful although variability remains (presence of diplopia precludes possibility of successful eyelid elevation)
    - CN III palsy:
      - Ptosis with normal or reduced levator function
      - Non-comitant strabismus
      - Mydriasis
      - Aberrant regeneration with the ptotic eyelid elevating with contraction of the MR or IR muscle, pupil constriction with eye movements
    - Horner's syndrome:
    - Mild ptosis with normal levator function, miosis, lower lid elevation

    Myogenic (normal innervation and abnormal muscle — reduced levator function is typical, facial muscle activity and ocular motility are also reduced):
    - Oculopharyngeal dystrophy (see Fig. 3.27):
      - Autosomal dominant inheritance
      - Progressive bilateral ptosis (good levator function initially) with facial weakness and difficulty swallowing (ask patient to drink glass of water rapidly)

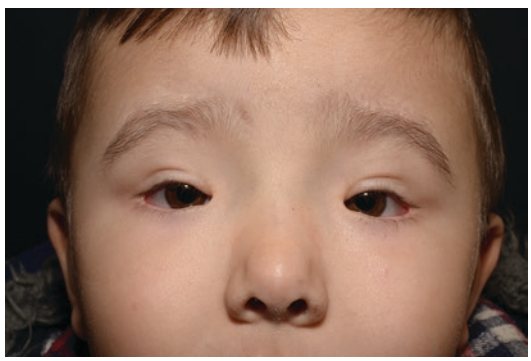

Fig. 3.26 Facial photo of a patient with BPES

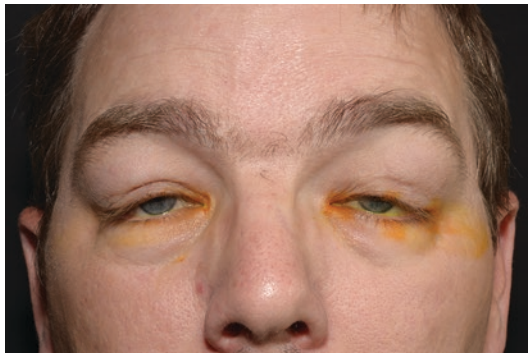

Fig. 3.27 Facial photo of a patient with oculopharyngeal dystrophy

- Myotonic dystrophy:
  - Autosomal dominant inheritance
  - Slowly progressive bilateral mild or moderate ptosis
  - Failure of muscles to relax after a sustained contraction
  - Facial and peripheral skeletal muscle weakness
  - Associated abnormalities in other organ systems (frontal balding, christmas tree cataract, testicular atrophy, weak cognitive function)
- Chronic Progressive External Ophthalmoplegia (CPEO):
  - Mitochondrial inheritance
  - Bilateral symmetrical ptosis with poor levator function
  - Facial weakness
  - An extreme loss of ocular motility (often to the point of no movement — frozen globe) with no diplopia
  - Pupils are spared
  - Kearns-Sayre syndrome: CPEO, heart block, pigmentary retinopathy
- Post-traumatic (damage to levator muscle)

  Post traumatic (damage to levator aponeurosis):
- Lid swelling
- Blepharochalasis:
  - Recurrent bouts of idiopathic lid swelling with secondary dermatochalasis

  Pseudoptosis (MRD1 and levator function are normal):
- Hemifacial spasm
- CN VII palsy with aberrant regeneration
- Contralateral lid retraction

3.16.2 History

- Adult patients
  - Questions to help identify type of ptosis:

    Is the diagnosis involutional ptosis?
    - Indefinite onset
    - Gradual progression
    - No other associated eye or systemic problems
    - Ptosis usually about the same severity throughout the day

    Is the ptosis acquired or has it been present since birth? When was the onset? What is the rate of progression?
    - Most adults will have an acquired form of ptosis, usually the common involutional type. The onset is difficult to identify, as the progression is usually so gradual over several years that no particular time is clearly identified as the onset. An acute onset suggests a diagnosis other than involutional ptosis — an exception to this is the onset of involutional ptosis after cataract surgery
    - Occasionally an adult will have pre-existing congenital ptosis that has slowly gotten worse over time or may have asymmetric congenital ptosis that can no longer be ignored because the "normal" side has progressively drooped more — physical exam will confirm the reduced levator function of congenital ptosis
  - Questions to identify factors that may modify the treatment plan:

    Is there a history of previous ptosis operations?
    - History of previous lid operations may be a warning sign that the

levator aponeurosis has already been shortened so that further tightening may cause lagophthalmos

Does the patient have symptoms of "dry" eye?

Is there a history of facial nerve palsy?

- A history of CN VII palsy signals the potential for poor blinking and lagophthalmos after surgery

– Questions to help identify an "unusual" type of adult ptosis:

Positive family history

Associated diplopia

Variation in degree of ptosis: minute to minute, with eye movements, better after naps

Associated facial movement problems: history of facial nerve palsy, history of facial spasms

- Paediatric patients
  – Questions to help identify type of ptosis:

Is the diagnosis simple congenital ptosis?

- Simple congenital ptosis involves only a ptotic upper eyelid in an otherwise healthy child with no abnormal eye finding

Is the ptosis congenital?

- When a ptosis is seen in a child, it is almost always congenital. Any onset after birth suggests a different diagnosis

Is the ptosis unilateral or bilateral?

- Congenital ptosis is usually bilateral, but often asymmetric

Does the lid change position? Is the lid ever open all the way?

- Wide variations in the day are not typical of simple congenital ptosis

Does the lid position change with chewing or sucking?

- Variation of lid position from movement to movement suggests a synkinetic form of ptosis.
- Ptosis associated with abnormal lid movements caused by chewing, sucking, or other changes in jaw position is known as Marcus-Gunn jaw winking
- Ptosis associated with abnormal lid movements caused by changes in eye position is seen in CN III palsy with aberrant regeneration

Is there a family history of ptosis?

- Strict inheritance of simple congenital ptosis is rare
- A positive family history (autosomal dominant inheritance) may suggest the presence of blepharophimosis syndrome
- Congenital ptosis is not commonly associated with any ocular or systemic abnormalities. Dystophy of the levator muscle is the only abnormality present

– Questions to identify factors that may modify the treatment plan:

Is the eyelid open above the pupil? During which part of the day? (how many times is the eyelid above the pupil?): assess risk of amblyopia

Surgical repair of a simple congenital ptosis is usually done before the child starts school (age 4). Features in the history suggesting the possibility of amblyopia should alter the timing of treatment

History of previous ptosis surgery:

- Previous ptosis repair, especially levator aponeurosis advancement procedures, puts the patient at risk for corneal exposure after more advancement

– Questions to help identify an "unusual" type of congenital ptosis:

Associated strabismus

Family history: blepharophimosis syndrome

Developmental delay: many syndromes associated with ptosis

Extreme variation of ptosis from minute to minute or throughout the day: lid movement associated with chewing or sucking, lid movement associated with eye movements

3.16.3 Examination

- Adult patients
  - Measure eyelid vital signs:
    Palpebral aperture (PA): measure from upper lid margin to lower lid margin in mm (normal 9–10 mm). For the PA measurement to be meaningful in describing the upper lid position, the lower lid must be in the normal position
    Marginal reflex distance 1 (MRD1): distance of upper lid margin from the corneal light reflex (normal 4–5 mm), measures degree of ptosis, with patient at your eye level, ask him/her to look straight ahead at a distance target, shine the penlight at the patient's eye
    Marginal reflex distance 2 (MRD2): distance of lower lid margin from the corneal light reflex
    Levator function (LF): block action of the brow with your thumb and don't allow the head to tip up with eye elevation
    Skin crease height: distance from upper lid margin to the skin crease (normal 8–10 mm in women and 6–8 mm in men)
  - Does the patient have normal facial expression?
    Weakness of the facial muscles is associated with the myogenic types of unusual ptosis
    Is there hyperkinetic movement of the face suggesting hemifacial spasm or aberrant regeneration of the facial nerve?
  - Measure the motility:
    Eye movements should be normal for the patients age in involutional ptosis
    Any reduction in motility or symptoms of diplopia suggest a diagnosis of other than involutional ptosis (MG, CN III palsy, CPEO)
    Any bizarre association of the upper eyelid position (ptosis or lid retraction) with eye movements should suggest aberrant regeneration of the third nerve
  - Is the pupil normal? Are there signs of Horner's syndrome? Do you see any miosis or lower eyelid elevation to suggest that a loss of sympathetic tone is responsible for the patient's mild ptosis (Horner's syndrome — upper lid ptosis, lower lid elevation, miosis, and anhidrosis of the ipsilateral side of the face)
  - Look for risk factors that increase the chance of post-operative corneal exposure:
    Bell's phenomenon — a poor Bell's phenomenon is only a relative contraindication for ptosis repair
    Look for lagophthalmos — possibly from previous ptosis surgery, look for lower eyelid retraction from any cause,
    Slit lamp examination to evaluate the tear film and if minimal do a Schirmer's test — if corneal exposure is present preoperatively it will be worse after elevating the lid, use the maximal treatment of any corneal exposure before proceeding with ptosis repair — consider the use of punctal plugs
- Paediatric patients
  - Measure eyelid vital signs:
    Palpebral aperture (PA): measure from upper lid margin to lower lid margin in mm (normal 9–10 mm). For the PA measurement to be meaningful in describing the upper lid position, the lower lid must be in the normal position
    Marginal reflex distance 1 (MRD1): distance of upper lid margin from the corneal light reflex (normal 4–5 mm), measures degree of ptosis, with patient at your eye level, ask him/her to look straight ahead at a distance target, shine the penlight at the patient's eye
    Marginal reflex distance 2 (MRD2): distance of lower lid margin from the corneal light reflex
    Levator function (LF): block action of the brow with your thumb and don't allow the head to tip up with eye elevation
    Skin crease height: distance from upper lid margin to the skin crease (normal 8–10 mm in women and 6–8 mm in men)

- Measure VA:
  - Fixation should be steady and maintained
  - Check for amblyopia: if amblyopia, due to deprivation or astigmatism, is present, consider earlier surgery to correct ptosis
- External appearance of child:
  - Appearance should be normal for simple congenital ptosis
  - Most common abnormal facies are seen in blepharophimosis syndrome
  - Many other syndromes can have ptosis as one of the associated findings
- Measure the motility:
  - Normal motility is associated with simple congenital ptosis
  - Most common motility disturbance seen in children with ptosis is a localised weakness of the superior rectus muscle (occurs in 5% of patients born with ptosis)
  - Any bizarre movement of the upper lid associated with eye movement should suggest aberrant regeneration of CN III
- Ask the child to open and close the mouth and move the jaw around:
  - No movement of the eyelid should occur with simple congenital ptosis
  - Any lid movement will diagnose a Marcus Gunn jaw winking ptosis
- Look for risk factors that increase the chance of corneal exposure (rare in children): facial nerve palsy, poor Bell's phenomenon, lagophthalmos (previous ptosis surgery), poor tear film, corneal exposure

3.16.4 Investigations

- Bloods: anti-Ach receptor/muscle-specific receptor tyrosine kinase (MuSK) antibodies if myasthenia gravis suspected
- Genetic testing: oculopharyngeal dystrophy, myotonic dystrophy
- CT angiography: indicated if partial CN III palsy (rule out a posterior communicating artery aneurysm) or a painful Horner's syndrome (rule out ICA dissection) is identified
- Skeletal muscle biopsy: look for red ragged fibers in CPEO

3.16.5 Treatment

- Adult patients
  - Indications for surgical correction of eyelid ptosis:
    - Symptoms: decreased central or peripheral vision, heaviness of the lids, brow ache or headache, difficulty reading, and neck ache (from chronic lifting of the chin)
    - Examination findings: elevated or arched eyebrows, prominent forehead furrows, and a chin up position
  - Preoperative considerations:
    - Stop aspirin or clopidogrel (7–10 days before operation), NSAIDS (24–72 h before operation), warfarin (5 days before operation), rivaroxaban (at least 24 h before operation), apixaban (at least 48 h before operation)
  - Choice of surgical procedure:
    - For simple congenital ptosis with levator function greater than 4 mm, a levator aponeurosis advancement is the correct treatment
    - For simple congenital ptosis with levator function less than 3 mm, a frontalis sling is appropriate
    - For simple ptosis with levator function between 3 and 4 mm, a generous advancement is usual, with the resection extending high above Whitnall's ligament into the muscle itself
    - For involutional ptosis with a normal levator function, a levator aponeurosis advancement is the procedure of choice
    - Decide if additional procedures such as a blepharoplasty or browplasty are necessary. Older patients often have dermatochalasis and brow ptosis accompanying involutional ptosis
- Paediatric patients

Table 3.15 Levator advancement procedure

- Procedure of choice for adults with involutional ptosis
- Tightening the levator muscle doesn't improve the levator function or movement of the eyelid; it essentially only resets the lid height
- Operation most easily done using a local anaesthetic under the skin (allows operation on aponeurosis but does not paralyse the deeper levator muscle — makes intraoperative adjustment of lid height and contour possible)
- Operation includes:
  - Patient preparation: mark upper lid skin crease, inject local anaesthetic with epinephrine
  - Skin incision: open orbicularis muscle
  - Identification of the levator aponeurosis: dissect orbicularis off orbital septum, open septum, dissect septum off preaponeurotic fat, dissect preaponeurotic fat off aponeurosis
  - Dissection of the levator aponeurosis off Muller's muscle: disinsert levator aponeurosis from anterior surface of tarsus, dissect aponeurosis free from Muller's muscle
  - Levator aponeurosis advancement
  - Intraoperative adjustment to height and contour: aim for 1 mm overcorrection
  - Closure: reform skin crease, running suture to close skin)

Table 3.16 Frontalis sling procedure

- Procedure of choice for any type of ptosis with poor levator function
- Eyelid is surgically "connected" to the brow with the action of the frontalis muscle lifting the upper eyelid
- Operation includes:
  - Patient preparation
  - Skin incisions
  - Suturing of the fascia to tarsus
  - Passing the fascia to the brow
  - Skin crease closure
  - Adjustment of height and contour
  - Closure of forehead incisions

  - Indications for surgical correction of eyelid ptosis:
  - Choice of surgical procedure:
    Ptosis with poor levator function (1–3 mm) requires a frontalis sling operation
    Ptosis with medium to good levator function (>4 mm: lowest amount of levator function that will allow eyelid to lift without creating corneal exposure) can be corrected with a levator aponeurosis advancement operation (Tables 3.15 and 3.16)

3.17 Approach to the Patient with Vertical Diplopia

3.17.1 Diagnoses to Consider for Monocular Vertical Diplopia

- Tear film abnormalities
- Uncorrected refractive error
- Corneal irregularity (e.g. keratoconus, refraction surgery) or scar
- Cataract
- Polycoria
- Dislocated lens
- Macular distortion (e.g. ERM)
- Non-organic

3.17.2 Diagnoses to Consider for Binocular Vertical Diplopia

- Neurogenic:
  - CN III palsy
  - CN IV palsy
- Mechanical:
  - TED
  - Myasthenia gravis
  - Orbital floor fracture
  - Congenital and acquired Brown's syndrome
  - Orbital inflammatory disease (myositis)
- Other:
  - Skew deviation
  - Ocular surgery, e.g. scleral buckling surgery
  - Decompensated hyperphoria
  - Superior oblique myokymia

3.17.3 History

- "Does the double vision resolve when either eye is covered?": In binocular diplopia, one of the images disappear when one eye is covered. In contrast, monocular diplopia ceases when covering the affected eye but persists when occluding the unaffected eye

- Patients with binocular diplopia should be asked the following questions:
  - "Is the double vision intermittent, constant, or variable?"
    Double vision that is worse in the mornings may suggest TED
    Double vision that is worse in the evenings or with fatigue could indicate myasthenia gravis or a decompensated phoria
  - "Does the double vision depend upon direction of gaze (left, down, distance, near)?"
  - Ask for old photographs to look for an anomalous head posture: suggests a chronic ocular misalignment
  - If patient 50 years or older, ask about headaches, jaw claudication, scalp tenderness and weight loss to rule out giant cell arteritis (GCA)
  - Ask about dysphagia, dyspnea, dysarthria, or proximal muscle weakness: suggests myasthenia gravis
  - Ask about oscillopsia: suggests a nystagmus or superior oblique myokymia
  - Ask about eyelid malpositions (retraction or ptosis): suggests myasthenia gravis, CN III palsy, or TED
  - Past medical and ocular history should include the following questions:
    Head or ocular trauma
    Thyroid disease
    Vasculopathic risk factors
    Childhood strabismus or amblyopia
    Previous eye muscle surgery

3.17.4 Examination

- Monocular vertical diplopia:
  - Examine anterior segment for any tear film abnormalities (early tear-film break up time, abnormal Schirmer test), areas of corneal thinning or cataract
  - Examine posterior segment for macular pathologies such as an ERM
  - Full ocular motility
- Binocular vertical diplopia:
  - Examine for an abnormal head posture: head tilt (e.g. CN IV palsy), chin-up position (e.g. TED)
  - Examine eyelid position
  - Perform exophthalmometry
  - Examine pupils
  - Examine ocular motility:
    Examine pursuits and saccades of the eyes individually (ductions) and together (versions):
    - Ophthalmoplegia secondary to a myopathy, neuropathy, or neuromuscular junction disorder reveals slowed saccades ± abnormal pursuits
    - Restrictive ophthalmoplegia demonstrates normal saccadic velocity

    Ocular alignment should be evaluated in primary position, upgaze, downgaze, and horizontal gaze positions, including distance and near:
- Cover-uncover test: distinguish phorias from tropias
- Alternate cover test: reveals full deviation of tropia plus latent phoria

3.17.5 Investigations

- Monocular vertical diplopia:
  - Refraction: reveal any unidentified or irregular astigmatism from corneal or lenticular causes
  - Corneal topography: detect an irregular corneal surface or contour
  - OCT: detect macular pathology
- Binocular vertical diplopia:
  - Bloods tests: anti-Ach receptor/ MuSK antibodies (myasthenia gravis), TSH/T3/T4 levels (TED), glucose levels (vasculopathic CN palsies), FBC/CRP/ESR (if patient 50 years or older to rule out GCA)
  - Blood pressure: vasculopathic CN palsies
  - ICE pack test/Tensilon test: myasthenia gravis
  - Repetitive stimulation electromyography (EMG): myasthenia gravis
  - Hess chart: for incomitant strabismus

  - CT scan: if orbital fracture is suspected, sight threatening TED is suspected, partial CN III palsy (rule out a posterior communicating artery aneurysm) is identified or multiple cranial nerves are involved
  - Forced duction testing: verify a restrictive process

3.17.6 Restriction of Extraocular Motility in Orbital Fractures

3.17.6.1 Differential Diagnosis of Enophthalmos

- Bony defects: orbital fractures, congenital orbital wall defects
- Small globe: microphthalmos, nanophthalmos, phthisis bulbi, orbital implant
- Soft tissue atrophy: post-irradiation, scleroderma, cicatrizing tumours

3.17.6.2 Classification of Blow Out Fractures

- Orbital rim remains intact: fracture affects the floor (antral blowout), medial wall (ethmoidal blow out), combined antral and ethmoidal blow out
- Orbital rim fractured in addition to an antral, ethmoidal, or combined blow out

3.17.6.3 Classification of Orbital Floor Blow Out Fractures

- Type I: limited elevation of affected eye from mechanical restriction
- Type II: limited depression of affected eye from IR muscle palsy
- Type III: combined limited elevation and depression from mechanical restriction and IR muscle palsy, respectively

3.17.6.4 Examination

- Orbital floor fracture: vertical diplopia with limitation of both upgaze and downgaze (upgaze is commonly more affected than downgaze resulting in downward displacement of the small field of BSV)
- Type I orbital floor blow out fracture:
  - Limitation of ocular movement on up gaze
  - Positive FDT for mechanical restriction with the greatest limitation in elevation and abduction
  - Field of BSV is reduced in upgaze
- Type II orbital floor blow out fracture:
  - Limitation of ocular movement on down-gaze
  - Negative FDT for mechanical restriction on depression
- Type III orbital floor blow out fracture:
  - Limitation of ocular movement on up-gaze with positive FDT for mechanical restriction, with the greatest restriction in elevation and abduction
  - Limitation of ocular movement on downgaze with negative FDT for mechanical restriction on depression
  - Patient often has small central island of BSV, but is considerably handicapped by diplopia on downgaze
- Medial wall fracture (most often seen in association with a blowout fracture of the orbital floor): horizontal diplopia with restriction of abduction (mechanical restriction) and adduction (either mechanical restriction or to a neurogenic palsy of the MR)
- Backwards (enophthalmos) ± downward displacement (herniation of fat from the inferior part of the orbit into the antrum) of the globe
- Retraction of the globe (on elevation in a floor blow out fracture and on abduction in medial wall blow out fracture): occurs when the eye moves away from the site of entrapment
- Infraorbital anaesthesia (damage to infraorbital nerve): loss of sensation to ipsilateral cheek and upper teeth
- >5 mm difference in IOP in primary position and in position of gaze in which movement is restricted

3.17.6.5 Investigations

- CT scan: tear drop sign (small clump of soft tissue lying outside the orbit), missing rectus sign (absence of IR above orbital floor), muscle rounding sign (rounding of IR muscle)
- Hess chart: mechanical restriction
- Field of binocular single vision (BSV)
- Forced duction testing (FDT)

3.17.6.6 Treatment

- Advise patients to refrain from nose blowing
- Antibiotic prophylaxis
- Type I orbital floor blow out fracture:
  - Conservative treatment: prisms, occlusion
  - Surgical treatment (avoid if it puts the field of BSV in the primary position and down-gaze at risk): recession of contralateral IO muscle ± contralateral SR muscle
- Type II orbital floor blow out fracture:
  - Conservative treatment (continued for at least 9–12 months from the time of injury to allow spontaneous recovery of IR muscle function): prisms, occlusion
  - Surgical treatment: recession of contralateral SR ± inverse Knapp procedure
- Type III orbital floor blow out fracture:
  - Conservative treatment: occlusion
  - Surgical treatment: IR and SR recessions of the unaffected eye
- Medial wall blow-out fracture:
  - Conservative (continued for at least 9–12 months from the time of injury to allow spontaneous recovery of IR muscle function): prisms, occlusion
  - Surgical treatment: limitation of adduction due to MR muscle palsy is corrected by an ipsilateral MR resection/LR recession if palsy is partial and by a transposition of the SR and IR to the MR + LR weakening by Botox if palsy is complete

3.17.6.7 Indications for Surgical Intervention in Orbital Floor Fractures

- Immediate:
  - Persistent oculocardiac reflex
  - Young patient with "white eyed" trapdoor fracture
  - Significant facial asymmetry
- Early (<2 weeks):
  - Persistent symptomatic diplopia (diplopia within 30° of fixation)
  - Significant enophthalmos (>2 mm)
  - Hypoglobus
  - Progressive infraorbital anesthesia
  - Fracture involving >50% of the orbital floor
- Observation:
  - Minimal diplopia (e.g. just in upgaze)
  - Minimal restriction
  - Minimal enophthalmos

3.17.7 Restriction of Extraocular Motility in TED

3.17.7.1 Examination

See Sect. 3.15.4.2.

3.17.7.2 Investigation

See Sect. 3.15.4.2.

3.17.7.3 Treatment

- Conservative:
  (a) Treatment of diplopia: prisms, Botox, occlusion (last resort)
- Surgical:
  (a) Aims of extraocular muscle surgery are to improve the patient's appearance and to establish a field of binocular single vision in the primary position and on down-gaze, extending the area into other fields of gaze if possible
  (b) Patient should be euthyroid and the ocular muscle imbalance should have remained stable for at least 3 months before considering surgery
  (c) Categorise the ocular motility disturbances into recognisable patterns:
    1. Unilateral or grossly asymmetrical bilateral restriction of elevation
       - Incomitant (increase in vertical deviation on upgaze and a reduction on downgaze, usually with an intact inferior field of BSV): mechanical restriction of ipsilateral IR — treat with ipsilateral IR recession
       - Concomitant (vertical deviation that is the same on upgaze and which decreases minimally or not at all on downgaze, usually with no field of BSV): mechanical restriction of ipsilateral IR + contralateral SR — treat with IR recession ± SR recession

2. Unilateral or grossly asymmetric bilateral restriction of abduction
   - Incomitant (ET which increases in the direction of mechanical restriction and reduces in the opposite field of gaze + face turn away from the side with the mechanical restriction + intact field of BSV): mechanical restriction of ipsilateral MR — treat with ipsilateral MR recession
   - Concomitant (ET in all positions of gaze): bilateral mechanical restriction of both MR — treat with unilateral or bilateral MR recession
3. Unilateral or grossly asymmetric bilateral restriction of both elevation and abduction: management is the same as for pattern (1) and (2)
4. Bilateral symmetric restriction of elevation
   - Neither eye is able to maintain fixation in primary position
   - Asymmetrical mechanical restriction of elevation, with a − 2 to −3 restriction in the more mobile eye
   - A pattern ET is present on upgaze, with a convergence retraction movement as the eyes attempt to move into the field of maximum restriction
   - Contraction of the SR, if present, will restrict movement on down-gaze
   - Treat with bilateral IR recession
5. Bilateral restriction of both elevation and abduction
6. Mechanical restriction of the superior rectus muscles resulting in limited down-gaze
   - Limitation of depression that is greatest in abduction
   - Treat with SR recession

3.18 Angle Closure (Table 3.17)

3.18.1 Risk Factors for Angle Closure

- Inuit/South East Asians/Chinese
- Hyperopia with short axial length

Table 3.17 Angle closure terminology

- Angle closure is characterised by apposition of the peripheral iris against the trabecular meshwork, resulting in obstruction of aqueous outflow
- Primary angle closure suspect (PACS)/Occludable angle: ≥2 quadrants (180°) of iridotrabecular contact (ITC), normal IOP, no PAS, normal optic nerve (ZAP trial - see Table 3.20)
- Primary angle closure (PAC): ≥2 quadrants (180°) of ITC, raised IOP (>21 mmHg) and/or PAS, normal optic nerve (EAGLE study - see Table 3.19) — 30% in 5 years develop PACG
- Primary angle-closure glaucoma (PACG): PAC with disc or reproducible field defects consistent with glaucoma (EAGLE - see Table 3.19)

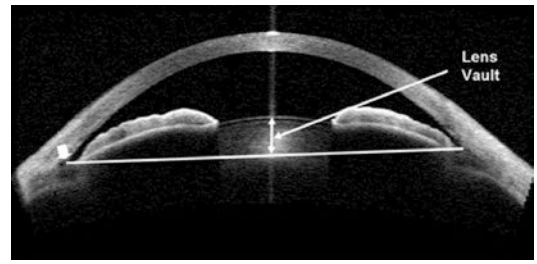

Fig. 3.28 Anterior lens vault

- Older age: reduced depth and volume of the AC
- Anterior lens vault (see Fig. 3.28): perpendicular distance between the anterior pole of the lens and the horizontal line joining the two scleral spurs on horizontal anterior segment OCT — eyes with angle closure have greater lens vault compared with normal eyes

3.18.2 Mechanisms of Angle Closure

- Pupil-block (most common mechanism): strong apposition of iris sphincter to anterior lens capsule (mid-dilated pupil), increased fluid pressure in PC causes a forward shift of the iris, anterior movement of iris results in closure of AC angle
  - Acute angle closure ± glaucoma
  - Sub-acute angle closure ± glaucoma: symptoms intermittent (colour halos around lights from corneal epithelial oedema — blue-green central halo and yellow-red peripheral halo) or absent

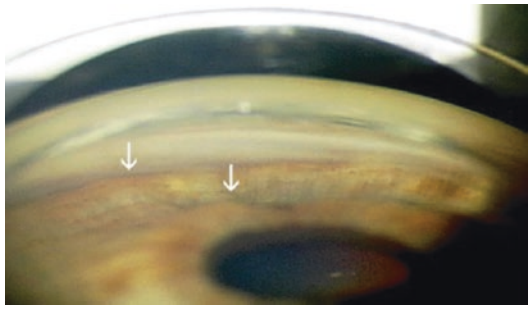

Fig. 3.29 Gonioscopic view of a patient with a plateau iris configuration showing the double hump sign (white arrows) on indentation gonioscopy

  - Chronic angle closure ± glaucoma: IOP chronically elevated with varying degree of PAS (usually broad based and starts in the superior quadrant — narrowest)
  - Combined mechanisms glaucoma: angle initially closed, PI performed, angle open but IOP remains high
- Plateau iris:
  - Plateau iris configuration (see Fig. 3.29): pre-iridotomy anatomic appearance, anterior position of ciliary body and processes, flat iris plane, closed AC angle, normal central AC depth, gonioscopy (double-hump sign on indentation gonioscopy — central iris moves posteriorly, peripheral hump created from anterior ciliary body pushing iris root forward, central hump created by iris sitting on anterior lens capsule)
  - Plateau iris syndrome: angle closure in eye with plateau iris configuration despite presence of a patent PI
  - Secondary angle closure

3.18.3 History

- Ask about risk factors for angle closure (see Sect. 3.18.1)

3.18.4 Examination

- Bilateral (PAC) or unilateral (secondary angle closure, e.g. phacomorphic) shallow peripheral AC: Van Herick's method — direct a narrow-slit beam at 60° onto the cornea just anterior to the limbus, AC considered narrow if distance between the anterior iris and posterior cornea is <1/4 of the corneal thickness
- Normal Central AC depth
- Fixed semi-dilated pupil with diffuse iris atrophy/transillumination defects: suggestive of previous acute angle closure attack
- Glaucomflecken: small anterior subcapsular opacities (lens epithelial necrosis) suggestive of previous acute angle closure attack
- Check IOP
- Perform gonioscopy: open or closed angle, PAS
- Examine the optic disc for signs of glaucoma:
  - Generalised signs: CDR 0.7 or more, asymmetry of CDR of 0.2 or more, progressive enlargement of cup
  - Focal signs: rim thinning/notching (ISNT rule), regional pallor, NFL haemorrhage, NFL loss

3.18.5 Investigations

- HVF: early: paracentral defect, nasal step (IT or ST rim thinning), temporal wedge (nasal disc thinning) / late: arcuate defect, double arcuate defect, central vision only

3.18.6 Treatment

- If IOP raised:
  - Immediate IOP reduction with IV acetazolamide (Diamox), topical β blockers, PGAs, α2 agonists ± IV mannitol
  - Instillation of miotic once IOP reduced to break the pupil block
- PACS: prophylactic Yag PI's (see Table 3.18)
- PAC: Yag PI (see Table 3.18), lens extraction ± goniosynechialysis, trabeculectomy
- PACG: Yag PI (see Table 3.18), lens extraction ± goniosynechialysis, trabeculectomy
- Plateau iris syndrome: iridoplasty, lens extraction

Table 3.18 Yag PI procedure

- Indications: therapeutic — angle closure with pupil block, prophylactic — PACS, fellow eye in AACG (approximately 50–75% of patients who develop acute angle closure in one eye will have an attack in the fellow, unoperated eye within 5–10 years)
- Consent: risks — bleeding, inflammation, pressure spike, monocular diplopia, failure/need for retreatment, corneal burns (if shallow AC)
- Pre-procedure: instill topical pilocarpine 2% (tightens the iris), topical Iopidine 1% (prevents IOP spike + reduce bleeding), topical anaesthetic, set up laser — two to three pulses of 3–6 mJ, angle the beam (beam should not be perpendicular), position the Abraham CL
- During procedure: identify suitable iridotomy site — superior (hidden by normal lid position), peripheral, and ideally in an iris crypt, focus and fire laser — success indicated by a forward gush of pigment loaded aqueous
- Post-procedure: check IOP at 30–60 min post PI, topical steroid, follow-up in outpatient's clinic in 2 weeks

3.18.7 Other Diagnoses to Consider

- Trauma (surgical or non-surgical): sectoral iris atrophy/transillumination defects, mydriasis

3.18.8 Management of Acute Angle Closure (AAC) Attack

- Lowering of IOP in affected eye:
  - Systemic: IV acetazolamide (Diamox) 500 mg STAT (then 250 mg PO QDS)
  - Topical:
    - β-blocker
    - α2 adrenergic agonists
    - Prostaglandin analogues
    - Topical steroids
  - Check IOP hourly until adequate control
  - If IOP not responding to above treatments: admit patient, systemic mannitol 20% IV 1 g/kg
  - If IOP still not responding: acute YAG PI (if corneal oedema not obscuring view)
  - If IOP still not responding: review diagnosis (? malignant glaucoma) ± repeat YAG PI ± AC paracentesis ± cyclodiode ± surgical PI ± laser iridoplasty ± emergency cataract extraction
- Break the pupillary block and open the AC angle in affected eye (once IOP reduced):
  - Pilocarpine 2%
  - Yag PI
- Prevention of AAC attack in contralateral non-affected eye (50% to 75% of patients who develop acute angle closure in one eye will have an attack in the fellow eye):
  - Pilocarpine 2% followed by Yag PI

3.19 Normal Tension Glaucoma (NTG) (Table 3.21)

3.19.1 History

- History of Raynaud's disease
- History of migraines

3.19.2 Examination

- Check VA, colour vision, RAPD
- Check IOP: <21 mmHg
- Perform gonioscopy: open angle
- Examine the optic nerve for signs of glaucoma:
  - Generalised signs: CDR 0.7 or more, asymmetry of CDR of 0.2 or more, progressive enlargement of cup
  - Focal signs: rim thinning/notching (ISNT rule), regional pallor, NFL haemorrhage, NFL loss

3.19.3 Investigations

- HVF: early: paracentral defect, nasal step (IT or ST rim thinning), temporal wedge (nasal disc thinning) / late: arcuate defect, double arcuate defect, central vision only
- Phasing: look for IOP spikes (diurnal fluctuations in IOP)

Table 3.19 Summary of the effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE) study (Azuara-Blanco et al. 2016)

- Primary outcome: a multicentre RCT to assess the efficacy, safety, and cost-effectiveness of clear-lens extraction (CLE) compared with standard care (SC) with laser PI plus topical medications as first line treatment in people with newly diagnosed PACG or PAC with IOP ≥30 mmHg
- Methods:
  - Inclusion criteria: phakic, age ≥50, newly diagnosed PAC with IOP ≥30 mmHg or PACG
  - Exclusion criteria: symptomatic cataract, advanced glaucoma (MD >−15 dB or CDR ≥0.9), previous AAC attack or who has undergone previous laser or ocular surgery
  - Groups: SC group — PI, laser trabeculoplasty if angle closure persisted, escalation of medical treatment, trabeculectomy / CLE group — phaco + IOL, escalation of medical treatment, trabeculectomy (target IOP 15–20 mmHg for both groups)
  - Primary endpoints: European QOL 5-dimension (EQ5D) questionnaire, IOP, incremental cost-effectiveness ratio (ICER — cost to NHS/QALY)
  - Secondary endpoints: trabeculectomy rate. Field loss
  - Follow up: 3 years
- Results: 419 patients
  - Primary endpoints: EQ-5D questionnaire scores and IOP (16.6 CLE vs 17.9 SC) at 36 months was statistically significantly better in the CLE group, at 3 years 61% of the CLE group and 21% of the SC group were on no glaucoma medications and the mean number of drops was 0.4 in the CLE group and 1.3 in the SC group
  - Secondary endpoints: VF severity at 3 years was similar in the two treatment groups, there was six trabeculectomies in the SC group but only one in the CLE group
  - Safety/complications: 3% (6 patients with one having irreversible loss of two lines) had intraoperative complications from the CLE group, 8% (16 patients) had minor bleeding from PI
- Conclusion of study: In the context of newly diagnosed PAC with IOP ≥30 mmHg or PACG with no visually significant cataract, CLE results in greater overall QOL, lower IOP, and fewer drops when compared to standard care (PI and topical medications). Immediate CLE would seem likely to be cost effective, particularly in the longer term

Table 3.20 Summary of the Zhongshan Angle Closure Prevention (ZAP) trial (He et al. 2019)

- Primary outcome: Assess the efficacy of laser PI in preventing the development of primary angle-closure or acute angle closure in Chinese people with primary angle closure suspects (PACS)
- Methods:
  - Inclusion criteria: age 50–70 years old; bilateral PACS (defined as six or more clock hours of angle circumference in which the posterior trabecular meshwork was not visible under non-indentation gonioscopy) in the absence of primary angle-closure or primary angle-closure glaucoma; IOP 21 mmHg or less; vertical CDR less than 0.7; cup to disc asymmetry was no greater than 0.2; borderline or normal glaucoma hemifield test
  - Exclusion criteria: PAS observed on gonioscopy; severe health problems resulting in life expectancy of less than 1 year; previous intraocular surgery or penetrating eye injury; media opacity preventing laser PI; BCVA worse than 20/40; IOP greater than 15 mmHg after dilation or after a 15-min dark room prone provocative testing
  - Groups: Laser PI in one randomly selected eye, with the contralateral eye serving as an untreated control
  - Primary endpoint: Incidence of primary angle closure (IOP above 24 mmHg on two separate occasions, development of at least 1 clock hour of PAS in any quadrant, or an episode of acute angle closure) by eyes by 72 months
  - Secondary endpoint: presenting VA, IOP, total angle width on gonioscopy, limbal AC depth, adverse events during laser PI or at any follow up visits
  - Follow up: 72 months
- Results: 889 patients
  - Primary endpoint: incidence of PAC in 4.19 per 1000 eye-years in treated eyes compared with 7.97 per 1000 eye-years in untreated eyes ($p = 0.024$). Eyes that underwent laser PI had a 47% reduction in the risk of developing PAC or an acute attack compared to untreated eyes. One in 20 untreated eyes developed PAC at 72 months. NNT was 44 to prevent one case of new PAC disease over 72 months. Rate of developing any angle closure endpoint in PACS eyes was less than 1% per year.
  - Secondary endpoint: similar presenting VA and IOP measurements between the two arms; laser PI itself was safe and no long-term adverse events were identified; angles were significantly larger after laser PI than in untreated eyes
- Conclusions of study: Benefit of prophylactic laser PI is limited; therefore, widespread prophylactic laser PI for PACS is not recommended

Table 3.21 Definition of NTG

• Open normal appearing angles who have glaucomatous optic nerve head and VF damage despite pressures that have never been documented above 21 mmHg

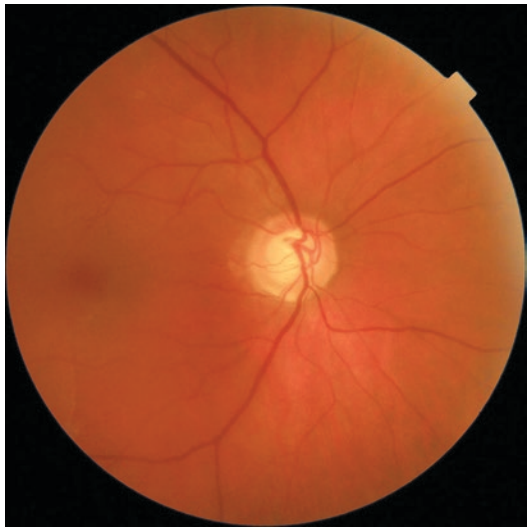

Fig. 3.30 Colour fundus image of a patient with NTG showing increased optic disc cupping and prominent inferior notching with loss of normal sheen of NFL radiating temporally from notch

- 24-hour BP monitoring: nocturnal hypotension
- Ensure correlation between optic nerve head findings and VF defects (see Figs. 3.30 and 3.31)
- Neuro-imaging (see Table 3.22 for indications)

3.19.4 Treatment

- Reduce IOP by 30% (see Table 3.23): medical treatment initially and surgical treatment (laser trabeculoplasty, trabeculectomy, GDI) after failure of maximal tolerated medical therapy (MTMT)
- Avoid drug induced nocturnal systemic hypotension: liaise with GP/physicians

3.19.5 Risk Factors for Progression of NTG

- Female sex
- History of migraines
- Disc haemorrhages at diagnosis

3.19.6 Other Diagnoses to Consider

- POAG
- Secondary open angle glaucomas: steroid induced, PDS, PXF
- PACG
- Ischaemic optic neuropathy
- Compressive lesions of the optic nerve and tract
- Optic neuritis
- Trauma

3.20 Chronic Open Angle Glaucoma (COAG) (Table 3.24)

3.20.1 Risk Factors for COAG

- Age
- African-Caribbean: more frequent, younger onset, more severe
- Positive Family History
- High myopia: scleral canal morphology making disc more vulnerable
- Raised IOP

3.20.2 History

- Ask about family history of glaucoma

3.20.3 Examination

- NICE Guidance [NG81]:
  - IOP measurement using Goldmann applanation tonometry (slit-lamp mounted)

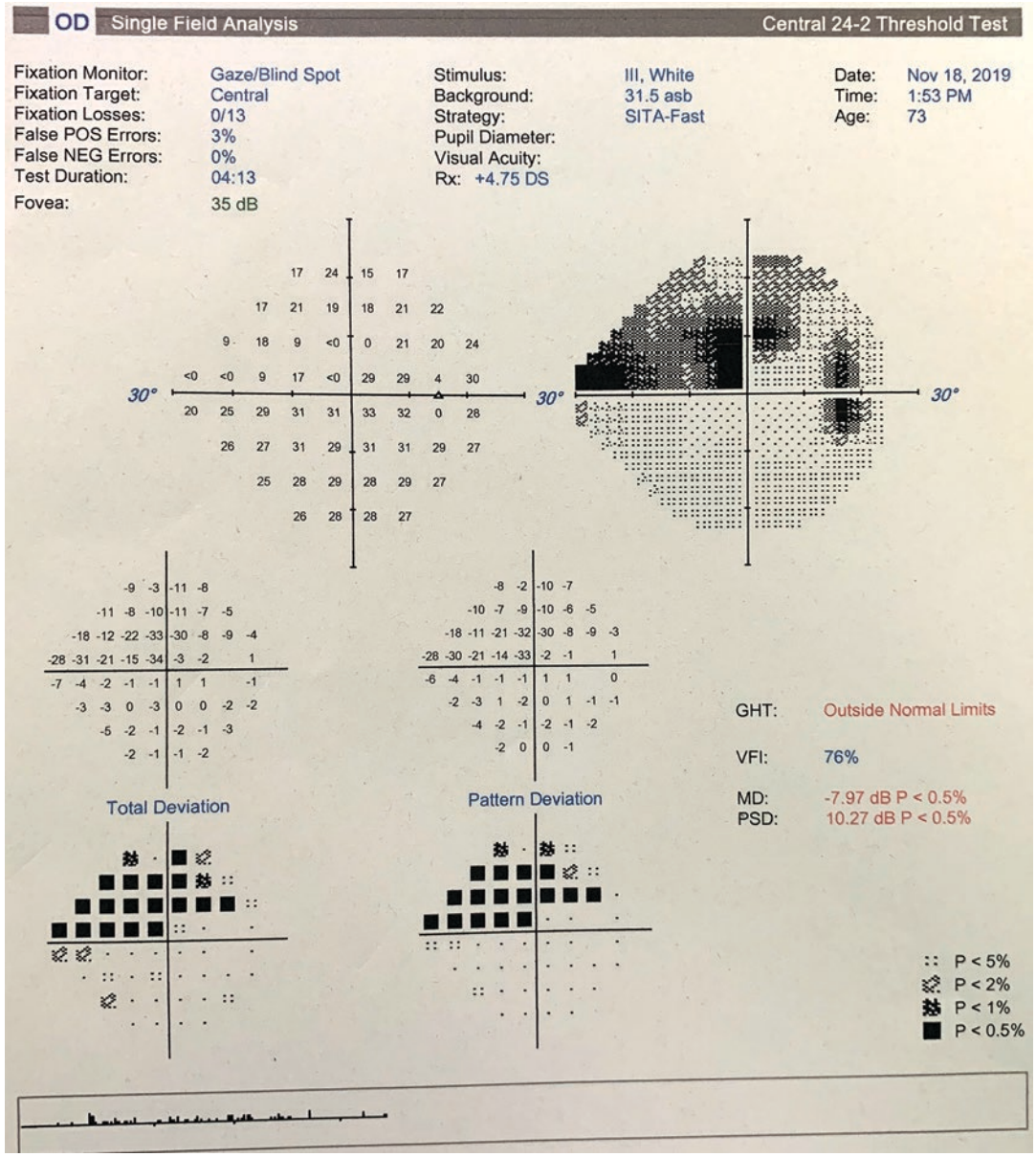

Fig. 3.31 30-2 HVF of the same patient as in Fig. 3.30 showing a superior arcuate scotoma which correlates to the prominent inferior optic disc notching as shown in Fig. 3.30

Table 3.22 Indications for neuro-imaging

- General factors: age <50, new onset or increased severity of headaches, localising neurologic symptoms other than migraines
- Ocular factors: positive visual symptoms, colour vision abnormalities, lack of disc and VF correlation, VF defect respecting the vertical midline, optic disc pallor, unexplained VA reduction, RAPD

– Central corneal thickness (CCT) measurement
– Peripheral anterior chamber configuration and depth assessments using gonioscopy: open angle
– Optic nerve assessment and fundus examination using stereoscopic slit lamp biomicroscopy, with pupil dilatation.

Table 3.23 Summary of the Collaborative Normal Tension Glaucoma Study (Collaborative Normal-Tension Glaucoma Study Group 1998)

- Primary outcome: An RCT conducted to determine whether IOP played a part in the pathogenic process of NTG
- Methods:
  - Inclusion criteria: unilateral or bilateral NTG with optic disc abnormalities and VF defects characteristic of glaucoma, no single IOP reading of >24 mmHg with median IOP reading (from ten baseline IOP readings) of ≤20 mmHg, age >20 years and <90 years, pupil diameter ≥2.5 mm
  - Exclusion criteria: patients taking systemic β-blockers or clonidine, eyes with previous laser treatment, previous ocular surgery, or cyclodestructive procedures, non-glaucomatous conditions that might later affect the visual field, narrow angles or advanced field loss, BCVA <20/30
  - Groups: One eye of each patient was randomised to either the untreated control arm or to the 30% IOP reduction (from the mean of the last three pre-randomisation pressure readings) arm by medical (pilocarpine) or surgical (ALT or trabeculectomy) intervention. Randomisation began if eye had VF defect that threatened fixation, VF progression was demonstrated, a change in the optic nerve head appearance was confirmed, or a disc haemorrhage was noted.
  - Primary end points: VF progression, change in degree of glaucomatous optic disc damage, or both
  - Follow up: 5 years (initial report)
- Results: 145 eyes of 145 patients
  - Lowering of IOP by 30% reduces the rate of VF progression from 35% to 12%
  - 12% of eyes showed VF progression despite an IOP reduction of 30%
  - 65% of patients showed no progression during follow up of 5 years or more
  - 30% IOP reduction could be achieved and maintained in 57% of patients with topical medications, ALT, or both
  - Females, especially those with a hx of migraine and patients with disc haemorrhages at diagnosis were all more likely to progress
- Conclusions: IOP is part of the pathogenic process of NTG. Therapy that is effective in lowering IOP and free of adverse effects would be expected to be beneficial in patients who are at risk of disease progression

Table 3.24 Useful information about COAG

- Adult onset optic neuropathy with glaucomatous optic disc and/or VF changes, open angles, IOP >21 mmHg and no other underlying disease
- Prevalence (proportion of a population with the disease at a given time point) of 1% >40 years old/ prevalence of 10% >75 years old + Caucasian

- Optic disc signs in glaucoma:
  - Generalised signs: CDR 0.7 or more, asymmetry of CDR of 0.2 or more, progressive enlargement of cup
  - Focal signs: rim thinning/notching (ISNT rule not obeyed), regional pallor, NFL haemorrhage, NFL loss

3.20.4 Investigations

- NICE Guidance [NG81]:
  - Visual field assessment using standard automated perimetry (central threshold testing)
  - Optic nerve head (ONH) image for baseline documentation
- HVF signs in glaucoma:
  - Early: paracentral defect, nasal step (IT or ST rim thinning), temporal wedge (nasal disc thinning)
  - Late: arcuate defect, double arcuate defect, central vision only
  - Ensure correlation between optic nerve head findings and VF defects

3.20.5 Diagnosis

- NICE Guidance [NG81]
  - COAG: any IOP, ONH damage, normal/ uncertain/defects on VF
  - Suspected COAG: any IOP, suspicious of possible glaucoma on ONH, normal or uncertain VF

3.20.6 Treatment (see Tables 3.25, 3.26 and 3.27)

- Suspected COAG pathway (NICE Guidance [NG81])
  - If IOP less than 24 mmHg:
    Do not offer treatment initially and reassess
    - If conversion to COAG is present at reassessment: manage patient according to COAG pathway (see below)
    - If uncertain of conversion to COAG and IOP controlled at reassessment: further reassess at 6–12 months.
    - If IOP not controlled and conversion to COAG uncertain or not detected at reassessment: offer generic prostaglandins as first line treatment if IOP is 24 mmHg or more. Review at 1–4 months after starting treatment. Further reassess at 6–12 months if IOP controlled and COAG uncertain or 12–18 months If IOP controlled with treatment and conversion to COAG not detected
    - If conversion to COAG not detected and IOP controlled at reassessment: further reassess at 12–18 months — patient can subsequently be discharged if patient is not on any treatment, IOP remains controlled and results no longer suggest COAG
  - If IOP 24 mmHg or more:
    Offer generic prostaglandins and reassess at 1–4 months after starting treatment:
    - If conversion to COAG is present at reassessment: manage patient according to COAG pathway (see below)
    - If IOP is not controlled and conversion to COAG is uncertain at reassessment: review management plan (use alternative second line treatments) and further reassess at 1–4 months
    - If IOP is controlled and conversion to COAG is uncertain at reassessment: reassess at 6–12 months
    - If IOP is controlled and conversion to COAG not detected at reassessment: reassess at 12–18 months
- COAG pathway (NICE Guidance [NG81])
  - For patients with early or moderate COAG: offer a generic prostaglandin.
  - For patients with advanced COAG: offer surgery with augmentation and interim pharmacological treatment. Offer a generic prostaglandin if patient is not keen for surgical intervention
  - Check treatment is effective and tolerated at 1–4 months for people starting or changing treatment. If prostaglandins have not been effective then offer alternative second line treatments
  - Follow up regime:
    If IOP controlled:
    - Reassess at 2–6 months if progression or uncertain progression. If progression of COAG is subsequently detected then offer patient surgery with augmentation
    - Reassess at 6–12 months if progression not detected and high clinical risk
    - Reassess at 12–18 months if progression not detected and low clinical risk

    If IOP not controlled:
    - Reassess at 1–2 months if uncertain progression or progression. If progression of COAG or IOP remains uncontrolled then offer patient surgery with augmentation
    - Reassess at 1–4 months if progression not detected
- Other options to consider:
  - Selective laser trabeculoplasty (see Table 3.28)
  - Glaucoma drainage implants
  - Cyclodiode

Table 3.25 Summary of the Early Manifest Glaucoma Trial (Heijl et al. 2002)

- Primary outcome: Compare the effect of immediate therapy to lower the IOP, vs no treatment or later treatment, on the progression of newly detected open-angle glaucoma (OAG) as measured by increasing VF loss or optic disc changes
- Methods:
  - Inclusion criteria: diagnosis of early manifest open angle glaucoma (POAG, NTG, PXF glaucoma), age between 50 and 80 years, reproducible glaucomatous VF defects in at least one eye
  - Exclusion criteria: advanced VF loss (MD > −16 dB) or a threat to fixation, VA <20/40, mean IOP >30 mmHg or any IOP >35 mmHg in at least one eye, any condition precluding reliable results of perimetry or optic disc photography, the use of study interventions, or 4 years of follow up, cataractous lens changes exceeding gradings of N1, C2, or P1 according to the lens opacification classification system (LOCS) II
  - Groups: Treatment group — 360° ALT + betaxolol 0.5% BD (reduced mean IOP by 25%, a reduction maintained throughout follow up — IOP reduction was larger in eyes with a baseline IOP of ≥21 mmHg [29%] than in eyes with a baseline IOP of <21 mmHg [18%])/ non-treatment group
  - Primary endpoints: Progression of either glaucomatous VF defects or optic disc cupping
  - Follow up: median 6 years (initial report)
- Results: 255 patients
  - Primary endpoints: After a median of 6 years of follow-up, progression was less frequent in the treatment group (45%) than in controls (62%) and occurred significantly later in treated patients (median time to progression was 18 months longer in the treatment group than the control group). Each 1 mmHg of decreased IOP was related to an approximately 10% lowering of risk.
  - Safety/complications: Nuclear cataract developed faster in the treated group and six had surgery (compared to two controls)
  - Risk factors for progression (in decreasing order of risk): PXF, bilateral glaucoma, higher baseline IOP (≥21 mmHg), worse baseline MD (more than −4 dB), older age, frequent disc haemorrhages post treatment (not associated with IOP or treatment)
- Conclusion of study: Clear beneficial effects of lowering IOP on delaying the onset of progression, with lower rates of progression in the treatment group than the control group

3.21 Aqueous Misdirection (Fig. 3.32)

3.21.1 Definition

- Posterior misdirection of aqueous into the vitreous causing anterior displacement of vitreous, ciliary processes, and lens/IOL with secondary angle closure

3.21.2 Risk Factors

- Short axial length
- Nanophthalmos
- Uveal effusion syndrome
- History of angle closure: previous acute angle closure, chronic angle closure
- Post procedures: trabeculectomy, GDI, cataract extraction, surgical iridectomy, Yag PI

3.21.3 History

- Ask about history of angle closure
- Ask about previous ocular surgeries including trabeculectomy, GDI, cataract extraction, surgical iridectomy, Yag PI

3.21.4 Examination

- Raised IOP
- Shallow/flat central and peripheral AC — significant myopic shift
- Patent PI — no iris bombe
- No suprachoroidal haemorrhage or detachments on fundus examination

3.21.5 Treatment

- Ensure patent PI before commencing treatment
- Medical:
  - Atropine
  - Reduction of IOP with systemic and topical medications

Table 3.26 Summary of the Advanced Glaucoma Intervention Study (The AGIS Investigators 1998, 2001)

- Primary outcome: Assess the effects of two surgical intervention sequences in patients with advanced POAG after the failure of medical therapy.
- Methods:
  - Inclusion criteria: eyes with either advanced (glaucoma not controlled adequately despite MTMT in the presence of glaucomatous VF defect) POAG without previous surgery or advanced POAG in a phakic eye 4 weeks or more after PI, phakic VA better than 20/80 [6/24]), age 35–80 years old, reproducible glaucomatous VF defects in at least one eye, a table of specific combinations of elevated IOP and VF defect was used to define uncontrolled glaucoma and was used to determine if a second or third operation was required
  - Exclusion criteria: secondary glaucoma or congenital angle anomalies, other active eye diseases that cause field loss or previous surgery
  - Groups: A-T-T group: ALT followed if necessary by trabeculectomy, followed if necessary by repeat trabeculectomy/T-A-T group: trabeculectomy followed if necessary by ALT, followed if necessary by repeat trabeculectomy
  - Primary endpoints: VA and/or VF (score 0 normal to-20 blind)
  - Follow up: 7 years (initial report)
- Results: 332 black patients, 249 white patients, 10 patients of other races
  - Low post intervention IOP is associated with reduced progression of VF defect

    Predictive analysis (IOP averaged over the first three 6-month visits: designed to assess whether IOP during early follow up is predictive of subsequent change from baseline in VF defect score): Initial mean IOP <14 mmHg over the first 18 months after surgery had a mean VF score deterioration of less than one point from baseline and those with an initial IOP ≥18 mmHg had a mean score deterioration of three points over 7 years

    Associative analysis (% of visits over the first 6 years of follow up for which an eye presented with IOP <18 mmHg): IOP <18 mmHg on 100% of follow up visits over 6 years resulted in a mean score deterioration of close to zero, but those achieving IOP <18 mmHg on <100% of visits had a mean deterioration of two to three points
  - After 7 years of follow-up, overall (both races) the mean decrease in IOP from baseline is greater in eyes assigned to T-A-T than in those assigned to A-T-T
  - In white patient's VF was better preserved by T-A-T only after the first year of follow-up and thereafter favour the A-T-T sequence, and acuity was better preserved by A-T-T throughout follow up.
  - For black patients, VF and acuity loss were less for eyes in the A-T-T sequence
  - Complications of trabeculectomy: relative risk of cataract in the 5 years after trabeculectomy was 1.78 compared to those participants who avoided trabeculectomy. Youth and high IOP were key risk factors for failure of either ALT or trabeculectomy. Diabetes mellitus or persistent postop inflammation were also significant risk factors for trabeculectomy failure
- Conclusion of study: Low IOP reduces risk of VF progression. Data supports the use of the A-T-T sequence for all black patients. For white patients the data supports the use of the T-A-T sequence

- Laser:
  - Yag disruption of posterior capsule (if pseudophakic) + anterior vitreous face
  - Trans-scleral cyclodiode photocoagulation of the ciliary body in one quadrant
- Surgical:
  - If pseudophakic: pars plana vitrectomy + posterior capsulotomy
  - If phakic: cataract extraction + posterior capsulotomy + pars plana vitrectomy

3.22 Vernal Keratoconjunctivitis (VKC) (Fig. 3.33 and Table 3.29)

3.22.1 Associated Diseases

- HSV keratitis
- Keratoconus
- Anterior capsular cataract

Table 3.27 Summary of the Collaborative Initial Glaucoma Treatment Study (Lichter et al. 2001)

- Primary outcome: Determine whether patients with newly diagnosed OAG are best treated by initial treatment with topical medications or by immediate trabeculectomy
- Methods:
  - Inclusion criteria: newly diagnosed OAG (POAG, PXF glaucoma, pigmentary glaucoma); one of three combinations of qualifying IOP (IOP ≥20 mmHg), VF changes, and optic disc findings; BCVA of 20/40 or better in both eyes; age 25–75 years; no prior ocular surgery; little (≤14 cumulative days of topical therapy) or no prior treatment of glaucoma
  - Exclusion criteria: use of glaucoma medication >14 cumulative days; CIGST VF score >16 in either eye; ocular disease that might affect measurement of IOP, VA, or VF; undergone ophthalmic laser, refractive, conjunctival, or intraocular surgery in either eye; PDR, DMO, or NPDR with >10 MA's by clinical count; current or expected chronic use of corticosteroids; likely require cataract surgery within 1 year of randomisation
  - Groups: topical medication group — escalating drops, if further treatment was required start with ALT, then trabeculectomy ± 5-FU drops, then trabeculectomy + anti-fibrotic agent, then medication/trabeculectomy group — trabeculectomy ± 5-FU, if further treatment was required start with ALT, then escalating drops, then repeat trabeculectomy + anti-fibrotic agent, then medication
  - Primary endpoint: increasing CIGST VF score reflecting increased VF loss
  - Secondary endpoints: change in VA, change in IOP, occurrence of cataract extraction, QOL (questionnaire)
  - Follow up: 5 years (initial report)
- Results: 607 patients
  - Primary endpoint: no significant difference in VF scores at 5 years in both groups
  - Secondary endpoints: initial VA decrease in the trabeculectomy group that was not observed in the topical medication group, resulted in lower mean VA in the trabeculectomy group that persisted through 3.5 years after surgery. After that time, mean VA levels were comparable in the two treatment groups up to 5 years of follow up (VA less in trabeculectomy group compared to topical medications group); there were no significant differences in the QOL between the two groups; both groups had significantly decreased mean IOP after treatment initiation (3 mmHg better reduction with trabeculectomy) although the amount of decrease was greater in the trabeculectomy group (48% in trabeculectomy group vs 35% in the topical medication group), and the difference was maintained over 5 years of observation; the trabeculectomy group had a higher cataract extraction probability over time; risk factors for VF progression: older age, non-white race, DM, development of cataract, maximal IOP, IOP fluctuation between visits
- Conclusion of study: CIGTS clinical outcomes do not suggest a change in the way ophthalmologists currently manage their patients with newly diagnosed OAG

3.22.2 History

- History of atopy: eczema, hayfever, asthma

3.22.3 Examination

- Skin of the lids may be eczematous with excoriation at the canthi ± reactive ptosis
- Palpebral VKC: giant papillae (>1 mm diameter) giving a cobblestone appearance ± mucus accumulation between the papillae
- Limbal VKC: white Horner-Trantas dots (aggregates of degenerated eosinophils and epithelial cells) on the apices of papillae at the limbus
- Cornea:
  - Punctate epithelial erosions on the superior and central cornea with adherent mucus
  - Macroerosion: confluent area of epithelium breakdown
  - Vernal plaque (shield ulcer): deposition of calcium and mucus deposited on Bowman's layer — prevent re-epithelialisation

3.22.4 Treatment

- Inflammation:
  - Topical mast cell stabilisers (e.g. cromolyn sodium)/topical anti-histamines (e.g. emedastine)/topical mast cell stabilisers + anti-histamines (e.g. olopatadine, lodoxamide)
  - Topical corticosteroids: risk of glaucoma, ocular herpetic infection, cataract
  - Topical acetylcysteine: reduces mucus adherence to the cornea during exacerbations

Table 3.28 Summary of the selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT) trial (Guzzard et al. 2019)

- Primary outcome: To compare eye drops versus selective laser trabeculoplasty (SLT) as first line treatment for OAG or OHT
- Methods:
  - Inclusion criteria: newly diagnosed untreated OAG or OHT in one or both eyes; qualified for treatment according to NICE guidelines; VF loss with MD not worse than −12 dB in the better eye or −15 dB in the worse eye with corresponding damage to the optic nerve for those with OAG; VA 6/36 or better in eyes to be treated; no previous intraocular surgery except uncomplicated phacoemulsification at least 1 year prior to randomisation
  - Exclusion criteria: patients with contraindications to SLT (history of uveitis, unable to sit at slit-lamp, poor view of trabecular meshwork); patients unable to use eye drops; patients who had a symptomatic cataract; patients who were under active treatment for another ophthalmic condition
  - Groups: eye drops group, SLT group
  - Primary endpoint: health-related quality of life measured using the EuroQol EQ-5D 5 levels utility scores
  - Secondary endpoint(s): glaucoma-specific treatment related quality of life assessed with the Glaucoma Utility Index (GUI); patient-reported disease and treatment-related symptoms assessed using the Glaucoma Symptom Scale (GSS); patient-reported visual function assessed using the Glaucoma Quality of Life-15 questionnaire (GQL-15); clinical effectiveness (proportion of visits at target IOP, number of treatment escalations); visual function (VA, VF); safety
  - Follow up: 36 months
- Results: 652 patients
  - Primary endpoint: no significant difference in EQ-5D scores at 36 months
  - Secondary endpoints: mean GUI score, mean GQL-15 and mean GSS scores were similar between the two groups at 36 months; two groups had similar endpoint VA, IOP, and VF loss MD; 74.2% of eyes in the SLT group remained drop free at 36 months; SLT was more cost effective; 11 eyes (1.8%) required trabeculectomy in the eye drops group compared with none in the SLT group
- Conclusions of study: SLT should be offered as first line treatment for OAG and OHT

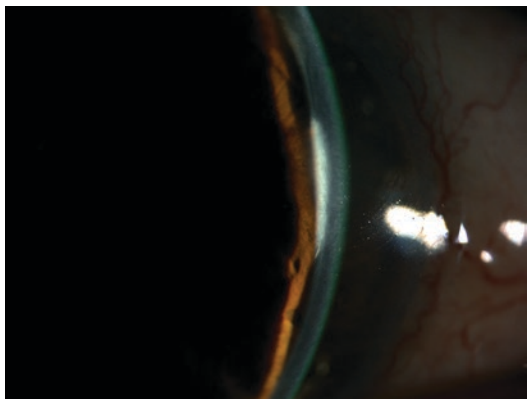

Fig. 3.32 Anterior segment image of a patient with aqueous misdirection showing a shallow central AC

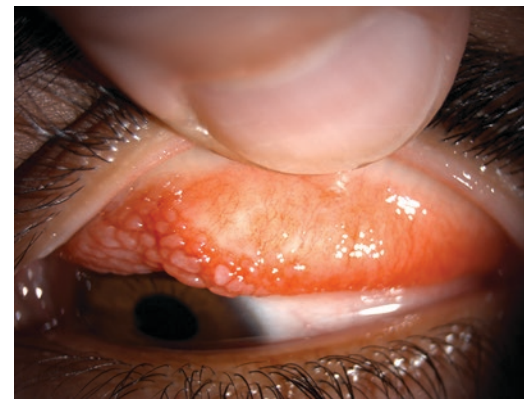

Fig. 3.33 Anterior segment image of a patient with VKC showing giant papillae

  - Steroid (e.g. triamcinolone 40 mg/mL) injected into the supratarsal space after lid eversion: reserved for severe disease not responding to topical treatment or given following surgery for a vernal plaque
  - Topical cyclosporin A: alternative to topical corticosteroid
  - Oral steroid: reserved for severe unremitting disease with corneal complications
- Vernal plaque:
  - Debridement of plaque
  - Superficial keratectomy after the local allergic inflammatory disease has been medically controlled

Table 3.29 Key facts about VKC

- Atopic disease in which an allergic response is mounted to common environmental allergens, dust, or pollen
- Usually develops in the first decade of life (82% by age 10 years with a mean age of 7 years)
- More common in males
- Seasonal propensity

Table 3.30 Key facts of AKC

- Bilateral, chronic inflammation of the conjunctiva and lids associated with atopic dermatitis
- Onset of disease usually in the second through fifth decade
- Male:Female ratio as 2.4:1
- Consists of type I and type IV hypersensitivity reactions

3.23 Atopic Keratoconjunctivitis (AKC) (Table 3.30)

3.23.1 History

- Periocular itching associated with dermatitis
- History of seasonal or exposure-related exacerbations is usually present
- Family History of atopic disease in one or both parents
- History of atopy: asthma, eczema, hayfever
- History of CL wear: lack of CL wear aids in differentiating AKC from GPC

3.23.2 Examination

- Periocular and lid dermatitis — scaling, flaking skin with reddened base
- Loss of cilia, meibomianitis, keratinization, and punctal ectropion.
- The conjunctiva of the tarsal surfaces has a papillary reaction and possibly a pale white oedema ± subepithelial fibrosis
- Inferior fornix shortening with symblepharon
- Perilimbal gelatinous hypertrophy ± Horner-Trantas dots
- Punctate epithelial keratopathy, persistent epithelial defects, scarring, microbial ulceration, and neovascularisation
- Anterior or posterior subcapsular cataract.
- Signs of KC (see Sect. 8.21)

3.23.3 Investigations

- Skin testing to determine nature of the irritants
- Corneal topography if clinical signs of KC is present

3.23.4 Treatment

- Environmental control: removal of environmental irritants in both the home and the employment or school setting
- Correction of trichiasis or lid position abnormalities if contributing in any way to corneal compromise, correction of blepharitis, lubricants for dry eye
- Topical medications: anti-histamines, topical steroids (for 7–10 days) — potential for cataract or glaucoma, mast-cell stabilisers — recommended for patients with perennial symptoms, mast cell stabilisers + anti-histamines (olopatadine, azelastine, epinastine, ketotifen), ciclosporin A, tacrolimus
- Systemic medications: oral prednisolone in cases of uncontrolled dermatitis with vision threatening complications

3.23.5 Other Diagnoses to Consider

- Vernal keratoconjunctivitis (VKC) — AKC patients are usually older and have major lid involvement compared to patients with VKC
- Giant papillary conjunctivitis (GPC) — history of CL wear
- Seasonal allergic conjunctivitis (SAC) — no or markedly diminished symptoms out of their season and show no evidence of chronic inflammation in the conjunctiva
- Perennial allergic conjunctivitis

3.24 Bacterial Keratitis (Fig. 3.34)

3.24.1 Risk Factors

- Ocular
  - Contact lens wear (gram negative pseudomonas is the most common cause of bacterial keratitis in CL wearers)
  - Trauma causing a corneal abrasion or epithelial defect: chemical and thermal injuries, foreign bodies, local irradiation
  - Corneal surgery: LASIK, RK, PK ± loose sutures
  - Ocular surface disease: dry eye, bullous keratopathy, chronic keratitis (e.g. HSV), neurotrophic keratitis (e.g. HSV, HZV, tumours of the cerebellopontine angle with CN VII palsy), OCP, SJS, atopic keratoconjunctivitis
  - Lid abnormalities: entropion, lagophthalmos, trichiasis
- Systemic
  - Immunosuppression: diabetes, drugs
  - Vitamin A deficiency
- Other
  - Male sex

3.24.2 History

- Ask about risk factors for bacterial keratitis (see Sect. 3.24.1)

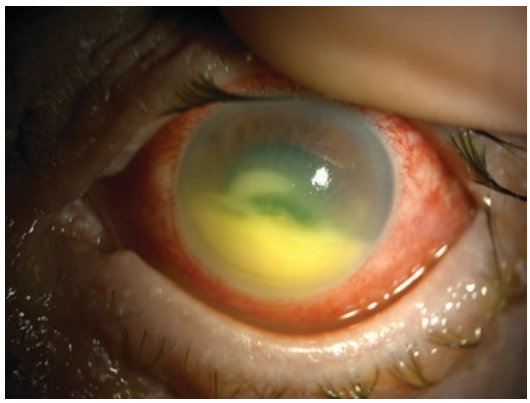

Fig. 3.34 Anterior segment image of a patient with a bacterial keratitis

- For contact lens wearers, enquire about the following
  - Type of contact lens worn
  - Duration of contact lens wear
  - Hygiene of contact lenses
  - Does the patient sleep, swim or shower with contact lens in their eyes?
  - Lifestyle: wearing of contact lenses for sports or at work
  - Purchasing of contact lenses: over the internet, from opticians

3.24.3 Examination

- Features suggestive of bacterial keratitis
  - Suppurative stromal infiltrate (particularly those greater than 1 mm in size) with indistinct edges, oedema, and white cell infiltration in surrounding stroma
  - Epithelial defect is typically present
  - An AC reaction is often seen ± hypopyon
- Pseudomonas: stromal necrosis exhibiting a shaggy surface and adherent mucopurulent exudate

3.24.4 Investigation

- Corneal scrapes
  - Stain: gram stain, giemsa stain, Ziehl-Neelson stain
  - Culture: blood agar, chocolate agar, Lowenstein-Jensen
- If patient wears CL's — send lenses, solutions, cases for culture

3.24.5 Treatment

- Admit and daily review if
  - Severe infection: >1.5 mm diameter infiltrate, central corneal ulcer, hypopyon
  - Poor compliance likely: either with administering drops or returning for daily review
  - Only eye
  - Failing to improve

- Stop CL wear if patient wears CL
- Medications
  - Intensive topical broad-spectrum antibiotics
  - Cycloplegia
  - Topical corticosteroids: no difference in BCVA at 3 months (Srinivasan et al. 2012) but corticosteroid use was associated with a mean one-line improvement in BCVA at 12 months among patients with non-Nocardia ulcers (Srinivasan et al. 2014)
- If an initial scrape result in no growth and current regimen proves clinically ineffective, consider withholding treatment for 12–24 h before re-scraping or performing a formal corneal biopsy
- Surgery
  - Cyanoacrylate tissue adhesive: progressive corneal thinning, corneal perforation
  - Therapeutic PK: impending or overt perforation
  - Optical PK: can be used after complete resolution of the corneal infection to remove corneal scarring and to rehabilitate vision
  - Conjunctival flap: non healing corneal ulcer

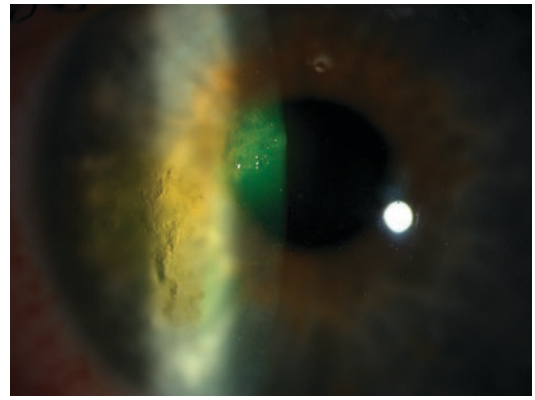

Fig. 3.35 Anterior segment image of a patient with a dendritic ulcer

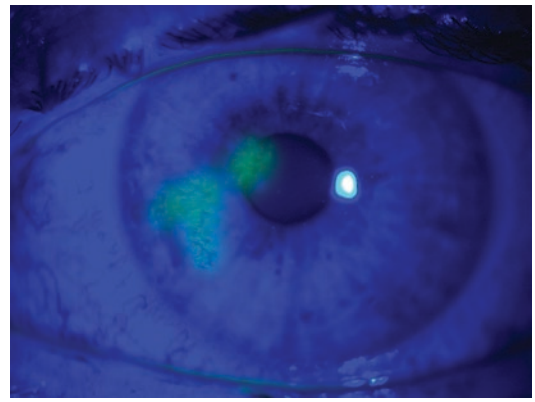

Fig. 3.36 Anterior segment image of the same patient in Fig. 3.35 showing fluorescein staining of the dendritic lesion

3.25 Herpes Simplex Virus (HSV) Keratitis

3.25.1 History

- History of cold sores
- History of previous attacks of HSV keratitis

3.25.2 Examination

- Epithelial keratitis (see Figs. 3.35 and 3.36)
  - Dendritic ulcer: branching linear lesion with terminal bulbs (stain with fluorescein) and raised swollen epithelial borders (negative staining with fluorescein + stain with rose bengal), lesion extends through basement membrane (true ulcer) — pseudodendrites are raised rather than ulcerated and do not stain with fluorescein
  - Geographic ulcer: non-linear enlarged dendritic ulcer, scalloped borders of swollen epithelial cells
  - Marginal ulcer: anterior stromal infiltrate with overlying ED, limbal injection with neovascularisation of the infiltrate, progresses centrally
  - Corneal vesicles: small raised clear vesicles in the epithelium
- Stromal keratitis (see Fig. 3.37)
  - Necrotising stromal keratitis: stromal infiltration with overlying epithelial defect
  - Interstitial keratitis: stromal infiltration with intact overlying epithelium, stromal oedema, stromal neovascularisation ± ghost vessels ± lipid exudation

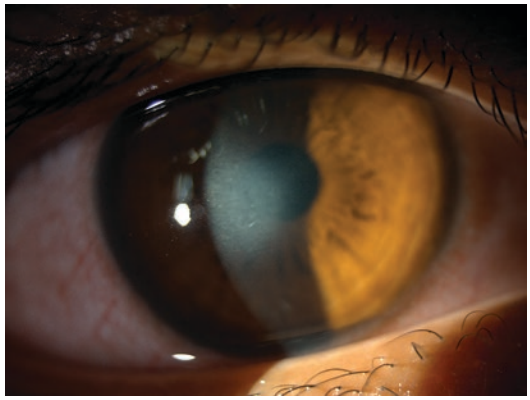

Fig. 3.37 Anterior segment image of a patient with HSV stromal keratitis

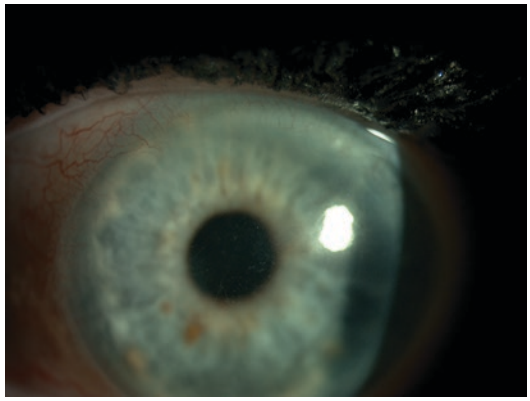

Fig. 3.38 Anterior segment image of a patient with HSV endotheliitis

- Endotheliitis (see Fig. 3.38)
  - Disciform endotheliitis: round area of stromal ± epithelial oedema without stromal infiltrate overlying KP's, iritis
  - Diffuse endotheliitis: diffuse stromal oedema with diffusely scattered KP's
  - Linear endotheliitis: line of KP's accompanied by stromal + epithelial oedema between the KP's and the limbus
- Iridocyclitis
  - Sectoral iris atrophy
  - Raised IOP

3.25.3 Treatment

- Epithelial keratitis
  - Topical aciclovir 3% 5×/day for 10–14 days
  - Cycloplegia
- Stromal keratitis
  - Topical corticosteroids (defer where possible until epithelium intact)
  - Topical aciclovir 3% 5×/day to prevent outbreak of epithelial keratitis
  - Cycloplegia
  - Monitor IOP and treat if necessary
- Endotheliitis
  - Topical corticosteroids (defer where possible until epithelium intact)
  - Topical aciclovir 3% 5×/day to prevent outbreak of epithelial keratitis
  - Oral aciclovir 400 mg 5×/day for 7 days then 400 mg BD
  - Cycloplegia
  - Monitor IOP and treat if necessary
- Iridocyclitis
  - Topical corticosteroids
  - Oral aciclovir 400 mg 5×/day for 7 days
  - Cycloplegia
  - Monitor IOP and treat if necessary

3.25.4 Herpetic Eye Disease Study (HEDS)

- A set of multicentre RCT's designed to address six HSV-associated clinical questions:
  - Topical corticosteroids in treating stromal keratitis already on a topical antiviral (Wilhelmus et al. 1994)

    Time to failure (new focal stromal inflammation, increase in area of inflammed cornea) comparison was highly in favour of the treatment group at 10 weeks (73% vs 26%)

    Delaying steroid initiation does not affect visual outcome at 6 months

- Oral aciclovir in treating stromal keratitis already on a topical steroid and antiviral (Barron et al. 1994)
  Time to treatment failure at 16 weeks was not delayed significantly in the treatment group
  No benefit of adding oral aciclovir (400 mg 5×/day) in patient on topical antiviral and topical corticosteroids
- Oral aciclovir in treating iridocyclitis already on topical steroid (The Herpetic Eye Disease Study Group 1996)
  The rate ratio for the protective effect of aciclovir on time to failure at 10 weeks bordered on significant
- Oral aciclovir in preventing recurrence of epithelial and stromal keratitis (The Herpetic Eye Disease Study Group 1998)
  Aciclovir prophylaxis (400 mg BD) reduced recurrence of ocular HSV from 32% (placebo group) to 19% (aciclovir group) at 12 months
  Effect applied to both epithelial (14% to 9%) and stromal keratitis (28% to 14%) — greatest for stromal keratitis patients with at least one prior episode
- Demographic and disease-specific predictors of recurrent HSV keratitis (Herpetic Eye Disease Study Group 2001)
  History of epithelial keratitis was not a risk factor for recurrent epithelial keratitis
  The more prior episodes of stromal keratitis, the higher the likelihood of recurrence
- Risk factors for recurrence of ocular HSV (Herpetic Eye Disease Study Group 2000)
  Stress, systemic infection, sunlight exposure, menstruation, CL wear, and eye injury were not deemed significant

3.26 Acanthamoeba Keratitis (Fig. 3.39)

3.26.1 Risk Factors

- Contact lens wear: poor CL hygiene (e.g. rinsing in tap water), extended wear CL (soft — 90% or rigid CL), swimming with CL insitu (ponds, hot tubs, swimming pools)
- Trauma: agricultural or rural setting

3.26.2 History

- Disproportionate incapacitating ocular pain to clinical findings
- Ask about risk factors (see Sect. 3.26.1)

3.26.3 Examination

- Radial keratoneuritis: represents amoebic migration along the corneal nerves (can also be seen in pseudomonas keratitis)
- Epitheliitis (flat diffuse microcystic form with perilimbal sparing) ± epithelial ridges ± pseudodendrites
- Anterior stromal infiltrate ± overlying ED that progresses circumferentially to form a

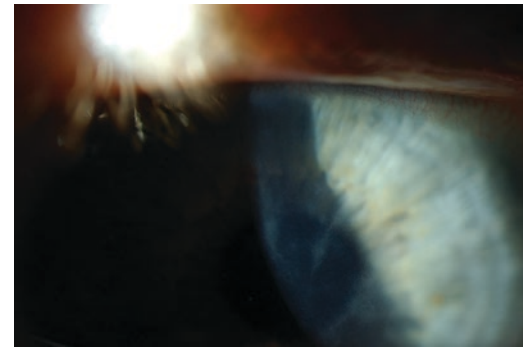

Fig. 3.39 Anterior segment image of a patient with acanthamoeba keratitis showing radial keratoneuritis

stromal ring infiltrate with subsequent stromal scarring
- Scleritis
- Uveitis

3.26.4 Investigations

- Corneal scrape:
  - Culture on non-nutrient agar with E. coli overlay
  - Stain with Calcofluor white (stains cysts visualised under UV light) or gram stain (stains organisms)
  - DNA detection using PCR
- If patient wears CL's — send lenses, solutions, cases for culture
- Invivo confocal microscopy (IVCM):
  - Direct visualisation of cysts (high contrast round bodies — see Fig. 3.40)
- Corneal biopsy for culture if other tests negative but there is a strong suspicion of acanthamoeba keratitis

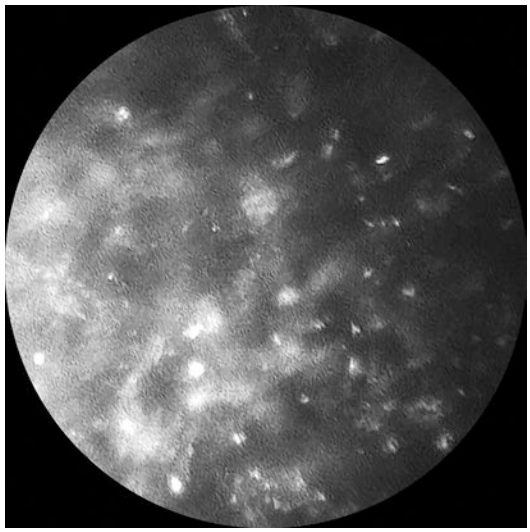

Fig. 3.40 IVCM of a patient with acanthamoeba keratitis showing high contrast round bodies suggestive of acanthamoeba cysts

3.26.5 Treatment

- Admit and daily review
- Stop CL wear if patient wears CL
- Educate patient about CL wear and hygiene
- Medical:
  - Intensive topical anti-amoebic agents:
    Biguanides: PHMB 0.02% or chlorhexidine 0.02%
    Diamidine: propamidine 0.1% or hexamidine 0.1%
  - Cyclopentolate
  - Scleritis: systemic steroids ± steroid sparing agent
- Surgical:
  - Severe stromal scarring: PK an option once free of infection — 3 months after discontinuation of anti-acanthamoebal medications
  - Extensive stromal necrosis and impending or overt perforation: emergency PK — high risk of persistent or recurrent disease in grafted tissue
  - Severe intractable pain: enucleation

3.27 Fungal Keratitis (Fig. 3.41)

3.27.1 Risk Factors

- Trauma involving plant matter
- Contact lens wear
- Immunosuppression: topical corticosteroids, alcoholism, diabetes, HIV positive, systemic immunosuppression
- Corneal surgery: PK, LASIK, RK
- Chronic keratitis: neurotrophic cornea (HSV, HZV, topical anaesthetic abuse), dry eye

3.27.2 History

- Ask about risk factors (see Sect. 3.27.1)

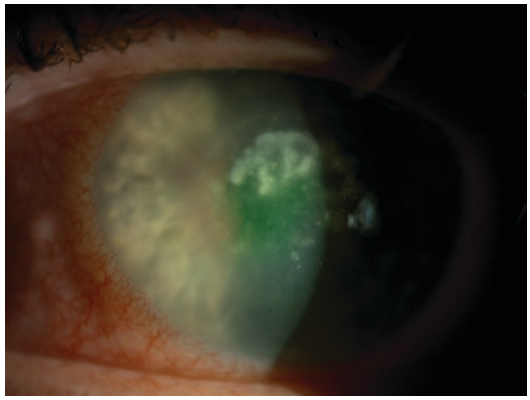

Fig. 3.41 Anterior segment image of a patient with a fungal keratitis

3.27.3 Examination

- Non-specific: conjunctival injection, epithelial defect, stromal infiltration, AC reaction or hypopyon
- Filamentous fungi: stromal infiltrates with irregular feathery margins, elevated edges, dry rough texture, satellite lesions
- Yeast: localised with "button" appearance, expanding stromal infiltrate, relatively small epithelial ulceration
- It is not always possible to differentiate clinically between bacterial and fungal keratitis, especially in cases where yeasts are the infecting fungi

3.27.4 Investigations

- Corneal scrapes
  - Stains: gram stain, giemsa stain, Grocott's methenamine silver (GMS) stain
  - Culture: Sabouraud's dextrose agar (for most fungi), sheep blood agar (for fusarium)
- In vivo confocal microscopy (IVCM): look for filaments (see Fig. 3.42)
- Corneal biopsy if corneal scrapings for culture are negative and there is a strong suspicion of fungal keratitis

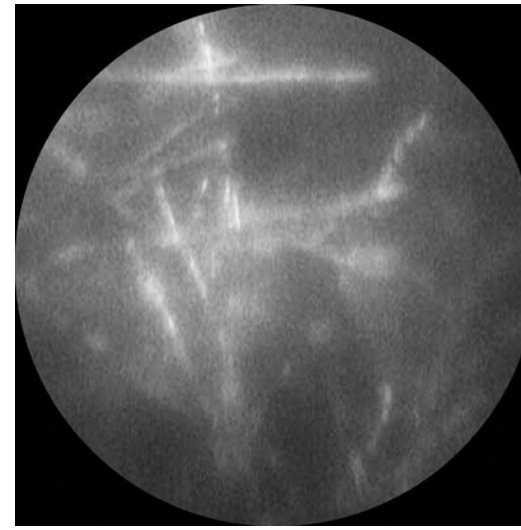

Fig. 3.42 IVCM of a patient with a fungal keratitis secondary to a filamentous fungus

3.27.5 Treatment

- Admit and daily review, stop CL wear if patient wears CL
- Medical treatment:
  - Topical:
    Intensive topical broad spectrum anti-fungal agents: natamycin 5% (fusarium infection), voriconazole 1% (candidal infection), amphotericin 0.15% (candida, aspergillus): natamycin treatment is associated with significantly better clinical and microbiological outcomes than voriconazole treatment for filamentous fungal keratitis (Prajna et al. 2013)
    Cyclopentolate
  - Systemic:
    Oral fluconazole (candida and aspergillus)
    Oral voriconazole
- Visual rehabilitation after a treated fungal infection begins with spectacle correction and hard contact lenses. If these modalities fail to improve vision sufficiently — surgery
- Surgical treatment: PK in a quiet but visually compromised eye or therapeutic PK or for

impending or overt perforation, conjunctival flap for a non-healing ulcer

3.28 Ectopia Lentis (Fig. 3.43)

3.28.1 Differential Diagnosis

- Systemic
  - Marfan syndrome (AD — fibrillin gene on chromosome 15, clinical diagnosis):
    Ocular: bilateral superotemporal lens subluxation, accommodation intact, RD, glaucoma, keratoconus, high myopia, blue sclera
    Musculoskeletal: arachnodactyly, disproportionately long limbed, joint laxity, high-arched palate
    Cardiovascular: mitral valve prolapse, aortic dilatation, aortic regurgitation, aortic dissection
  - Weill-Marchesani syndrome (AR):
    Ocular: bilateral inferonasal lens subluxation, microspherophakia, RD, high myopia
    Musculoskeletal: brachydacytyly, short stature
    Neurological: reduced IQ
  - Homocystinuria (AR):
    Ocular: bilateral inferonasal lens subluxation, myopia, glaucoma
    Musculoskeletal: marfanoid habitus
    Haematological: thromboses, especially associated with GA
    Neurological: reduced IQ3.28.2
  - Hyperlysemia (AR)
  - Sulfite oxidase deficiency (AR)
  - Ehlers-Danlos syndrome (AR)
- Ocular
  - Trauma
  - PXF
  - High myopia
  - Hypermature cataract
  - Buphthalmos
  - Ciliary body tumour
  - Aniridia
  - Hereditary ectopia lentis
  - Ectopia lentis et pupillae: lens subluxation with pupil displacement in opposite direction

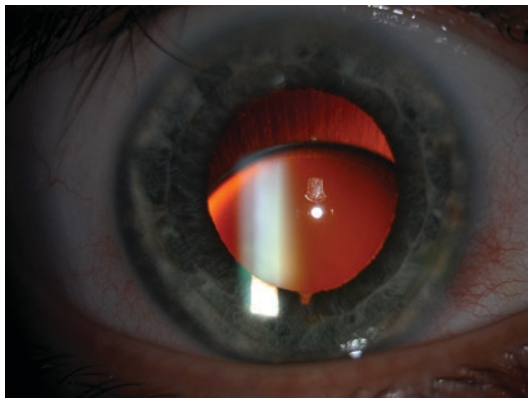

Fig. 3.43 Anterior segment image of a patient with ectopic lentis

3.28.2 History

- History of trauma
- Positive family history
- Cardiovascular or musculoskeletal abnormalities in patient or family

3.28.3 Examination

- Ectopia lentis ± uveitis ± corneal decompensation ± pupil block
- Check IOP
- Perform gonioscopy to look for angle closure
- Perform a dilated fundus examination to look for RD, signs of glaucoma
- Systemic examination

3.28.4 Investigations

- Refraction
- Cardiac evaluation (echocardiography) in Marfan's syndrome
- Plasma homocysteine level in homocystinaemia

3.28.5 Treatment

- Genetic counselling
- Vision
  - Correction of refractive error: spectacles, CL
  - Surgical: Lensectomy ± vitrectomy with post-op aphakia correction or secondary artisan IOL, or scleral sutured PCIOL
- Ectopia lentis
  - Migration of lens into AC: mydriatics + lie patient on their back to permit posterior migration of lens behind the iris
  - Pupil block glaucoma: Yag PI and topical medications to reduce IOP
  - Lensectomy ± vitrectomy ± artisan IOL ± scleral sutured PCIOL:
  - Indications:
    Lens induced glaucoma/uveitis
    Lens in AC with corneal decompensation
    Lens opacity is mature or hypermature
    Inadequate VA not correctable by refraction
    RD

3.29 High Myopia and Cataract Surgery

3.29.1 Preoperative Considerations

- Assess visual potential: myopic degeneration, macular holes, myopic foveoschisis, previous RD repair with silicone oil
- Discuss refractive outcome: anisometropia — less need for second eye operation if patient already wears CL
- Biometry
  - Use of IOL master rather than A-scan to measure the axial length (AL) of the eye (posterior staphyloma can generate an erroneously long axial length when measured with the A scan giving rise to a postoperative hypermetropic refractive surprise)
  - Convert speed of sound through vitreous to 987 m/s on IOL master to measure true AL in a silicone oil (viscosity 1000 cSt) filled eye/true AL of a silicone oil filled (viscosity 1300 cSt) eye can be estimated from the measured AL (MAL) obtained on A/B scan US by multiplying MAL by a conversion factor of 0.71
  - Formula choice: SRK/T if axial length >26.5 (NICE Guidance [NG77])
  - IOL power choice: A constant increases as IOL power is lower, which leads to selection of a higher dioptric power implant to lessen the odds of a postoperative hyperopic surprise — select a power of IOL which leaves some residual of postoperative myopia
  - IOL material selection: avoid silicone lenses

3.29.2 Intraoperative Considerations

- Anaesthesia: retrobulbar and peribulbar anaesthesia carry the risk of perforation of the globe in a long, myopic eye
- Deeper AC: break reverse pupillary block by using the chopper to slightly tent up the iris at the pupillary margin to establish a channel for anterior-posterior fluid flow (equalise anterior and posterior chamber pressures), decrease infusion pressure by lowering bottle height (increase risk of surge)
- Increased risk of post-op RD (0.9–3.8% risk if AL >26.0 mm): prevent collapse of the AC when removing the phaco probe or I&A probe from the eye to avoid traction or tension on the vitreous during surgery (once AC collapses, the vitreous has a tendency to move anteriorly) — inject viscoelastic via the paracentesis prior to removing the phaco probe or IA probe from the eye
- Zonular weakness: minimise nuclear manipulation to protect damaged zonules from a previously vitrectomised eye

3.29.3 Postoperative Considerations

- Floppy large bag: postop refraction can take time to stabilise due to the variation in effective

lens position as the capsular bag shrinks and wraps around the IOL
- Repeat fundus exam to search for retinal breaks that may have been created during the surgery
- Timely surgery on the fellow eye (within 6 weeks) will minimise the imbalance caused by the large degree of anisometropia

3.30 Pseudoexfoliation and Cataract Surgery

3.30.1 Preoperative Considerations

- Risk of wipe out (progression of VF) to a vulnerable nerve
- Control of high IOP: risk for suprachoroidal haemorrhage
- Phacodonesis: when there is severe zonular instability, the surgeon may consider pars plana lensectomy with an ACIOL or sutured PCIOL
- Zonular dialysis: quantified by the number of clock hours involved — a capsular tension ring (CTR) can be used if 4 clock hours or less of zonule loss
- AC depth: AC depth <2.5 mm centrally may indicate anterior displacement of the lens-iris diaphragm from zonular weakness
- Poor mydriasis: look for iris atrophy and transillumination defects

3.30.2 Intraoperative Considerations

- Pupil size: ensure adequate pupil dilation by use of intracameral injection of phenylephrine, iris stretching or iris hooks
- Avoid overinflating AC with viscoelastic causing posterior pressure on the lens can further weakening the zonules
- Capsulorrhexis: large capsulorrhexis (risk of post-op anterior capsular phimosis), provide counter traction via the non-dominant hand using a second instrument via the paracentesis (if wrinkling of the anterior capsule when piercing the anterior capsule)
- Hydrodissection: avoid overfilling of the AC causing excessive zonular stress
- Nucleus removal: for soft nuclei consider prolapsing the nucleus anteriorly, for denser nuclei consider chopping techniques
- Cortex removal: lower flow rate and maximum vacuum settings, perform circumferential removal of cortex rather than radial stripping (less stress on zonules)
- Consider insertion of CTR if up to 4 clock hours of zonular dehiscence present
- IOL insertion: IOL placed in the capsular bag — orientation of haptics towards the area of zonular loss to bolster support at the equator / IOL placed in the ciliary sulcus — orientation of haptics 90° away from the area of zonular loss

3.30.3 Postoperative Considerations

- IOP spike: diamox for 3 days postoperatively

3.31 Intraoperative Floppy Iris Syndrome (IFIS)

3.31.1 Features

- Syndrome characterised by a triad of occurrences
  - Fluttering and billowing of the iris stroma in response to normal irrigation currents
  - A propensity for the floppy iris stroma to prolapse towards the phaco and side incisions
  - Progressive pupillary constriction that occurs during the surgical procedure

3.31.2 Preoperative Considerations

- Past or present use of α1-antagonists (tamsulosin, alfuzosin, doxazosin) in the treatment of BPH and HTN

3.31.3 Intraoperative Considerations

- Pupil size: intracameral injection of phenylephrine (0.25 mL 2.5% phenylephrine mixed with 1 mL BSS — 1:200 solution), iris hooks
- Wound construction: longer incision within the clear cornea and move incisions more anteriorly into the cornea to help with flow dynamics and iris prolapse

3.32 Corneal Endothelium in Cataract Surgery

3.32.1 Endothelial Cell Counts

- 4000 cells/mm^2 at birth
- 2500 cells/mm^2 in middle age
- 2000 cells/mm^2 in old age

3.32.2 Ophthalmic Viscosurgical Devices (OVDs)

- OVDs are solutions of long chain polymers
- Dispersive OVDs:
  - Lower viscosity + cause less IOP spikes (more difficult to remove from the eye)
  - Uses: isolate part of surgical field, e.g. protect cornea or keeping the iris or vitreous out of the way
  - Examples: Viscoat (sodium chondroitin sulfate + sodium hyaluronate with molecular weight of 100–500 kDa)
- Cohesive OVDs:
  - Higher viscosity + cause higher IOP spikes (easier to remove from the eye)
  - Uses: deep AC creation, opening the bag prior to IOL implantation
  - Examples: Healon (sodium hyaluronate with molecular weight of 1000–2000 kDa), Provisc (sodium hyaluronate with molecular weight of 1000–2000 kDa), Healon GV (sodium hyaluronate with molecular weight of 4000–8000 kDa)
- Viscoadaptive OVDs:
  - Has components of both cohesive and dispersive OVDs
  - At high flow rates (e.g. phacoemulsification) it acts like a dispersive OVD and stays within the eye to protect the corneal endothelium
  - At low flow rates (e.g. I/A) it acts like a cohesive OVD for easier removal
  - Example: Healon 5 (sodium hyaluronate with molecular weight of 4000–8000 kDa)

3.32.3 Soft-Shell Technique

- Dispersive OVD to protect the corneal endothelium
- Cohesive OVD to maintain the AC space

3.32.4 Ultimate Soft-Shell Technique

- Viscoadaptive OVD + Basic Salt Solution

3.32.5 Irrigating Solutions

- Basic Salt Solution
  - Composition per 1 mL: sodium and potassium chloride, calcium chloride dehydrate, magnesium chloride hexahydrate, sodium acetate trihydrate, sodium citrate dehydrate, sodium hydroxide, hydrochloric acid
- Basic Salt Solution Plus
  - Has been shown to minimise endothelial pleomorphism and polymegathism though Invivo studies
  - Part I: 480 mL solution in a 500 mL single dose bag to which the part II concentrate is added. Each mL of part I contains (five salts and a buffer): sodium and potassium chloride, dibasic sodium phosphate, sodium bicarbonate, hydrochloric acid, sodium hydroxide
  - Part II: sterile concentrate in a 20 mL single dose vial for addition to part I. Each mL of part II contains: calcium chloride dehydrate, magnesium chloride hexahydrate, dextrose (energy source), glutathione disulfide (antioxidant)

3.33 Endophthalmitis (Table 3.31)

3.33.1 Other Diagnoses to Consider

- Toxic anterior segment syndrome (TASS)
  - Acute post-operative non-infectious inflammatory reaction due to inadvertent entry of toxic substances in the AC
  - Rapid onset: 12–24 h post-surgery
  - Mild/moderate or no pain
  - Corneal oedema (limbus to limbus) with moderate-to-severe AC inflammation ± fibrin/hypopyon, raised IOP
  - Vitritis is rare
  - Highly sensitive to topical steroids
- Occult retention of lens cortex or nucleus
- Hypopyon uveitis (e.g. Behcet's)
- Inflammatory reaction to intravitreal drug

3.33.2 Investigations

- B-scan
  - Indication: significant media opacification prevents adequate view of the fundus
  - Findings: dispersed vitreous opacities with vitritis, chorioretinal thickening
  - Rule out RD or choroidals, dislocated lens material, retained foreign bodies

Table 3.31 Key facts about endophthalmitis

- National rate of post cataract surgery endophthalmitis was 0.14% in the BOSU study (Kamalarajah et al. 2004) and 0.055% in the Bolton study (Kelly et al. 2007)
- Acute post-operative endophthalmitis: usually 3–5 days after ocular surgery
- Chronic post-operative endophthalmitis: usually 6 weeks after ocular surgery
- White plaque on posterior capsule suggest Propionobacterium acnes infection
- Current advice is to continue with the local arrangements for preventative treatment of endophthalmitis if audited figures reveal a rate similar to the Bolton study. If figures are higher, the use of intracameral cefuroxime should be considered

3.33.3 Treatment of Acute Endophthalmitis

- Admit
- If VA hand motion (HM) or better
  - Perform a vitreous needle tap (27G needle attached to a TB syringe) ± AC tap (30G needle attached to a TB syringe) with simultaneous injection of intravitreal antibiotics (vancomycin 1 mg/0.1 mL + amikacin 0.4 mg/0.1 mL or ceftazidime 1 mg/0.1 mL)
  - Oral ciprofloxacin 750 mg BD: no evidence of clinical benefit
  - Corticosteroids: topical (e.g. dexamethasone 0.1% hourly), systemic (e.g. oral prednisolone 1 mg/kg OD rapidly reducing to zero over 7–10 days): no evidence it improves VA and should be avoided in fungal infections
  - If failure to respond at 48–72 h consider repeating needle vitreous tap ± AC tap with simultaneous injection of intravitreal antibiotics (repeat intravitreal antibiotics may increase the risk of retinal toxicity)
- If VA light perception (LP) of worse
  - Pars plana vitrectomy (PPV) with intravitreal injection of antibiotics:

    In the Endopthalmitis Vitrectomy Study (Endophthalmitis Vitrectomy Study Group 1995), patients with postop endophthalmitis within 6 weeks of cataract surgery who presented with LP only VA had a significant threefold improved chance of obtaining 6/12 vision after immediate vitrectomy compared to tap and inject
  - Oral ciprofloxacin 750 mg BD: no evidence of clinical benefit. Potential resistance from pseudomonas and gram-positive cocci organisms
  - Corticosteroids: topical (e.g. dexamethasone 0.1% hourly), systemic (e.g. oral prednisolone 1 mg/kg OD rapidly reducing to zero over 7–10 days): no evidence it improves VA and should be avoided in fungal infections

  - If failure to respond at 48–72 h consider repeating needle vitreous tap ± AC tap with simultaneous injection of intravitreal antibiotics (repeat intravitreal antibiotics may increase the risk of retinal toxicity)

3.33.4 Prevention

- Pre-operative
  - Identification and treatment of blepharitis, conjunctivitis, mucocele or chronic dacryocystitis before elective surgery is performed
  - Avoidance of intraocular procedures in patients with significant active non-ocular infections
- Intra-operative
  - Skin and conjunctival preparation with 5% povidone iodine 5 min before op
  - Eyelid speculum and careful draping to eliminate eyelashes from surgical field
  - Suturing of any leaking wounds at the completion of the operation
  - Avoidance of serious intraoperative complications such as PCR and vitreous loss and avoidance of overly prolonged surgery
  - Intracameral cefuroxime (1 mg in 0.1 mL) at the completion of cataract surgery:
    ESCRS study (ESCRS Endophthalmitis Study Group 2007): five-fold decrease in incidence of postoperative endophthalmitis with intracameral cefuroxime compared with topical levofloxacin
    NICE Guidance [NG77]: recommends use of intracameral cefuroxime during cataract surgery to prevent endophthalmitis
- Post-operative
  - Topical antibiotics

3.33.5 Prognosis

- Prognosis depends on organism (e.g. poor prognosis with pseudomonas, staphylococcus aureus and streptococcus pneumoniae), patient factors (e.g. diabetes, advanced age, post complicated cataract surgery), time to intravitreal injection

3.34 The RCOphth Ophthalmic Services Guidance on Managing an Outbreak of Post-Operative Endophthalmitis 2016

3.34.1 Outbreak Definition

- More than one case in a short time frame, e.g. days to weeks

3.34.2 Determine If There Is an Outbreak

- Incident report all cases
- Review cases for risk and causes with particular concern if
  - Analysis of the cases demonstrate a common organism especially an unusual organism
  - Analysis of the cases demonstrates the same apparent underlying cause of concern
  - Analysis of the cases demonstrates the cases related clearly to only one team member, one surgeon, one theatre/site, one session in the week, a particular instrument or consumables batch number
  - Two or more cases have arisen during the same theatre list
  - Cluster occurring over a very short time frame, e.g. days to weeks
- Regularly assess incidence
- Use agreed system as cut off for action

3.34.3 Notification

- Notify/involve colleagues: ophthalmology, risk team, microbiology, infection control, management (clinical and medical director)

- Make patients aware of symptoms and provide easy emergency postop access
- Consider resuming early follow up

3.34.4 Immediate Measures

- Consider cessation of all surgery/procedures
- Cease bilateral simultaneous cataract surgery if performed
- Ensure all know and follow current prophylaxis regime

3.34.5 Investigation

- Review cases and check all aspects for risks and common factors:
  - Patient factors — blepharitis, diabetes, concurrent systemic illness, vitreous loss, postop wound leak, duration of surgery, non-compliance with prescribed drops
  - Surgeon factors: surgical and draping technique
- Check theatre environment, cleanliness, airflow/ventilation system
- Microbiological sampling of intraocular tap samples (looking for a common organism or subtype), equipment, theatre, drugs, irrigating and viscoelastic solutions
- Review and obey theatre discipline and correct operating practices
- Ensure equipment/devices up to date, used properly, maintained well
- Check instrument cleaning and sterilisation procedures
- Keep detailed records of investigations and actions
- Eliminate specific cause if found
- If specific cause not found:
  - Revise and improve current prophylaxis protocol
  - Introduce intracameral antibiotics
  - Consider external review from other unit or College

3.35 Idiopathic Intracranial Hypertension (IIH) (Fig. 3.44 and Table 3.32)

3.35.1 Differential Diagnosis of Disc Swelling

- Pseudopapilloedema
  - Features:

No disc hyperaemia, no dilation of surface microvasculature, no blurring of retinal vessels at the disc margin

  - Causes:

    Optic disc drusen

    Myelinated peripapillary nerve fibers: dense white opacity

    Tilted discs

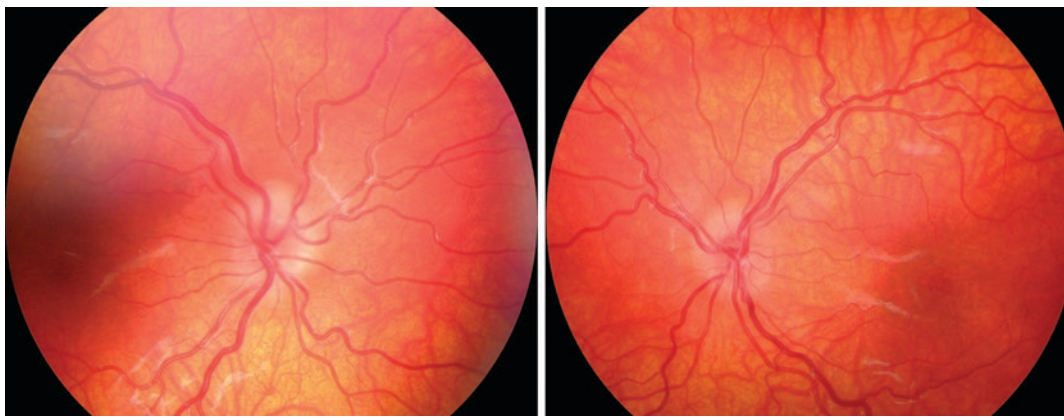

Fig. 3.44 Colour fundus image of a patient with IIH showing bilateral disc swelling

Table 3.32 Key facts about IIH

- The syndrome of increased ICP without ventriculomegaly or mass lesion, and with normal CSF composition
- Diagnosis of exclusion
- Obesity is the major risk factor

Hypermetropic discs
Myopic discs

- Papilloedema
  - Features:
    Patients retain good visual function (VA, VF, colour vision) until late in disease course regardless of how swollen the nerve appears
    Bilateral disc swelling
  - Causes:

Raised intracranial pressure (ICP)

- Local disc swelling
  - Causes:
    Inflammatory: optic neuritis, uveitis, scleritis
    Vascular: AION, CRVO, diabetic papillitis
    Granulomatous: TB, sarcoid
    Infiltrative: leukaemia, lymphoma
    Trauma causing hypotony
    Tumours of optic nerve: optic nerve sheath meningioma, glioma
    Hereditary: LHON
    Iatrogenic: surgery causing hypotony

3.35.2 Causes of Raised ICP

- Mass effect: tumours, haemorrhage, trauma — oedema, haematoma
- Increased CSF production: choroid plexus tumour
- Reduced CSF drainage: IIH
- Drugs ("I LOVE PTC"): isotretinoin, lithium, OCP, vitamin A derivatives, endocrine (synthetic growth hormone), prednisolone withdrawal, tetracyclines, cyclophosphamide
- Haematological: cerebral venous sinus thrombosis
- Endocrine: Addison's disease, hypoparathyroidism, obesity

3.35.3 Terminology

- Primary pseudotumor cerebri
  - IIH: includes patients with obesity, recent weight gain, polycystic ovarian syndrome, and thin children
- Secondary pseudotumor cerebri
  - Cerebral venous abnormalities:
    Cerebral venous sinus thrombosis
    Bilateral jugular vein thrombosis or surgical ligation
    Middle ear or mastoid infection
    Increased right heart pressure
    Superior vena cava syndrome
    Arteriovenous fistula
    Decreased CSF absorption from previous intracranial infection or subarachnoid hemorrhage
    Hypercoagulable states
  - Medications and exposures
    Antibiotics: tetracycline, minocycline, doxycycline, nalidixic acid, sulfa drugs
    Vitamin A and retinoids: hypervitaminosis A, isotretinoin, all-trans retinoic acid for promyelocytic leukaemia, excessive liver ingestion
    Hormones: human growth hormone, thyroxine (in children), leuprorelin acetate, levonorgestrel, anabolic steroids
    Withdrawal from chronic corticosteroids
    Lithium
    Chlordecone
  - Medical conditions
    Endocrine disorders: Addison disease, Hypoparathyroidism
    Hypercapnia: sleep apnoea, Pickwickian syndrome
    Anaemia
    Renal failure
    Turner syndrome
    Down syndrome

3.35.4 Criteria for Diagnosis of IIH

- Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children (Friedman et al. 2013)

1. Required for diagnosis of pseudotumor cerebri syndrome:
   - A diagnosis of pseudotumor cerebri syndrome is definite if the patient fulfils criteria A–E. The diagnosis is considered probable if criteria A–D are met but the measure CSF pressure is lower than specified for a definite diagnosis
     A. Papilledema
     B. Normal neurologic examination except for cranial nerve abnormalities
     C. Neuroimaging: normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on MRI, with or without gadolinium, for typical patients (female and obese), and MRI, with and without gadolinium, and magnetic resonance venography for others; if MRI is unavailable or contraindicated, contrast-enhanced CT may be used
     D. Normal CSF composition
     E. Elevated lumbar puncture opening pressure (at least 250 mm CSF in adults and at least 280 mm CSF in children [250 mm CSF if the child is not sedated and not obese]) in a properly performed lumbar puncture
2. Diagnosis of pseudotumour cerebri without papilledema:
   - In the absence of papilledema, a diagnosis of pseudotumor cerebri syndrome can be made if B–E from above are satisfied, and in addition the patient has a unilateral or bilateral sixth nerve palsy
   - In the absence of papilledema or sixth nerve palsy, a diagnosis of pseudotumor cerebri syndrome can be suggested but not made if B–E from above are satisfied, and in addition at least three of the following neuroimaging criteria are satisfied:
     I. Empty sella
     II. Flattening of the posterior aspect of the globe
     III. Distension of the perioptic subarachnoid space with or without a tortuous optic nerve
     IV. Transverse venous sinus stenosis

- IIH: consensus guidelines on management (Mollan et al. 2018)
  A. Papilloedema
  B. Normal neurological examination (except CN VI palsy)
  C. Neuroimaging: normal brain parenchyma (no hydrocephalus, mass, structural lesion or meningeal enhancement). Venous thrombosis excluded in all
  D. Normal CSF constituents
  E. Elevated lumbar puncture pressure of at least 25 cmCS
  - IIH without papilloedema (IIHWOP) diagnostic criteria:
    Presence of criteria B–E for IIH plus unilateral or bilateral CN VI palsy
    Suggestion of possible IIHWOP if presence of criteria B–E plus three neuroimaging finding (empty sella, flattening of posterior aspect of the globe, distension of the perioptic subarachnoid space ± a tortuous optic nerve, transverse venous sinus stasis) suggestive of raised ICP

3.35.5 History

- Symptoms (Mollan et al. 2018)
  - Headache worse lying down (76–96%)
  - Transient visual obscurations lasting 1–30 s precipitated by posture/straining (68–72%)
  - Pulsatile tinnitus (52–61%)
  - Back pain (53%)
  - Dizziness (52%)
  - Neck pain (42%)
  - Blurred vision (32%)
  - Cognitive disturbance (20%)
  - Radicular pain (19%)
  - Diplopia from CN VI palsy (18%)
  - Nausea or vomiting

3.35.6 Examination

- CN VI palsy
- True disc swelling
  - Elevated appearance of optic nerve head
  - Blurring of disc margins
  - Peripapillary NFL oedema with obscuration of retinal vessels
  - Hyperaemia and dilation of the disc surface capillary net
  - Peripapillary haemorrhages (acute) and exudates (chronic)
  - Retinal venous dilatation and tortuosity
- Optociliary shunt vessels in chronic papilloedema
- Enlarged blind spot

3.35.7 Investigations

- MRI head: rule out tumour, hydrocephalus, meningeal lesion
- MRV/CTV: rule out cerebral venous thrombosis
- LP (normal opening pressure <20 cmH_2O or <25 cmH_2O in the obese): confirm raised ICP and normal CSF composition to rule out a meningeal process
- VF: enlarged blind spot

3.35.8 Treatment

- Weight loss with sodium reduction
- Medical:
  - Diamox
  - Topiramate
  - Furosemide
- Surgical:
  - Optic nerve sheath fenestration: for progressive visual loss despite maximally tolerated medical therapy
  - CSF diversion procedure (lumboperitoneal or ventriculoperitoneal shunt): for intractable headache despite maximally tolerated medical therapy

3.36 Septo-Optic Dysplasia (De Morsier Syndrome) (Fig. 3.45)

3.36.1 Risk Factors for Optic Nerve Hypoplasia

- Young maternal age
- Maternal drug (LSD) and alcohol abuse (fetal alcohol syndrome) during pregnancy
- Exposure to sodium valproate or phenytoin during pregnancy
- Maternal diabetes: superior segmental optic nerve hypoplasia (topless disc syndrome — superior entrance of central retinal vessels, superior disc pallor)

3.36.2 Examination

- Optic nerve hypoplasia (subnormal number of optic nerve axons with normal mesodermal elements and glial supporting tissue): small optic nerves with crowded vessels and a pale ring around the nerve (double ring

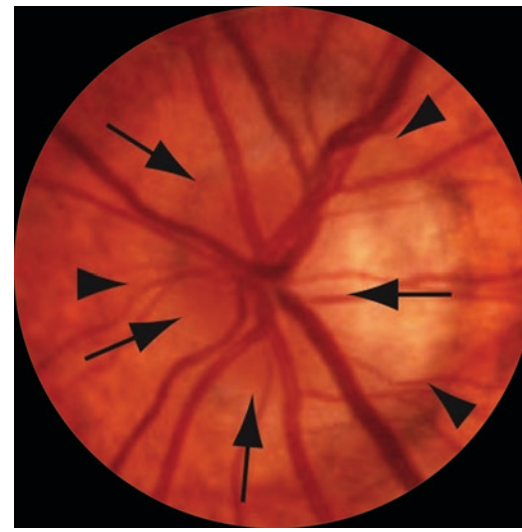

Fig. 3.45 Colour fundus image of a patient with optic nerve hypoplasia showing the double ring sign. Black arrows show the inner ring and the black arrowheads show the outer ring

sign — inner ring is the abnormal extension of the retina and RPE over the outer portion of the lamina cribrosa, outer ring is the consists of the normal junction between sclera and lamina cribrosa)

3.36.3 Investigations

- Bloods: hypopituitarism (GH, TSH, ACTH, ADH deficiency)
- MRI head and orbit: midline abnormalities — absent septum pellucidum and agenesis or thinning of corpus callosum

3.36.4 Treatment

- Refer to endocrinologists for hormonal supplementation
- Visual impairment registration

3.37 Tobacco-Alcohol Amblyopia

3.37.1 Pathophysiology

- Both smoking and alcohol can cause B12 deficiency. B12 and B9 (folate) deficiencies lead to increased formic acid production, which impairs the electron transport chain (mitochondrial oxidative phosphorylation). This leads to ATP deficiency, thus causing optic neuropathy
- Abuse of tobacco can lead to increased levels of cyanide in the body, which can impair the electron transport chain similarly to that of formic acid. Tobacco can also be toxic by causing disturbances in the metabolism of the vitamin B complex and by impairing vitamin B12 absorption
- Tobacco and alcohol act synergistically to cause optic nerve damage via a disease referred to as "tobacco-alcohol amblyopia". The theoretical mechanism of this disease is based on the decreased consumption of vitamin B12 from alcohol abuse combined with the decreased absorption of B12 from tobacco use leading to severely low levels of this vitamin in the body

3.37.2 Differential Diagnosis

- Toxic optic neuropathy
  - Drugs: vigabatrin, ethambutol, amiodarone, isoniazid, lead, methanol
- Inflammatory optic neuropathy
  - Typical/atypical optic neuritis
  - Sarcoidosis
  - Vasculitis, e.g. SLE, PAN
- Inherited
  - LHON: VA typically 6/60—HM
  - Kjer syndrome
  - Behr syndrome
  - Wolfram syndrome (DIDMOAD)
- Compressive/infiltrate optic neuropathy

3.37.3 History

- Symptoms:
  - Subacute, painless, bilateral progressive central vision loss
  - Colour desaturation (red desaturation)
  - Isolated numbness or paraesthesia
  - Gait abnormalities
  - Psychiatric or cognitive symptoms
- Alcohol abuse with malnourishment — caloric needs from alcohol. Which is lacking in the vitamin B complex — chronic alcohol abuse leads to systemic deficiencies in B1, B9, and B12
- Smoking
- FHx: inherited optic atrophy
- DHx: toxic optic neuropathy

3.37.4 Examination

- Bilateral decreased VA (typically 6/9–6/60) due to preferential damage to the papillomacular bundle3
- Reduced colour vision
- Sluggish pupil reactions; however, there may be no RAPD VF demonstrate bilateral central or cecocentral scotomas

- Optic discs may look normal initially or slight hyperaemic, progressing to temporal pallor over time
- Rule out any signs of intraocular inflammation

3.37.5 Investigations

- Bloods: vitamin B1 (thiamine), B2 (riboflavin), B3 (niacin or nicotinamide), B6 (pyridoxine), folate (B9), B12 (cobalamin)

3.37.6 Treatment

- Abstain from alcohol
- Abstain from tobacco
- Supplement deficient vitamins, specifically B12 (IM injections) and folate (oral)
- Pabrinex:
  - Indication: prophylaxis and treatment (to prevent irreversible Korsakoff's syndrome — reduced ability to acquire new memories) of Wernicke's encephalopathy (thiamine deficiency with triad of confusion, ataxia with wide spaced gait, ophthalmoplegia or nystagmus)
  - Contents: vitamins B and C (B1, B2, B3, B6, ascorbic acid)

3.38 Optic Atrophy in Infancy and Childhood

3.38.1 Causes

- Unilateral (other eye clinically normal with normal ERG/VEPs)
  - Tumour compression anterior to chiasm: optic nerve glioma — fusiform enlargement of optic nerve on MRI scan
  - Tumour infiltration anterior to chiasm: leukaemia
  - Trauma
  - Leber's hereditary optic neuropathy (LHON) before other eye affected (other eye usually affected within 2 months)
  - Glaucoma
- Bilateral ± nystagmus
  - Severe hypoxia
  - Hereditary optic neuropathies (LHON, ADOA — Kjer syndrome, AROA — Behr syndrome, Wolfram syndrome [AR] — DIDMOAD)
  - Tumour: glioma of the optic chiasm, craniopharyngioma
  - Increased ICP: congenital hydrocephalus, IIH
  - Optic neuritis
  - Toxic or nutritional optic neuropathy: drugs, avitaminosis
  - Neurometabolic

3.38.2 History

- History of birth (prematurity with IVH) or perinatal problems (whether child had to be in an incubator, have added oxygen, be ventilated, or had any difficulty in breathing, episodes of bradycardia or apnoea, resuscitation): perinatal asphyxia
- Family History of poor vision: hereditary optic neuropathy (LHON, ADOA, optic nerve gliomas in NF-1) or retinal dystrophies
- History of diabetes and hearing loss
- Headaches, vomiting: raised ICP
- History of trauma: traumatic optic neuropathy
- Sudden visual loss:
  - With pain: optic neuritis, infiltrations (leukaemia)
  - Without pain: LHON — peripapillary telangiectasia, NMO
- History of toxic drugs (anti-TB agents, e.g. ethambutol, systemic antibiotics, e.g. linezolid, immunomodulatory agents, e.g. infliximab), malnutrition (anorexia nervosa): toxic/nutritional optic neuropathy
- History of seizures: hereditary degenerative diseases

- History of other systemic disorders: syndromic optic neuropathy
- Any photophobia, blepharospasm, buphthalmos: congenital glaucoma

3.38.3 Examination

- Optic nerve function: VA, RAPD, colour vision (blue-yellow tritanopia of ADOA)
- Check for proptosis (axial for optic nerve glioma)
- Check IOP and measure the horizontal corneal diameter: glaucoma
- Examine parents and siblings: hereditary optic neuropathy (LHON, ADOA)
- Full systemic examination including dermatological (NF-1) and neurological

3.38.4 Investigations

- VF (age ≥5 years old): central or cecocentral scotomas for LHON or toxic/nutritional optic neuropathies
- MRI head/orbits: exclude tumours
- ERG: exclude a primary retinal disease (even if the retina appears normal)
- VEP: delayed with abnormal amplitude and waveform in the acute stage of optic neuritis
- Bloods: glucose, vitamin B1 (thiamine), B2 (riboflavin), B6 (pyridoxine), B12, folic acid levels
- Raised ICP: LP
- LHON: Mitochondrial DNA analysis for mutations (11,778, 14,484, 3460)

3.38.5 Treatment

- Treat the underlying cause
  - Nutritional optic neuropathy: Oral vitamin supplementation
  - Toxic optic neuropathy: stop drugs
  - Optic nerve glioma:
    Observation: isolated optic nerve involvement distant from the chiasm, good vision, non-disfiguring proptosis
    Surgical excision: reduced vision, pain, severe proptosis, posterior spread threatening the chiasm
    Chemotherapy/radiotherapy: chiasmal or midbrain involvement
- Visual impairment registration

3.39 Giant Cell Arteritis (GCA)

3.39.1 History

- Symptoms: abrupt onset headaches (usually unilateral in the temporal area), scalp tenderness, jaw claudication, visual symptoms (diplopia, reduced VA), constitutional symptoms (fever, weight loss, loss of appetite), vascular claudication of the limbs
- Osteoporotic risk factors and fractures

3.39.2 Examinations

- Abnormal superficial temporal artery: tender, thickened with reduced or absent pulsation
- RAPD suggesting AION or CRAO
- CN III, IV, VI palsy

3.39.3 Investigations

- Bloods: FBC (anaemia, thrombocytosis), raised CRP, raised ESR
- Temporal artery duplex US: hypoechoic halo due to vessel wall oedema in temporal arteries, positive for over 2 weeks post-steroid initiation
- Temporal artery biopsy: samples should be at least 2 cm in length, aim for within 1 week but sample can remain positive for 2–6 weeks after the commencement of treatment
  - Consent: risks — visible scarring, haematoma, wound infection, scalp or skin necrosis, facial nerve injury, cerebral infarction
  - Procedure:
    Map the artery by palpation or US doppler (mark skin overlying the artery)
    Hair removal for good surgical exposure

Clean the skin and inject local anaesthetic
Skin incision
Blunt dissection to artery — artery lies superficially in the superficial temporalis fascia
Tie the proximal and distal end of the artery with 4/0 silk or Vicryl before cutting
Close subcutaneous tissue with 5/0 interrupted Vicryl and skin closure with a running 6/0 Vicryl subcuticular suture
Compression bandage for 24 h

- MRI: in patients with suspected large vessel GCA, e.g. limb claudication or persistently high-inflammatory markers despite adequate glucocorticoid therapy
- CXR: every 2 years in patients with large vessel GCA

3.39.4 Interpretation of Investigations

- Bloods
  - ESR (upper limit in women: age + 10/2, upper limit in men: age/2): can be raised in patients with anaemia
- TAB
  - Length of specimen biopsied should be documented and known in order to be able to interpret findings correctly
  - TAB may be negative in some patients. Patients should be regarded as having GCA if there is a typical clinical picture and response to glucocorticosteroids. If features considered atypical or alternative explanations are available and TAB is negative, rapid glucocorticosteroid tapering (within 2 weeks).

3.39.5 Treatment

- British Society for Rheumatology guideline on diagnosis and treatment of giant cell arteritis (Mackie et al. 2020)
  - High dose glucocorticosteroid therapy should be initiated immediately when GCA is strongly suspected. 'Strongly suspected' GCA means that in the assessing clinician's judgement, GCA is a more likely explanation for the patient's symptoms that any other condition
  - Glucocorticoid starting dosages:
    The standard initial glucocorticoid dose for GCA is 40–60 mg oral prednisolone per day. The vast majority of patients with GCA symptomatically within 1–7 days to a 40–60 mg daily dose of prednisolone, apart from irreversible sequelae such as established visual loss, stroke or tissue necrosis. Failure to respond to this dose should prompt re-evaluation of the diagnosis
    GCA patients with acute or intermittent visual loss may initially be given 500 mg–1 g intravenous methylprednisolone daily for up to 3 consecutive days before commencing oral prednisolone therapy. If intravenous therapy is not immediately possible, this should not delay initiation of oral prednisolone (60–100 mg may be given for up to 3 consecutive days)
  - Glucocorticoid tapering regime:
    Glucocorticoid dose should be tapered to zero over 12–18 months, providing there is no return of GCA symptoms, signs or laboratory markers of inflammation. A more rapid dose reduction is appropriate for patients at high risk of glucocorticoid toxicity and/or those receiving concomitant glucocorticoid sparing therapy
    Initial dose of prednisolone continued until GCA symptoms and acute phase markers resolve (induction of clinical remission)
    Reduce daily dose by 10 mg every 2 weeks to 20 mg (aim to reach 20 mg prednisolone once the patient has been in remission for 4–8 weeks)

Reduce daily dose by 2.5 mg every 2–4 weeks to 10 mg
Reduce daily dose by 1 mg every 1–2 months
One week after any change in dose, review the person to exclude any relapse of symptoms (it may be possible to do this by telephone)
Return to previous higher prednisolone dose if headache symptoms return (and judged to be due to GCA relapse) during glucocorticoid taper
Consider high-dose oral prednisolone (40–60 mg) with or without glucocorticoid-sparing agent if jaw or tongue claudication occurs (and judged to be due to GCA relapse) during glucocorticoid taper
Investigate with vascular imaging (MRI, CT or FDG-PET/CT) and consider increasing oral prednisolone and/or adding glucocorticoid-sparing agent if weight loss, fever, night sweats, anaemia, persistent acute phase response, new/recurrent polymyalgia rheumatica symptoms, limb claudication, abdominal pain or back pain occurs (and judged to be due to GCA relapse) during glucocorticoid taper

- Methotrexate (MTX)
  MTX might be considered for GCA, in combination with a glucocorticoid taper, in patients at high risk of glucocorticoid toxicity or who relapse
- Proton pump inhibitors (recommended for GI protection — risk of GI bleed from corticosteroids)
- Osteoporosis prophylaxis
- The routine use of antiplatelet or anticoagulant agents for GCA is not recommended
- The routine use of cholesterol-lowering agents such as statins for GCA is not recommended
- Follow up:
  Weeks 0, 1, 3, 6, then months 3, 6, 9, 12 in the first year
  Arrange routine reviews a week after any change in dose
  After the first year, the person should be seen every 3–6 months (with extra visits for relapses or adverse events)

- Tocilizumab
  - Giant-Cell Arteritis Actemra (GiACTA) trial (Stone et al. 2017): tocilizumab with a tapering course of glucocorticosteroids was more effective than glucocorticosteroids alone at increasing the proportion of patients sustaining remission and time to first flare up at 52 weeks
  - NICE Guidance [TA518]: when used with a tapering course of glucocorticosteroids (and when used alone after glucocorticosteroids), is recommended as an option for treating GCA in adults only if:
    They have relapsing or refractory disease
    They have not already had tocilizumab
    Tocilizumab is stopped after 1 year of uninterrupted treatment at most

3.39.6 Complications

- Second eye involvement is 10% if treated and 95% if untreated
- Vascular: thoracic aortic aneurysms, TIA/CVA, MI
- Death

3.40 Comitant Esotropia (ET)

3.40.1 Other Diagnoses to Consider

- Type 1 Duane's syndrome: limitation of abduction, globe retraction in adduction
- Congenital CN VI palsy: limitation of abduction
- Convergence spasm: intermittent spasm of convergence, of miosis, and of accommodation, high myopia on dry retinoscopy accompanying the failure of abduction — treatment options include cycloplegia and bifocals

3.40.2 Classification of Comitant ET

- Primary ET
  - Accommodative ET:
    Refractive fully accommodative ET
    Refractive partially accommodative ET
    Non-refractive convergence excess ET with high AC/A ratio
  - Non-accommodative ET:
    Constant:
    - Starting <6 months: infantile ET
    - Starting >6 months: basic ET — muscle surgery

    Variable with distance:
    - Distance fixation only: distance ET (divergence insufficiency) — orthoptic exercises initially
    - Near fixation only: non-accommodative convergence excess — muscle surgery
    - Secondary sensory ET
    - Consecutive ET

3.40.3 Infantile ET

3.40.3.1 Definition

- Infantile esotropia is a constant non-accommodative ET with onset before 6 months of age in a neurologically normal child

3.40.3.2 Examination

- The angle is >30 PD with mild or no amblyopia (alternate fixation) and mild hyperopia
- Full extraocular motility: can elicit by monocular occlusion or performing a doll's head manoeuvre
- Dissociated vertical deviation (DVD): eye elevates and extorts and is not associated with a corresponding downwards movement of the other eye when fixation is resumed — can occur spontaneously or when the eye is occluded
- Inferior oblique overaction (IOOA): visible in adduction only and is associated with fundus excyclotorsion, if the eye elevates in adduction and there is a corresponding hypodeviation in the opposite eye the deviation is due to IOOA
- Latent nystagmus: horizontal jerk nystagmus that occurs on monocular occlusion, fast phase toward the uncovered eye (fixing eye), nystagmus lessened in adduction and worsened in abduction
- Optokinetic asymmetry: greater sensitivity to objects moving from temporal to nasal than from nasal to temporal
- Normal anterior/posterior segment examination

3.40.3.3 Investigations

- Cycloplegic refraction

3.40.3.4 Treatment

- Full hypermetropic correction if hyperopia ≥2.5 D
- Treat any amblyopia present: atropine penalisation or patching
- Muscle surgery (before age 2 — better stereopsis outcomes): bilateral MR recession, unilateral MR recession and LR resection, IO recession or myectomy for IOOA

3.40.4 Accommodative ET

3.40.4.1 Definition

- Accommodative ET describes an ET caused in whole, or in part, by the use of accommodation to clear vision in the presence of uncorrected hypermetropia

3.40.4.2 Classification

- Refractive fully accommodative ET
  - Equal distance and near deviation
  - ET resolves with full hypermetropic correction
- Refractive partially accommodative ET
  - Equal distance and near deviation
  - ET partially resolves with full hypermetropic correction
- Non-refractive accommodative convergence excess ET
  - Near ET
  - Little or no ET at distance
  - Deviation at least 10 PD more at near than at distance

3.40.4.3 Examination

- Full extraocular motility ± IOOA
- Normal anterior/posterior segment examination
- Determine AC/A ratio based on near-distance discrepancy (≥10 PD)

3.40.4.4 Investigations

- Cycloplegic refraction: hypermetropia ≥2.5 D

3.40.4.5 Treatment

- Refractive error correction
  - Full hypermetropic correction
  - Myopic correction if > −3.0 D
  - Executive bifocals (+3.00 near add) + full hypermetropic correction for non-refractive accommodative convergence excess ET
- Miotics: phospholine iodide — non-refractive accommodative convergence excess ET
- Treat any amblyopia present: atropine penalisation or patching
- Muscle surgery (for potential BSV or cosmesis when eyes not aligned adequately with glasses): bilateral MR recession

3.41 Comitant Exotropia (XT)

3.41.1 Other Diagnoses to Consider

- Sensory XT: abnormal anterior/posterior segment
- Type 2 Duane's syndrome: limitation of adduction, globe retraction in adduction
- Convergence insufficiency: near point of convergence greater than age for normal, no manifest deviation but may be exophoric for near — treatment options include full myopic correction, convergence exercises (e.g. pencil push ups), prisms, Botox, surgery

3.41.2 Classification of Comitant XT

- Primary XT:
  - Constant:
    Starting <6 months: Infantile XT
    Starting >6 months: Basic XT
  - Intermittent:
    Distance fixation only:
    - True divergence excess XT (normal AC/A ratio)
    - Simulated divergence excess XT (high AC/A ratio)

    Near fixation only: Near XT
- Secondary sensory XT
- Consecutive XT

3.41.3 Intermittent XT

3.41.3.1 Definition

- Intermittent XT is a strabismus condition with outward drifting of either eye interspersed with periods of good alignment or orthotropia
- Onset usually before 18 months of age
- XT at distance fixation with eyes remaining aligned for near fixation

3.41.3.2 Classification

- True divergence excess XT

Deviation ≥10 PD larger when measured at distance fixation than at near

- Simulated divergence excess XT

  Initial deviation ≥10 PD larger when measured at distance fixation than at near

  Misalignment at near fixation increases to <10 PD of the angle at distance following disruption of near binocular vision by 1 h of monocular occlusion or with +3.0 D lenses or pharmacological cycloplegia

3.41.3.3 Newcastle Control Score (NCS) for Intermittent XT

- A scoring system for grading the severity of intermittent distance XT (Haggerty et al. 2004). The components of the NCS are
  - Home control (subjective criteria):

    Score 0: XT or monocular eye closure never noticed

    Score 1: XT or monocular eye closure seen <50% of time child observed for distance fixation

    Score 2: XT or monocular eye closure seen >50% of time child observed for distance fixation

Score 3: XT or monocular eye closure seen for distance and near fixation
- Clinic control near (objective criteria):
  Score 0: Manifest only after cover test (CT) and resumes fusion without need for blink or refixation
  Score 1: Blink or refixate to control after CT
  Score 2: Manifest spontaneously or with any form of fusion disruption without recovery
- Clinic control distance (objective criteria):
  Score 0: Manifest only after cover test (CT) and resumes fusion without need for blink or refixation
  Score 1: Blink or refixate to control after CT
  Score 2: Manifest spontaneously or with any form of fusion disruption without recovery

- Total score 0–7
- Surgical intervention indicated for NCS ≥3 to achieve a cure (NCS 0 or 1)

3.41.3.4 Examination
- Full extraocular motility: can elicit by monocular occlusion or performing a doll's head manoeuvre
- Normal anterior/posterior segment examination

3.41.3.5 Investigations
- Cycloplegic refraction

3.41.3.6 Treatment
- Refractive error correction:
  - Full myopic correction in children
  - Hypermetropia correction if > +4.00 D
- Muscle surgery (NCS ≥3):
  - Simulated distance XT: unilateral MR resection and LR recession
  - True distance XT: bilateral LR recession

3.42 Amblyopia Management (Table 3.33)

3.42.1 Classification

- Strabismic amblyopia
- Refractive amblyopia
- Stimulus deprivation amblyopia

3.42.2 Methods of Detection

- Reduced BCVA in the absence of an organic cause
- Crowding phenomenon: scores better with single optotypes
- Tolerance of a neutral density filter: classically in amblyopia VA is reduced less by the addition of neutral density filters than in other causes of reduced VA

3.42.3 Methods of Treatment

- Refractive error correction alone first-spectacle adaptation phase of 18 weeks:
  - Correct anisometropia > 1.00 D and correct astigmatism > 1.50 D
  - Full myopic correction in children > 3.5 years old if VA <6/9 and myopia > −0.75 D
- Occlusion therapy (if reduced VA remains after 18 weeks of refractive error correction):

Table 3.33 Key facts about amblyopia

- Amblyopia is the decrease of best corrected visual acuity (BCVA) by one line or more caused by pattern vision deprivation or abnormal binocular interaction for which no causes can be detected by the physical examination of the eye
- Development of amblyopia occurs during the critical period of visual development (the first 7–8 years of life)

  - Moderate amblyopia (6/12 to 6/24): 2 h per day of total occlusion is as effective as 6 h per day of total occlusion for improving visual acuity in children aged 3–7 years (The Pediatric Eye Disease Investigator Group 2003a)
  - Severe amblyopia (6/30 to 6/120): 6 h per day of total occlusion is as effective as all-day full-time occlusion for improving visual acuity in children aged 3 to less than 7 years of age (The Pediatric Eye Disease Investigator Group 2003b)
  - Teenagers (13–17 years old) who have never before received amblyopia treatment may improve visual acuity from a trial of occlusion therapy for 2–6 h per day (The Paediatric Eye Disease Investigator Group 2005)
- Penalisation therapy:
  - Moderate amblyopia (6/12 to 6/24): atropine is as effective as 6 h per day of total occlusion for improving visual acuity in children aged 3 to less than 7 years (The Pediatric Eye Disease Investigator Group 2002)

3.43 Retinopathy of Prematurity (ROP)

3.43.1 Classification of ROP

The International Classification of ROP (An International Committee for the Classification of Retinopathy of Prematurity 2005):

- Plus disease
  - Retinal arterial tortuosity ± venous dilatation in the posterior pole in at least two quadrants
  - Pre-plus disease is the presence of retinal arterial tortuosity ± venous dilatation in the posterior pole in one quadrant only
- Zones
  - Zone I:
    Area in a circle twice the radius of the distance from the optic disc to the foveola
    Approximate temporal extent of Zone I can be determined by using a 25- or 28-D lens:
    - Place nasal edge of optic disc at one edge of the field of view
    - Limit of Zone I is at the temporal field of view
  - Zone II:
    Area in a circle centred on the optic disc with a radius of the distance from the optic disc to the nasal ora serrata
  - Zone III:
    Includes remainder of the fundus outside zones I and II
- Staging
  - Stage 1 (see Fig. 3.46):
    Flat demarcation line separating vascular and avascular retina
  - Stage 2 (see Fig. 3.47):
    Border thickens and appears elevated (ridge); small tufts of vessels may be present at border
  - Stage 3 (see Fig. 3.48):
    Presence of a ridge with extraretinal fibrovascular proliferations
    Blood vessels grow through the ILM of the retina at the ridge into the vitreous
  - Stage 4:
    4a - Macula on partial tractional RD
    4b - Macula off partial tractional RD
  - Stage 5:
    5a - Open funnel total tractional RD
    5b - Closed funnel total tractional RD

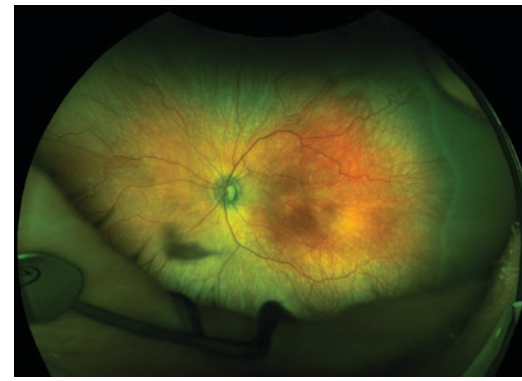

Fig. 3.46 Optos pseudocolour fundus image of a patient with stage I ROP with no plus disease

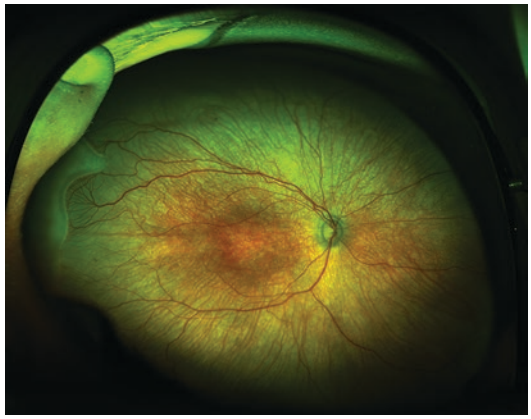

Fig. 3.47 Optos pseudocolour fundus image of a patient with stage II ROP with pre-plus disease

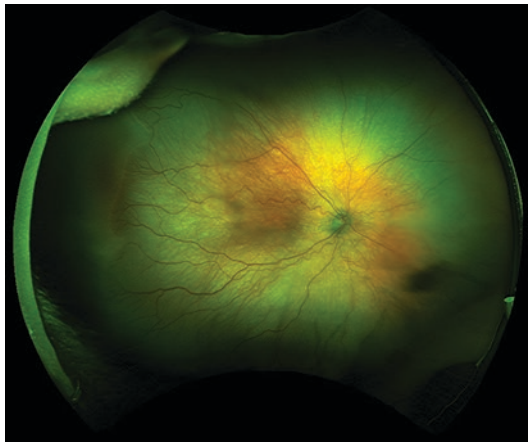

Fig. 3.48 Optos pseudocolour fundus image of a patient with stage III ROP with plus disease

3.43.2 UK ROP Guideline 2008

3.43.2.1 Screening Inclusion Criteria

- Must be screened: birth weight <1251 g and/or gestational age <31 weeks
- Should be screened: birth weight <1501 g and/or gestational age <32 weeks

3.43.2.2 First Screening Examination

- Gestational age <27 weeks: 30–31 weeks post-menstrual age
- Gestational age 27–32 weeks: 4–5 weeks postnatal age
- Gestational age >32 weeks: 4–5 weeks postnatal age

3.43.2.3 Frequency of Screening

- Weekly: vessels end in zone I or posterior zone II or any plus or pre-plus disease or any stage 3 disease (any zone)
- Fortnightly: all other circumstances where termination criteria not reached

3.43.2.4 Termination of Screening

- Babies with ROP that have two successive examinations showing any of
  - Lack of increase in intensity
  - Partial resolution progressing towards complete resolution
  - Change in colour in the ridge from salmon-pink to white
  - Transgression of vessels through the demarcation line
  - Commencement of the process of replacement of active ROP lesions by scar tissue
- Babies without ROP
  - Vascularisation has extended into zone 3

3.43.2.5 Treatment Criteria

- Stage 3 Zone 2 with plus disease
- Stage 3 Zone 1 without plus disease
- Any Stage Zone 1 with plus disease
- Stage 2 Zone 2 with plus disease (consider treatment)

3.43.2.6 Timing of Treatment

- Aggressive ROP: treat ASAP (<48 h)
- All other ROP requiring treatment: treat within 48–72 h

3.43.2.7 Treatment Technique

- Transpupillary diode laser to give near confluent (0.5–1 burn width) laser burn spacing to the entire avascular retina

3.43.2.8 Post-Treatment Follow Up

- First examination: 5–7 days post treatment
- Subsequent examination: Initially at least weekly, then as clinically indicated until at least 5 years of age

3.43.2.9 Re-Treatment

- Failure of ROP to regress: 10–14 days post-initial treatment

3.44 Penetrating Eye Injury

3.44.1 History

- Mechanism of injury
- Tetanus status

3.44.2 Examination

- IOP: may be reduced
- Lids: lid lacerations with or without involvement of the lid margin or canaliculus
- Conjunctiva: conjunctival lacerations, subconjunctival haemorrhage
- Cornea: penetrating corneal injury — perform a seidel test
- Sclera: penetrating scleral injury
- AC: formed or flat, hypopyon, hyphaema
- Iris: iris hole (transillumination), peaked pupil
- Perform gonioscopy to look for angle recession and occult intraocular foreign body (IOFB) in angle
- Lens: traumatic cataract (focal) ± disruption of anterior/posterior lens capsule ± zonular dehiscence ± subluxation/dislocation, IOFB
- Fundus: vitreous/retinal haemorrhage, retinal tear(s), RD, commotio retinae, choroidal rupture, IOFB (see Fig. 3.49)

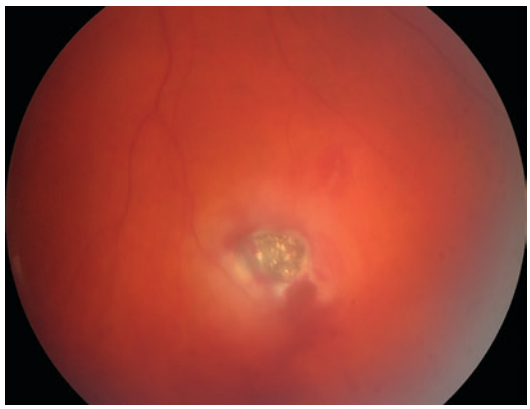

Fig. 3.49 Colour fundus image of a patient with a metallic IOFB dislodged in the retina

3.44.3 Investigations

- B-scan (if poor view of fundus): IOFB (highly reflective mobile appearing opacity), RD or choroidal haemorrhage
- CT orbit with 2 mm slices: orbital fractures, IOFB
- Full field ERG: siderosis causes a progressive reduction in the B-wave with eventual total extinguishing

3.44.4 Treatment

- Pre-operative
  - Admit and prepare for GA (NBM, determine last meal/drink, liaise with anaesthetist, ECG/bloods if indicated)
  - Protect globe with clear plastic shield
  - Systemic antibiotics, e.g. ciprofloxacin 750 mg BD ± topical antibiotics
  - Administer tetanus vaccine/toxoid if indicated
- Intraoperative
  - Primary globe repair:

    Limbus is repaired first typically with 9/0 nylon sutures

    Any corneal laceration is then repaired typically with 10/0 nylon sutures (longer compression suture throws are used in the peripheral cornea and shorter suture throws used in the central cornea) — rotate sutures to bury knots; return exposed viable iris tissue through perforation; abscise exposed tissue if non-viable

    Any scleral laceration is then repaired (following a conjunctival peritomy) in an anterior to posterior direction with 8/0 nylon sutures; return exposed viable uveal tissue through perforation; cut prolapsed vitreous flush to wound taking care not to induce vitreous traction
  - IOFB removal

    AC IOFB: corneal approach, removal with fine forceps

    Angle IOFB: scleral trapdoor approach

Lenticular IOFB: consider leaving in situ or remove with lens at cautious cataract surgery

Posterior segment IOFB: intraocular magnet or vitrectomy forceps

– Lid laceration repair
– Secondary procedures

Traditionally performed 4–10 days after initial injury, in part, to allow for the formation of a PVD

PPV + tamponade (C3F8 or silicone oil) ± membrane dissection (if PVR) ± encircling buckle (if breaks) ± lensectomy (if cataract; IOL commonly deferred) ± intravitreal antibiotics (if endophthalmitis)

3.44.5 Tetanus Prophylaxis

- Tetanus vaccine treatment (3 doses of 0.5 mL IM Td/IPD, separated by 4 weeks, with a booster after 10 years) if
  – Patient non-immune and wound is clean or tetanus prone
  – Patient is uncertain of vaccination status and wound is clean or tetanus prone
- Tetanus immunoglobulin treatment if
  – Patient non-immune and wound is tetanus prone
  – Patient is uncertain of vaccination status and wound is tetanus prone

3.45 Atypical Optic Neuritis (Table 3.34)

Table 3.34 Key facts about atypical optic neuritis

- Atypical optic neuritis is a heterogeneous collection of disorders whose presenting features suggest inflammation of the optic nerve
- Inflammation of the optic nerve may be divided into papillitis (disc is swollen), retrobulbar neuritis (disc is spared), and neuroretinitis (retinal involvement, macular star)
- If an acute optic neuropathy does not fulfil the criteria for typical optic neuritis (see Sect. 3.45.1) then it must be investigated further as an atypical optic neuritis to exclude a compressive lesion or other serious pathology

3.45.1 Features of Typical Optic Neuritis (Acute Demyelinating Optic Neuritis)

- Age 20–50
- Unilateral
- Worsens over hours/days
- Recovery starts within 2 weeks
- Retrobulbar pain (may be worse on eye movements) — present in 92% of cases
- Reduced colour vision
- RAPD — disc swelling only present in 1/3 of cases

3.45.2 Features of Atypical Optic Neuritis

- Absence of pain
- Grossly swollen optic disc with peripapillary haemorrhages
- Bilateral
- Severe loss of vision over several weeks
- Recurrence on cessation of steroids

3.45.3 Causes of Atypical Optic Neuritis

- Infection: syphilis, TB, lyme, HIV
- Lymphoproliferative (directly or indirectly related to the haematological disease): lymphoma, leukaemia, neurotoxic treatments post bone-marrow transplant
- Systemic immune mediated disorders: neurosarcoidosis, IBD, systemic vasculitis, connective tissue disease
- Antibody mediated neurological illness: NMO spectrum disorder (NMOSD), MOG antibody mediated demyelinating disease

3.45.4 History

- Course of optic nerve dysfunction both current and in the past: persistent visual loss, negligible spontaneous improvement
- Presence of paraesthesia, weakness of limbs — clumsiness with dropping things frequently, bowel and bladder incontinence — NMOSD
- Any recent infections or vaccinations — vaccinations induced optic neuritis

- History of lymphoproliferative diseases, IBD, connective tissue disorders
- History of autoimmunity (e.g. MG, hypothyroidism): NMOSD frequently associated with systemic autoimmune disorders
- Concurrent or recent treatments, e.g. bone marrow transplant, new biologic agents such as monoclonal antibodies

3.45.5 Examination

- Optic nerve function: VA, RAPD, colour vision, confrontational VF
- Cranial nerve: CN VII involvement in Sarcoidosis — Heerfordt's syndrome (CN VII palsy, uveitis, parotid/submandibular gland enlargement)
- Uveitis (anterior, intermediate or posterior): sarcoidosis, infective causes, lymphoproliferative causes
- Skin: erythema nodosum (red tender elevated lesions on the shins)

3.45.6 Investigations

- HVF
- MRI brain with gadolinium contrast ± spinal cord (transverse myelitis — lesion extending continuously over ≥3 vertebral segments)
- Bloods:
  - VDRL: syphilis
  - FBC, ESR: lymphoproliferative
  - ACE: sarcoidosis
  - Aquaporin-4 antibodies: NMOSD
  - Myelin oligodendrocyte glycoprotein (MOG) antibodies
- CXR: sarcoidosis (hilar lymphadenopathy, pulmonary fibrosis), TB

3.45.7 Treatment

- High dose oral/IV corticosteroids, followed by a reducing dose oral steroid programme
- Refer to respiratory team for bronchoscopy
- Refer to neurologists for full neurological examination

3.46 Carotid Artery Dissection (Table 3.35)

3.46.1 History

- Symptoms: headache, ocular pain, neck pain, Horner's syndrome (caused by compression of the ascending sympathetic supply within the carotid sheath), symptoms of TIA/CVA (over 50% of patients with a spontaneous ICA dissection present initially as a stroke or TIA with hemiplegia, dysarthria, dysphagia, or amaurosis fugax)
- History of neck trauma (e.g. from car accident with seat belt injury to neck)
- History of hereditary connective tissue disorders

3.46.2 Examination

- Horner's syndrome
- Deviation of tongue to affected side: compression of hypoglossal nerve (CN XII)
- Neurological examination

3.46.3 Investigation

- CTA or MRA

Table 3.35 Key facts about carotid artery dissection

- Dissection occurs when a tear forms within the inner wall of an artery
- Bloods enters tunica media of the vessel and forms an intramural haematoma along plane of the vessel wall — may cause vessel wall to bulge toward the lumen, leading to stenosis, or it may cause outward pseudoaneurysmal bulging of the vessel wall
- Cervical artery dissection accounts for only 1–2% of all ischaemic strokes, but in young and middle-aged people it accounts for 10–25% of strokes (Debette and Leys 2009)
- May occur spontaneously or secondary to trauma, hereditary connective tissue disorders (Marfan syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta)

3.46.4 Treatment

- Patients are treated empirically with either antiplatelet (aspirin, clopidogrel, dipyridamole) or anticoagulation (warfarin, heparin) therapy to prevent formation of a thrombus at the site of dissection and subsequent embolisation. However, there is no difference in efficacy of antiplatelet and anticoagulant drugs at preventing stroke and death in patients with symptomatic carotid and vertebral artery dissection (The CADISS Trial Investigators 2015; Markus et al. 2019)

3.46.5 Prognosis

- The risk of stroke is zero for patients who present with anything other than an initial stroke (The CADISS Trial Investigators 2015)
- For patients who present initially with symptoms of a stroke, only 2% will have a stroke recurrence (The CADISS Trial Investigators 2015)
- All stroke events occur in the first 10 days (The CADISS Trial Investigators 2015)

3.47 Transient Ischaemic Attack (TIA) and Stroke: NICE Guidance [TA128]

3.47.1 Prompt Recognition of Symptoms of Stroke and TIA

- FAST (Face Arm Speech Test):
  - Validated tool used outside of hospital to screen for a diagnosis of stroke or TIA in people with sudden onset of neurological symptoms:
  - Face: ask the person to smile
    Arm: ask the person to raise both arms
    Speech: ask the person to repeat a simple phrase

3.47.2 Assessment of People Who Have Had a Suspected TIA, and Identifying Those at High Risk of Stroke

- $ABCD^2$ score (0–9): A validated scoring system for assessing the risk of a subsequent stroke for people who have had a suspected TIA (that is, they have no neurological symptoms at the time of assessment and neurological symptoms lasted <24 h)
- Age ≥60 years old (1 point)
- BP ≥140/90 (1 point)
- Clinical features
  - Unilateral weakness (1 point)
  - Speech disturbance without weakness (1 point)
- Diabetes (1 point)
- Duration of symptoms
  - Symptoms lasting ≥1 h (2 points)
  - Symptoms lasting 10–59 min (1 point)
- People who have had a suspected TIA who are at high risk of stroke ($ABCD^2$ score ≥4) should have
  - Aspirin 300 mg OD started immediately
  - Specialist assessment and investigation within 24 h of onset of symptoms
  - Measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors
- People with crescendo TIA (two or more TIAs in a week) should be treated as being at high risk of stroke, even though they may have an $ABCD^2$ score of 3 or below
- People who have had a suspected TIA who are at lower risk of stroke (ABCD2 score ≤3) should have
  - Aspirin 300 mg OD started immediately
  - Specialist assessment and investigation ASAP, but definitely within 1 week of onset of symptoms
  - Measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors

- People who have had a TIA but who present late (more than 1 week after their last symptom has resolved) should be treated as though they are at a lower risk of stroke

3.47.3 Urgent Carotid Endarterectomy and Carotid Stenting

- People with stable neurological symptoms from acute non-disabling stroke or TIA who have symptomatic carotid stenosis of 50–99% according to the North American Symptomatic Carotid Endarterectomy (NASCET) Trial criteria (Ferguson et al. 1999), or 70–99% according to the European Carotid Surgery Trial (ECST) criteria (European Carotid Surgery Trialists Collaborative Group 1991) should
  - Be assessed and referred for carotid endarterectomy within 1 week of onset of stroke or TIA symptoms
  - Undergo surgery within a maximum of 2 weeks of onset of stroke or TIA symptoms
  - Receive best medical treatment (control of BP, antiplatelet agents, cholesterol lowering through diet and drugs, lifestyle advice)
- People with stable neurological symptoms from acute non-disabling stroke or TIA who have symptomatic carotid stenosis of less than 50% according to the NASCET criteria, or less than 70% according to the ECST criteria should
  - Not undergo surgery
  - Receive best medical treatment (control of BP, antiplatelet agents, cholesterol lowering through diet and drugs, lifestyle advice)

3.47.4 Pharmacological Treatments for People with Acute Stroke

- Thrombolysis with alteplase:
  - Recommended for treating acute ischaemic stroke in adults if:

    Treatment is started as early as possible within 4.5 h of onset of stroke symptoms and Intracranial haemorrhage has been excluded by appropriate imaging techniques
- Aspirin and anticoagulant treatment
  - People with acute ischaemic stroke:

    All people presenting with acute stroke who have had a diagnosis of primary intracerebral haemorrhage excluded by brain imaging should, ASAP but certainly within 24 h, be given:
    - Aspirin 300 mg PO if they are not dysphagic
    - Aspirin 300 mg PR or by enteral tube if they are dysphagic

    Thereafter aspirin should be continued until 2 weeks after the onset of stroke symptoms, at which time definitive long-term antithrombotic treatment should be initiated
  - People with stroke associated with acute arterial dissection:

    Treat with either anticoagulants or antiplatelet agents
  - People with acute venous stroke:

    People diagnosed with cerebral venous sinus thrombosis should be given full-dose anticoagulant treatment (initially full dose heparin and then warfarin INR 2–3) unless there are comorbidities that preclude its use

3.48 Amaurosis Fugax (Table 3.36)

3.48.1 Causes

- Embolic
  - Carotid artery disease:

    Atherosclerosis

    Dissection

    Aneurysms
  - Cardiac disease:

    Valvular heart disease

    Mural thrombi, e.g. lesions associated with AF or MI

    Intracardiac tumour, e.g. atrial myxoma

Table 3.36 Key facts about amaurosis fugax

- Defined as transient monocular visual loss attributed to ischaemia or vascular insufficiency
- Typically, patients describe diminished or absent vision in one eye that progresses over a few seconds and lasts for seconds to a few minutes followed by complete recovery

  - Drug abuse:
    Talc retinopathy
- Haemodynamic
  - Inflammatory arteritis:
    Takayasu's disease
  - Hypoperfusion:
    Heart failure
    Acute hypovolaemia
- Ocular
  - AION
  - CRAO/BRAO
  - CRVO
- Neurologic
  - Optic neuritis, optic nerve or chiasm compression
  - Papilloedema
  - MS
  - Migraine
- Idiopathic

3.48.2 History

- Ask about symptoms of GCA: headache, jaw claudication, scalp tenderness, weight loss, fever
- Ask about cardiovascular risk factors: HTN, DM, hypercholesterolaemia, smoking
- Ask about use of recreational drug use: talc
- Ask about symptoms of migraine: unilateral headache, photophobia/phonophobia, nausea/vomiting, aura that usually precedes the headache (visual — starts paracentrally and expands temporally with advancing edge forms a positive scotoma, motor — hemiparesis, speech — dysphasia, somatosensory — hemianaesthesia/paraesthesia)
- Ask about symptoms of MS
  - Ocular symptoms: pain on eye movements, rapid decrease of vision over hours/days with recovery starting at 2 weeks
  - Systemic symptoms: limb weakness, paraesthesia, urine retention, incontinence

3.48.3 Examination

- Ophthalmic examination to exclude
  - Retinal vascular diseases
  - Optic neuropathy

3.48.4 Investigations

- Bloods: FBC, CRP, ESR
- TAB
- Carotid doppler
- Cardiac echocardiography
- MRI head

3.48.5 Treatment

- Treat underlying cause
- Refer to TIA clinic with ABCD^2 score

3.49 Juvenile Idiopathic Arthritis (JIA) (Table 3.37)

3.49.1 International League of Associations of Rheumatologists Classification

- Systemic disease
- Polyarticular rheumatoid factor positive: five or more joints affected during the first 6 months of disease
- Polyarticular rheumatoid factor negative: five or more joints affected during the first 6 months of disease

Table 3.37 Key facts about JIA

- Chronic rheumatic disease of childhood characterised by chronic inflammatory arthritis (swelling within a joint or limitation in range of movement with joint pain or tenderness which persists for a minimum of 6 weeks)
- Onset prior to age 16 years old
- More common in girls but boys get higher rates of visual loss and complications
- Annual incidence in the UK is 1:10,000 with a prevalence of 1:1000 (The BSPAR and RCOphth guidelines for screening for uveitis in JIA 2006)
- Type of arthritis and the age at onset dictates the risk of developing uveitis
- Uveitis in JIA is asymptomatic until visual complications arise and therefore screening by slit-lamp is essential for diagnosis
- Visual impairment arises mainly from complications of the uveitis including cataract, glaucoma, macular oedema, hypotony

- Oligoarticular persistent: one to four joints affected throughout the first 6 months of disease
- Oligoarticular extended: one to four joints affected throughout and after the first 6 months of disease
- Psoriatic arthritis
- Enthesitis-related arthritis
- Undifferentiated arthritis

3.49.2 Risk Factors for Developing Uveitis in JIA

- Oligoarticular group
- ANA positive
- Female
- <7 years old at age of onset

3.49.3 Examination

- Articular
- Ocular
  - Chronic recurrent anterior uveitis with a white eye, usually bilateral
  - Complications of uveitis:
    Band keratopathy
    Macular oedema
    Cataract
    Glaucoma
    Hypotony that may lead to phthisis bulbi

3.49.4 Investigations

- Bloods: ANA
- OCT: macular oedema

3.49.5 Treatment

- Arthritis
  - Physiotherapy
  - Occupational therapy
  - Joint inflammation:
    NSAIDs
    Oral corticosteroids
    Immunosuppresants
    Biologics: adalimumab, etanercept, tocilizumab are recommended for treating polyarticular and extended oligoarticular JIA (NICE guidance)
- Anterior uveitis and macular oedema
  - Topical steroids + mydriatics
  - Subtenon injection of steroids/orbital floor injections
  - Oral corticosteroids
  - Immunosuppresants: methotrexate (MTX)
  - Biologics: infliximab, adalimumab
- Complications of ocular inflammation
  - Glaucoma:
    Topical medications
    Trabeculectomy
    GDI
  - Cataract:
    Cataract extraction once uveitis quiescent for at least 3 months

Preoperative considerations:
- Determine visual potential
- Concurrent surgery: co-existing ERM, vitreous opacity
- Frequent topical ± oral steroid 1–2 week before surgery

Intraoperative considerations:
- Maximise pupil size: synechialysis, intracameral phenylephrine, iris hooks
- Large capsulorrhexis to prevent post-operative capsular phimosis
- Meticulous removal of all nuclear matter and cortical matter

Postoperative considerations:
- Frequent topical ± oral steroids (if started preoperatively) that are tapered slowly to zero or maintenance dose
- Close follow up: 1 day post-op, 1 week post-op, 6 weeks post-op

– Band keratopathy:
  Chelation with ETDA
  PTK

3.49.6 BSPAR and the RCOphth Guidelines for Screening for Uveitis in JIA 2006

3.49.6.1 Principles
- Initial screening examination within 6 weeks of referral
- Symptomatic patients or patient suspected of cataracts or synechiae should be seen within 1 week of referral
- EUA should be considered if the patient is uncooperative at initial screening or for an urgent symptomatic examination in a young child
- Screening should restart at 2 monthly intervals after stopping MTX or any other immunosuppressant therapy during the period of maximum risk for 6 months before reverting to the previous screening arrangements

3.49.6.2 Specific Screening Schedules
- First screening within 6 weeks of referral
- 2 monthly intervals from onset of arthritis for 6 months, then 3–4 monthly screening for time outlined below:
  – Oligoarticular JIA, Psoriatic arthritis onset and Enthesitis related arthritis irrespective of ANA status onset under 11 years:
    <3 years old at onset: screen for 8 years
    3–4 years old at onset: screen for 6 years
    5–8 years old at onset: screen for 3 years
    9–10 years old at onset: screen for 1 year
  – Polyarticular ANA + JIA onset under 10 years:
    <6 years old at onset: screen for 5 years
    6–9 years old at onset: screen for 2 years
  – Polyarticular ANA-JIA onset under 7 years:
    All children need 5 years of screening
- Alternative method is to screen all these groups until age 11–12 years
- Older patients presenting for the first time after the age of 11 should undergo 1 year of screening

3.50 Paediatric Cataract

3.50.1 History

- Any family history of childhood cataracts (parents, siblings)
- Exposure to corticosteroid or radiation therapy
- Ocular trauma: accidental or non-accidental
- Co-morbidities suggesting systemic disease:
  – Galactosaemia: failure to thrive
  – Lowe syndrome: hypotonia, problems with weight gain, delayed milestones, feeding difficulties
  – Dysmorphic features suggestive of a syndrome
- Intrauterine infections (TORCH): associated with severe intraocular disease

- Age child was first noted to squint or have leukocoria
- If bilateral cataracts, ask parents when they first noted abnormal visual behaviour or nystagmus

3.50.2 Examination

- Vision testing
  - Fix and following a target (CSM method: **C**entral — location of corneal light reflex under monocular conditions, **S**teady — steadiness of fixation as light is held motionless and slowly moved around under monocular conditions, **M**aintained — binocular conditions): 3 months onwards
  - Forced choice preferential looking tests (e.g, Teller acuity card): 0–1 year
  - Cardiff cards: 0–2 years
  - 3 m logMAR uncrowded Kay pictures: 18 months to 3 years
  - 3 m logMAR crowded Kay pictures: 2–4 years
  - 3 m logMAR crowded letters: Above 3 years
- Pupillary reflexes for an RAPD: suggests poor visual potential
- Look for nystagmus: suggests severe visual impairment and poor visual potential
- Slit lam exam
  - Evaluate cornea
  - Evaluate iris
  - Evaluate morphology of cataract:
    Anterior polar: AD inheritance, minimal visual deprivation, non-progressive
    Anterior subcapsular: atopic dermatitis
    Posterior subcapsular: radiation
    Lamellar: rubella, diabetes, galactosaemia
    Sutural: Fabry's disease, mannosidosis
    Posterior cortical with lenticonus: Alport's syndrome
    Nuclear: rubella, galactosaemia ("oil droplet" cataract)
- Dilated fundus examination
  - Optic nerve
  - Retina
- Examine parents and siblings: presence of asymptomatic cataracts may establish the heredity

3.50.3 Investigations

- B-scan: if density of cataract precludes an adequate view of the fundus
- Unilateral cataracts: no tests required as most are isolated ocular problems
- Bilateral cataracts
  - No tests required if positive family history and child has no other medical problems
  - If no family history — investigate for systemic associations:
    Paediatric systemic evaluation
    Galactosaemia: urinalysis for reducing substances, galactokinase levels
    Lowe syndrome: urine amino acids, serum electrolytes, enzyme assay on cultured skin fibroblasts, OCRL gene testing
    TORCH screen: serology for toxoplasma, syphilis, rubella, CMV, HSV
    Karyotyping and geneticist involvement if dysmorphic features are present in child

3.50.4 Treatment

- Non-surgical
  - Observation: cataracts that are not in the visual axis, <3 mm in diameter, partial density
  - Dilation
- Surgical
  - Indications: visually significant cataracts: cataracts that are dense, central/axial, posterior, >3 mm in diameter
  - Determining whether a cataract is visually significant in young children who can't use an eye chart:

Retinoscopy: blackening of the retinoscopic reflex in the visual axis (i.e. how much of the pupil has an absent red reflex) is suggestive of a visually significant cataract

Fixation behaviour of the cataractous eye

– Preoperative considerations:

Timing of cataract surgery:

- 6 weeks for a unilateral cataract
- 10 weeks for a bilateral cataract (1–2 week period between lensectomy for each eye)

IOL implantation:

- Infant Aphakia Treatment Study (Infant Aphakia Study Treatment Group 2010, 2014): IOL implantation vs CL for the correction of aphakia in infants aged 1–7 months with unilateral congenital cataracts. No significant difference in VA for infants with a unilateral congenital cataract who were corrected with a CL compared to an IOL after cataract surgery at 5 years. IOL may be better for families who have a developmentally delayed child or are expected to have difficulty caring for the contact lenses
- IoLunder2 study (Solebo et al. 2018): children aged 2 years or younger who had cataract surgery with IOL implantation versus cataract surgery with aphakic correction with contact lenses or glasses. IOL implantation does not confer better vision or protection against postoperative glaucoma. IOL implantation increases the risk of requiring early reoperation in children younger than 2 years with bilateral or unilateral cataract

Biometry: performed in the operating room with the child under anaesthesia, A-scan to determine axial length, handheld keratometer to determine K readings.

– Intraoperative considerations:

Suturing of corneal wound incisions (absorbable 10/0 sutures): corneal tissue is less likely to self-seal in children and children more prone to traumatising the eye

Posterior capsulotomy + anterior vitrectomy (up to age 6 or 7): secondary opacification of the posterior capsule is more frequent and thicker in children

Subconjunctival dexamethasone: IATS showed similar rates of pupillary membrane formation with or without subconjunctival dexamethasone

– Postoperative considerations:

Glaucoma: 28% risk in the IOL group and 35% risk in the contact lens group at 5 years in the Infant Aphakia Treatment Study (Infant Aphakia Treatment Study Group 2014), no significant difference in glaucoma incidence between the CL and IOL groups at 5 years in the Infant Aphakia Treatment Study (Infant Aphakia Treatment Study Group 2014)

Amblyopia: occlusion therapy of the preferred eye

Inflammation (due to increased tissue reactivity, inflammatory complications, e.g. AC cell and flare, cell deposits on IOL optic, PS) are more frequently observed in children: topical (6×/day for 1 month) ± oral steroids postoperatively

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