Choroidal Neovascular Membrane

11

Contents

11.1 Age-Related Macular Degeneration

11.1.1 Clinical Features

Choroidal neovascular membranes (CNVs) most commonly occur with age-related macular degeneration (ARMD). Features of 'dry' AMD include hard drusen, soft drusen, retinal pigment epithelial disruption and geographic atrophy. Patients with extensive small drusen, non-extensive intermediate size drusen or pigment abnormalities have only a 1.3 % 5-year probability of progression to advanced AMD according to the ARED Study (Age-Related Eye Disease Study Research Group 2001). Those with extensive intermediate size drusen, at least one large druse, noncentral geographic atrophy in one or both eyes, or advanced AMD or vision loss due to AMD in one eye, are at risk of vision loss from advanced AMD in up to 50 % (large drusen with pigmentary changes) after 5 years (Ferris et al. 2005).

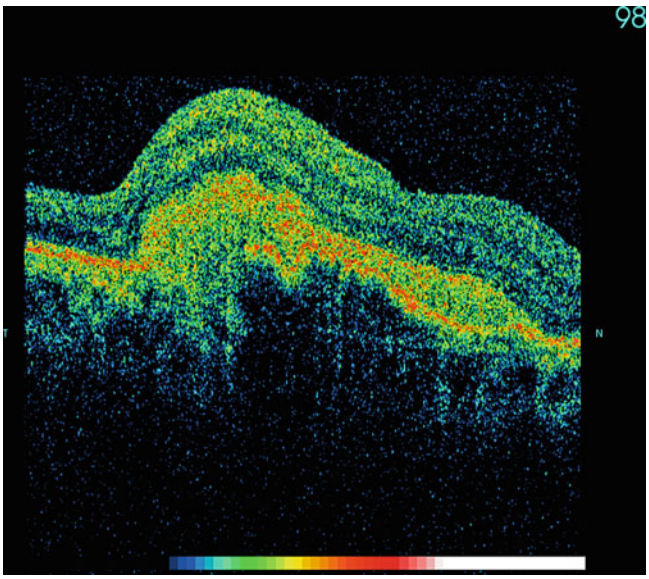

Fig. 11.1 OCT can demonstrate CNV membranes and be used to detect fluid around the membrane indicating a need for repeat anti-VEGF therapy. This membrane is currently dry

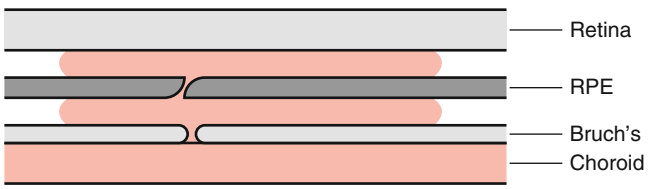

Fig. 11.2 Type 1 CNV is associated with age-related macular degeneration, presenting in all layers of the retina: sub-RPE in occult membrane, sub-neuroretina in classic membrane and possibly in the retina in retinal angiomatous proliferation (RAP)

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Simplified AREDS scoring system:

- 1 or more large drusen (≥125 μm, width of a large vein at disc margin) in an eye = 1 risk factor
- Any pigment abnormality in an eye = 1 risk factor
- Risk factors summed across both eyes
- The 5-year risk of developing advanced AMD in at least one eye:

0 factors	0.5 %
1 factor	3 %
2 factors	12 %
3 factors	25 %
4 factors	50 %

- If no large drusen but intermediate drusen present in both eyes = 1 risk factor

This risk can be reduced by taking a cocktail of high-dose vitamins (commercially available in combination preparations) such as 500 mg vitamin C; 400 IU vitamin E; 15 mg beta-carotene (to be avoided in smokers or ex-smokers of less than 10 years because of an increased risk of lung carcinoma); zinc, 80 mg, as zinc oxide and copper, 2 mg, as cupric oxide (Age-Related Eye Disease Study Research Group 2001). This cocktail has been shown to reduce the chance of advancement in patients with high-risk characteristics by approximately 30 %.

Patient's CNVs already in one eye are at particular risk of progressing to 'wet' ARMD with CNV production. The CNVs cause distortion and loss of vision with serous elevation of the retina, subretinal haemorrhage and finally disciform scar formation.

The CNVs are usually classified on fluorescein angiography into:

Classic: appear early and thought to be beneath the neuroretina

Nonclassic, indistinct and slower appearance: thought to be under the RPE

Mixed: can be either predominantly classic or nonclassic

The frequent bilaterality of the condition results in a high proportion of patients who are technically blind, with severe loss of central vision. For this reason, surgical approaches have been tried. However, these are much less commonly used since the effectivity of anti-VEGF treatments bevaci-

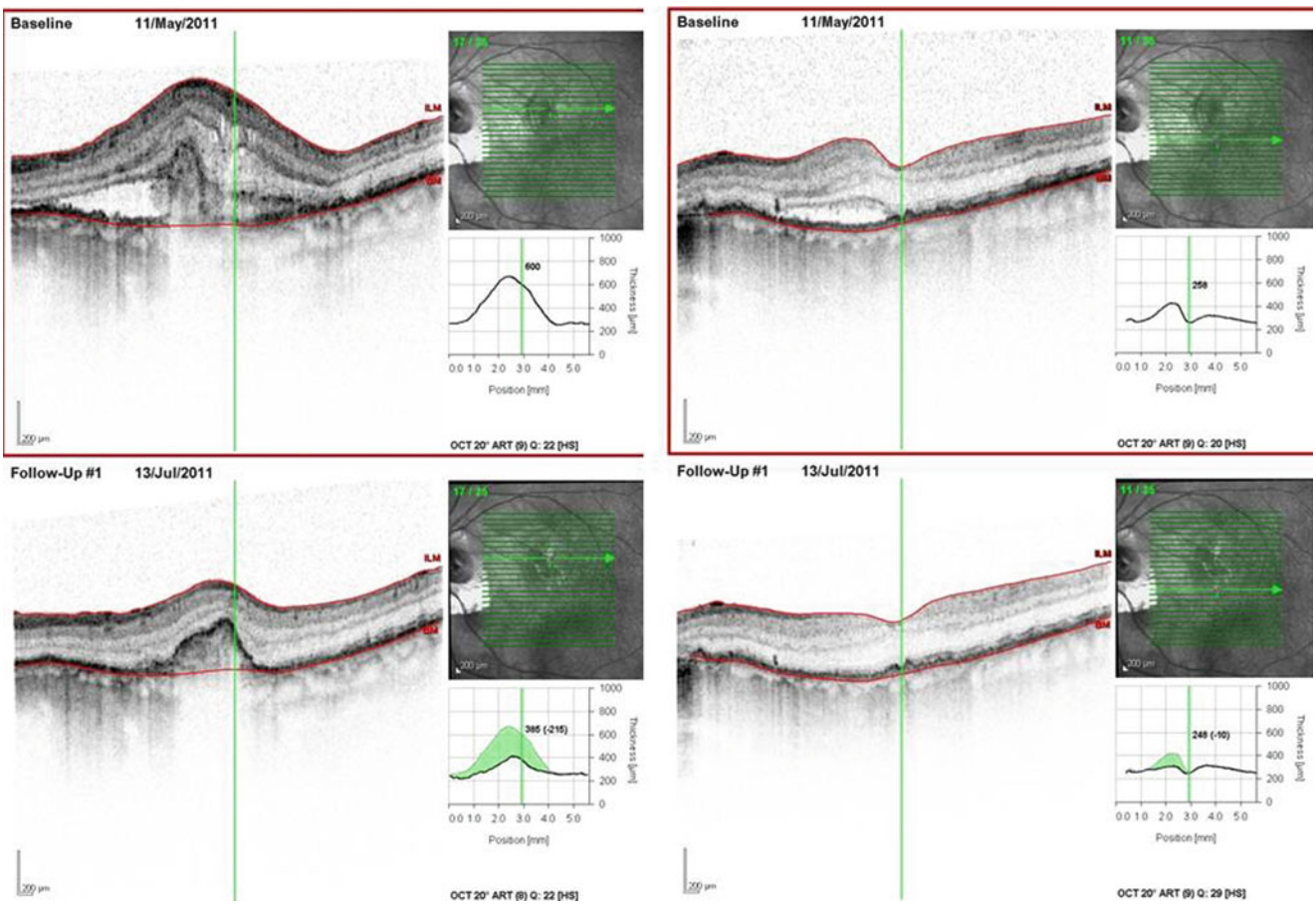


Fig. 11.3 A CNV shrunken with resolution of fluid leakage after ranibizumab injection, resulting in 20/20 vision

Table 11.1

Drug	Structure	Dosage	Route of administration
Ranibizumab (Lucentis) (Rosenfeld et al. 2006a, b; Brown et al. 2006)	Antibody fragment	0.5 mg/0.05 ml	Intravitreal
Pegaptanib (Macugen)	Aptamer (oligonucleotide)	0.3–1.0 mg/0.1 ml	Intravitreal
Bevacizumab (Avastin)	Complete immunoglobulin	1.25 mg/0.05 ml	Intravitreal

zumab (Avery et al. 2006), pegaptanib (Chakravarthy et al. 2006) and ranibizumab (Rosenfeld et al. 2006a, b; Brown et al. 2006) has been proven. The last is now established as the therapy of choice for CNVs from AMD.

Vitreomacular traction is more common in eyes with exudative AMD (38 %) compared with nonexudative AMD (10 %) and PVD that are less common (21 and 68 %, respectively), suggesting to some investigators a role for the vitreous in exudative AMD (Robison et al. 2009).

There may be situations where the surgery can be of use:

- Vitreous haemorrhage with CNV and subretinal haemorrhage
- Pneumatic displacement of subretinal haemorrhage
- Failure of anti-VEGF regimes

11.1.2 Vitreous Haemorrhage and CNV

A patient with sudden onset vitreous haemorrhage with evidence of a large subretinal craggy mass on ultrasound is very likely to have suffered a subretinal bleed from a CNV from AMD (Orth and Flood 1982). The subretinal haemorrhage is usually in the macular area but occasionally is due to a peripheral CNV, and the macula is clear of blood. Removing the vitreous haemorrhage is useful to restore peripheral vision. The haemorrhage is often very thick and may be altered to an ochre colour seen in severe bleeds. The vitreous may or may not be detached. If attached, separate it from the retina as in macular hole surgery. If there are large bullae of subretinal haemorrhage, there is a temptation to remove some of the subretinal blood via retinectomy; however, this is often not very effective in removing the blood as fibrinous mass has a 'cottage cheese' consistency and cannot be washed out. The retinectomies may allow fluid blood to egress in the postoperative period causing severe hyphaema and the potential for raised IOP and corneal staining. A larger 180° retinectomy will allow access to the blood for removal but runs the risk of postoperative

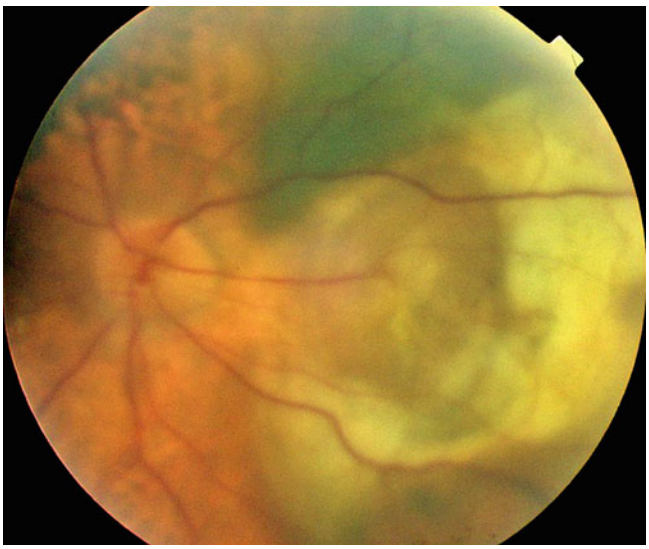


Fig. 11.4 Very large subretinal bleeds from CNV can cause severe vitreous haemorrhage. These are usually obvious on ultrasound as a crenated posterior mass

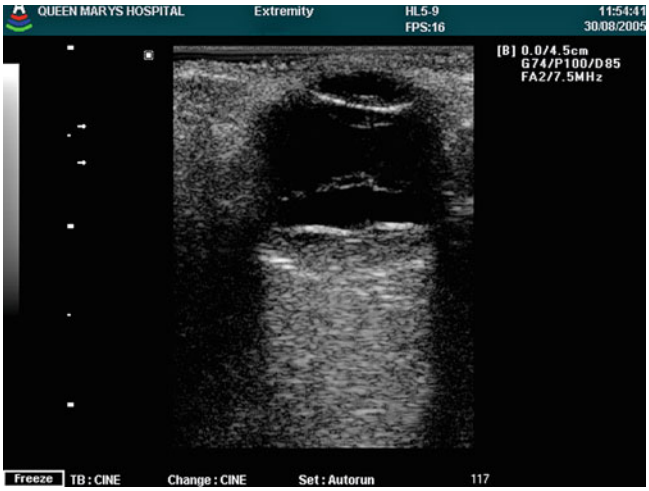


Fig. 11.5 An ultrasound of a patient with vitreous haemorrhage from subretinal bleed and age-related CNV, note the PVD and large craggy mass at the posterior pole

PVR, and visual recovery is unlikely to be much improved after prolonged surgery. If the subretinal blood is localised, leave it in situ; in most circumstances, it will remain localised, allowing the patient to achieve vision from unaffected parts of the retina.

Often these patients are on antiplatelet or anticoagulation therapy (Kuhli-Hattenbach et al. 2010). Examine the other eye for evidence of AMD.

Preoperative injection of intravitreal tissue plasminogen activator can be used to try to liquefy the clot (Oshima et al. 2007).

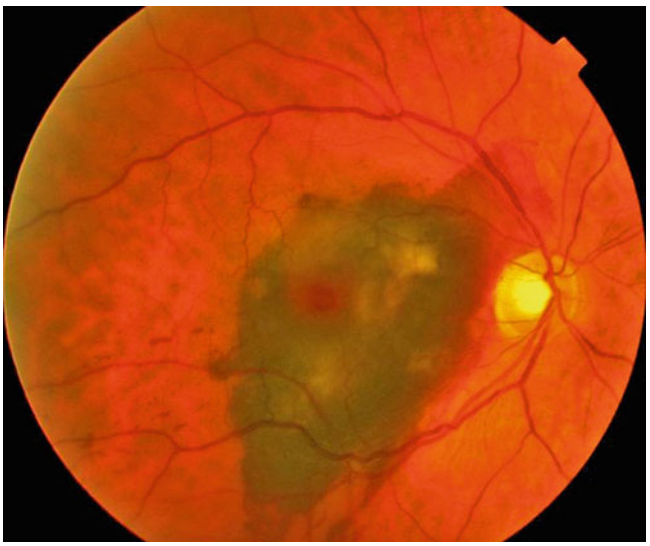


Fig. 11.6 Subretinal blood can occur from a number of reasons including type I choroidal neovascular membranes and macular aneurysms. Often, the blood will break through the retina, as seen in this case, into the posterior vitreous gel

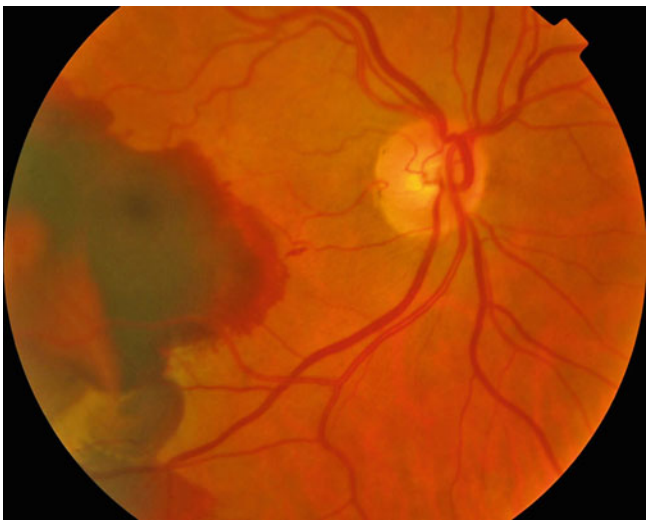


Fig. 11.8 Some CNV in ARMD will bleed into the subretinal space; a PPV and gas insertion (with or without subretinal tissue plasminogen activator, TPa) can displace the blood away from the fovea, thereby increasing vision despite a persistent CNV. This sequence of images shows the preoperative status and sequential improvement in the retinal appearance over months (see Figs. 11.9–11.11)

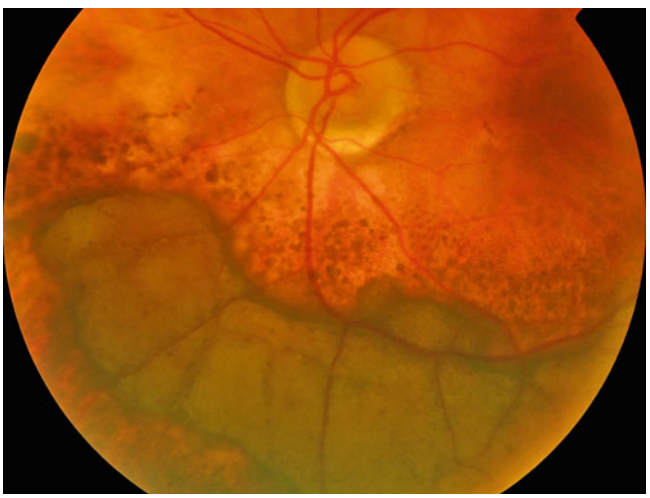


Fig. 11.7 An eccentric CNV caused a vitreous haemorrhage after a subretinal haemorrhage which did not affect the macula

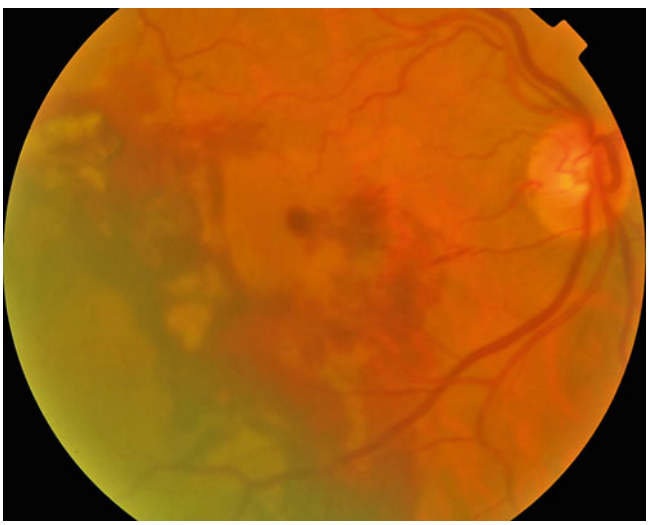


Fig. 11.9 See previous figure

11.1.3 Pneumatic Displacement of Subretinal Haemorrhage

A bleed from a CNV may spread under the macula, giving a rise to a large central scotoma. It is possible to facilitate resorption of the haemorrhage and perhaps to displace the bleed away from the fovea by performing a PPV and gas. The patient is required to posture upright to allow the gas bubble to act on the haemorrhage displacing it inferiorly. There is a debate whether either intravitreal tissue plasminogen activator (tPA, 0.05 ml, 50 μg) or subretinal tPA should be injected to facilitate the breakup of the clot (Gopalakrishan et al. 2007; Ohji et al. 1998; Hesse et al. 1996; Singh et al. 2006). The molecular size of tPA is similar to bevacizumab which is able to cross the retina in AMD. Any agent injected into the vitreous cavity in a vitrectomised eye however tends to have a shorter half-life because of more rapid clearance of the drug in the fluid-filled vitreous cavity in comparison to the gel-filled cavity. If injecting tPA into the subretinal space, the drug can be inserted using a 40-gauge needle to raise a bleb of fluid under the retina. As with any injection under the macula, take care that the pressure rise in the subretinal space does not 'blow' a hole in the fovea, the weakest point in the macula.

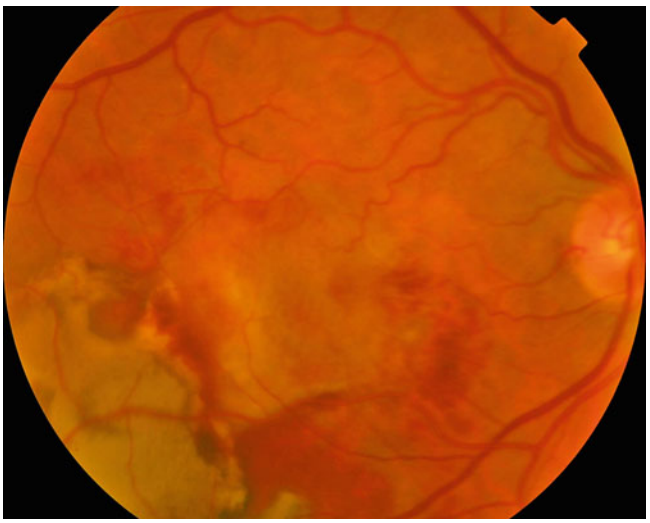


Fig. 11.10 See Fig. 11.8

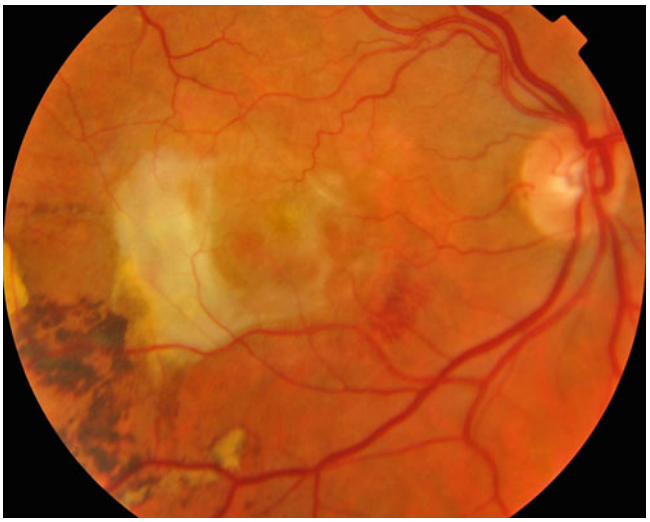


Fig. 11.11 See Fig. 11.8

11.1.4 Surgery for Failed Anti-VEGF Therapy

11.1.4.1 Introduction

Surgical approaches have been applied to subfoveal CNV. The most established strategy has been 360° macular translocation (Machemer and Steinhorst 1993a, b; Eckardt et al. 1999). Success rates are reportedly 33 % improvement in vision, but the usual benefit is for reading speed (bdel-Meguid et al. 2003; Wong et al. 2004) with 10 % recurrence. Translocation for geographic atrophy has been complicated by the rapid return of the atrophy in the translocated macula (Khurana et al. 2005).

Various other methods such as limited macular translocation and transplant of a RPE and choroidal patch are of unproven benefit (van Meurs et al. 2004; Stanga et al. 2002; Lappas et al. 2004; Angunawela et al. 2005; Thomas et al. 1992; Phillips et al. 2003; Fujii et al. 2003; Pieramici et al. 2000; Joussen et al. 2006). Removal of peripapillary

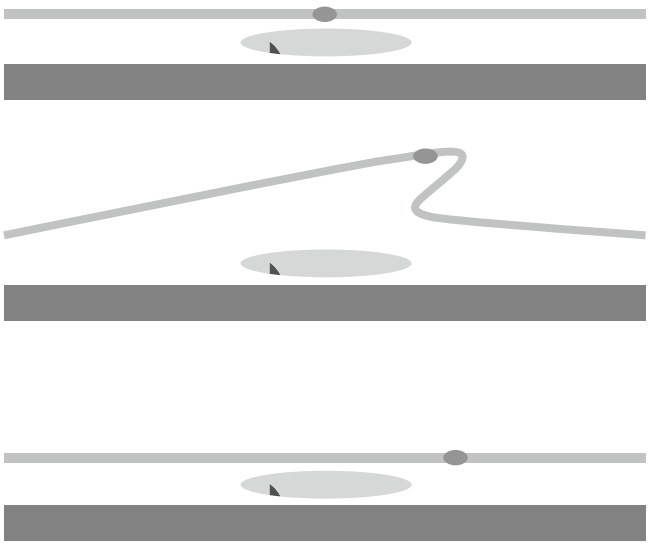


Fig. 11.12 The principle of retinal translocation is to move the fovea onto an undamaged area of RPE

CNV on its own is of doubtful benefit (Bains et al. 2003). Clinicopathologic studies of eyes with surgically removed CNV reveal breaks in Bruch's membrane and persistent sub-RPE CNV (Grossniklaus et al. 2006).

In most circumstances, the monthly injection of ranibizumab is the current treatment of choice for CNV from AMD. However, the long-term dosage regimes for these agents are not well understood, and combination therapy with intravitreal steroid and PDT are being investigated to try to reduce the need for years of repeated injections. In those patients with loss of vision in their second affected eye who are not responsive to these agents, there may still be a role for 360° macular translocation surgery.

11.1.4.2 360° Macular Translocation

Additional surgical steps

Phacoemulsification of the lens with IOL

Artificial inducement of retinal detachment via infusion of fluid through a retinotomy

Removal of the CNV

Drainage of subretinal fluid and insertion of heavy liquids

Translocation of the retina

Reattachment of the retina

360° Laser retinopexy

Silicone oil tamponade

Perform a phacoemulsification cataract extraction. Set up the PPV using a shortened infusion cannula preferably. Perform the PPV with close removal of the peripheral gel at the vitreous base with indentation if required.

Table 11.2 Difficulty rating for 360° macular translocation

Difficulty rating	Very difficult
Success rates	Low
Complication rates	High
When to use in training	Late

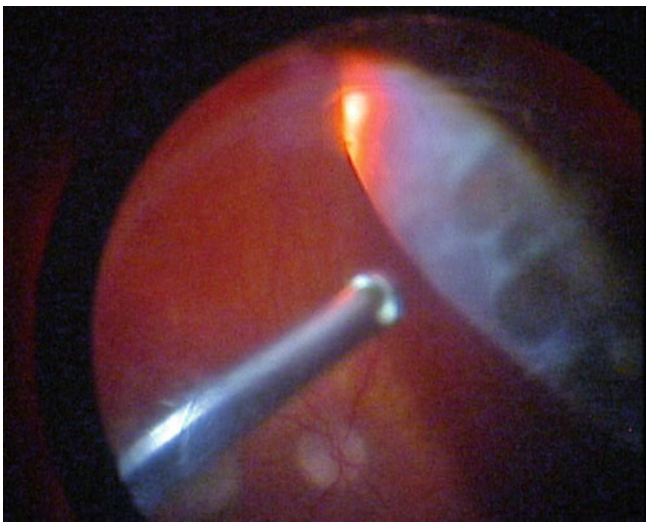


Fig. 11.13 For 360° macular translocation after cataract extraction and lens implantation, trim the vitreous base with a high-speed cutter. With a 40-gauge cannula, create a retinal detachment and then spread the SRF with fluid–air exchange. Create the 360° retinectomy, dissect off the CNV, rotate the retina, laser the retinectomy and insert silicone oil (see Figs. 11.14–11.19)

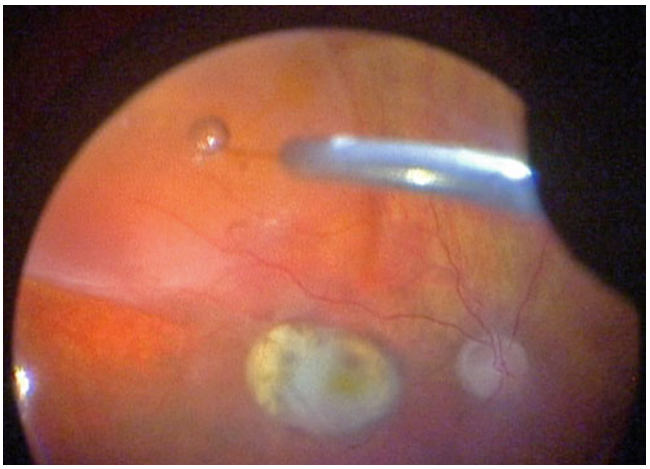


Fig. 11.14 See previous figure

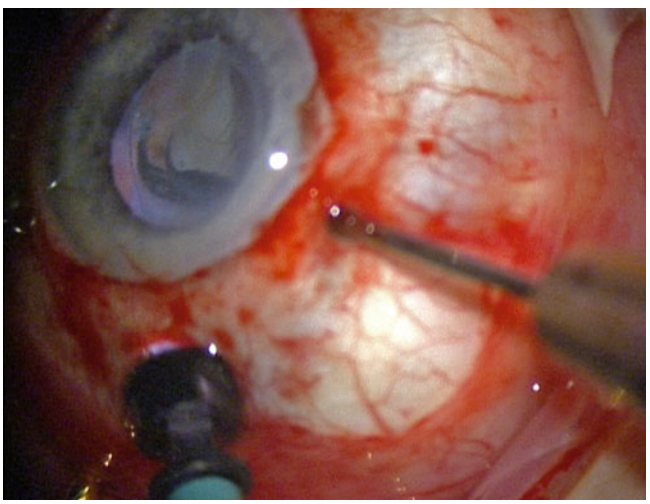


Fig. 11.15 See Fig. 11.13

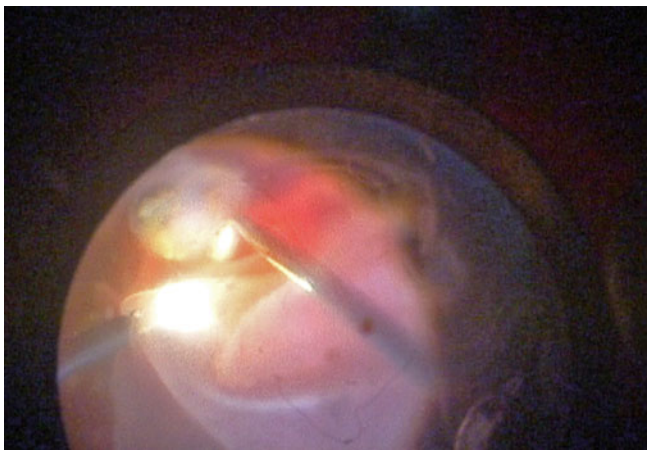


Fig. 11.16 See Fig. 11.13

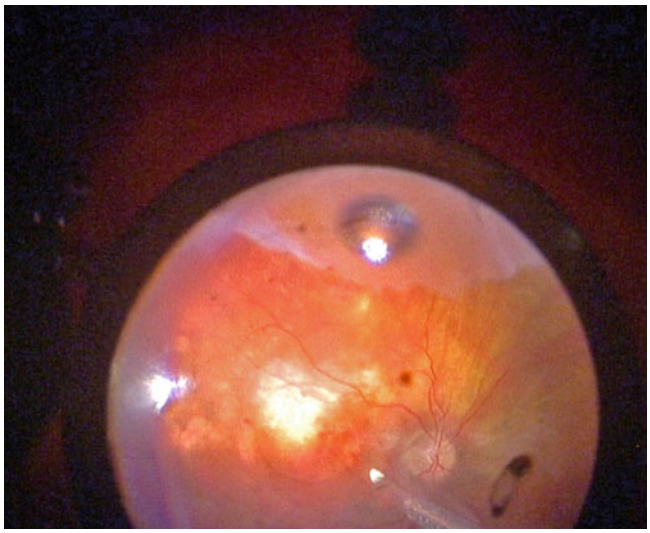


Fig. 11.17 See Fig. 11.13

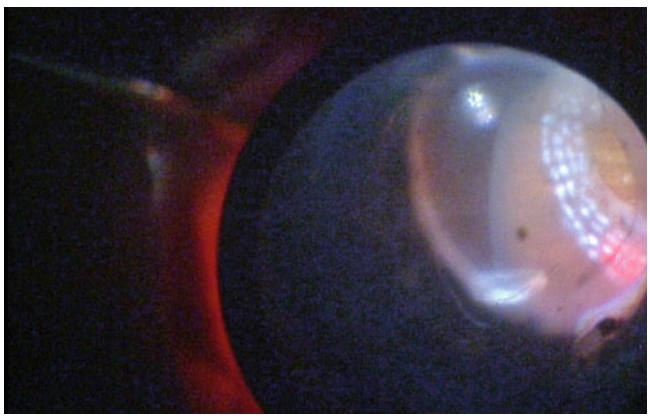


Fig. 11.18 See Fig. 11.13

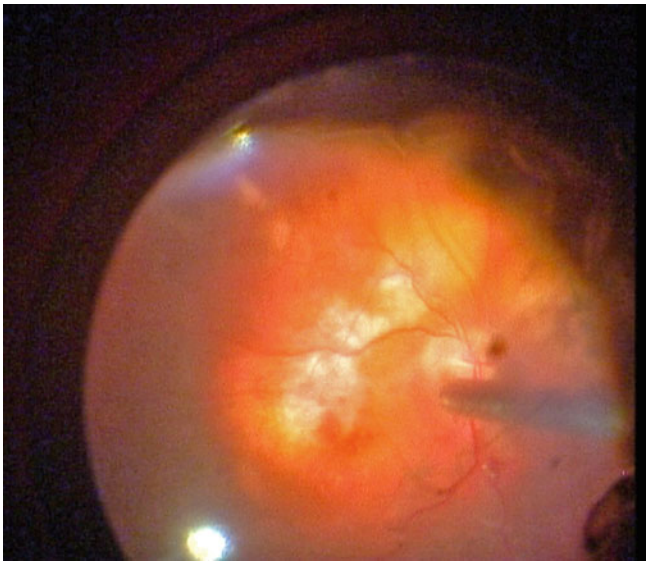


Fig. 11.19 See Fig. 11.13

Note: It is very important not to create an iatrogenic break as this will create difficulty during the induction of the retinal detachment by the loss of infusion fluid through the break.

Insert a high-gauge (40-G) cannula through the retina at the equator. Inject fluid, gradually increasing the pressure until retinal bullae are formed. Use air injection to spread the SRF to undetached retina and then replace with fluid. Repeat until the entire retina is detached. Perform a 360° retinectomy as anteriorly as possible. Remove the CNV. Use a small bubble of 'light heavy' liquids to open out the retina again. Rotate the retina by gentle traction with a diamond-dusted silicone-tipped manipulator so that the fovea reaches healthy RPE. Use additional 'light heavy' liquids to reattach the retina completely. Apply laser retinopexy to the 360º retinectomy. Exchange the liquid for the silicone oil and close.

At a second operation (3–6 months), the silicone oil is removed and the extraocular muscles moved to compensate for torsional displacement of the image.

11.1.5 Specific Complications

- Retinal detachment associated with proliferative vitreoretinopathy in approximately 10–20 % (Aisenbrey et al. 2002; Pertile and Claes 2002)
- Diplopia 6 %
- Recurrent CNV 10 %
- Choroidal haemorrhage
- Macular hole and pucker
- Severe hypotony has also been described (Ichibe et al. 2002)

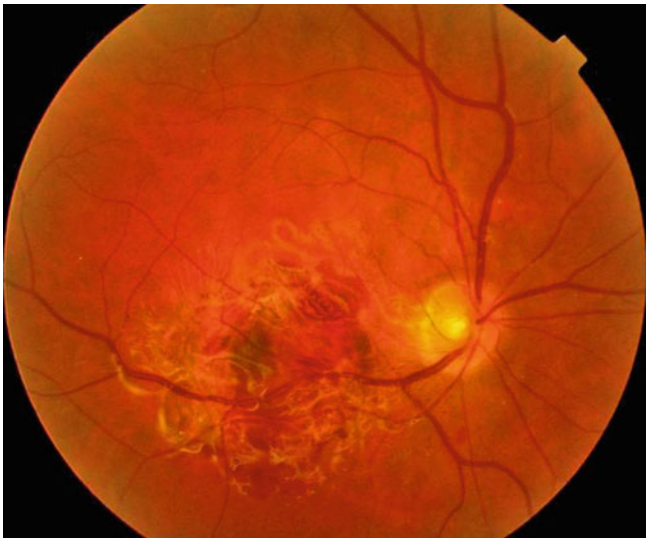


Fig. 11.20 The retina has been moved in this patient; the fovea is now situated over healthy RPE providing 20/120, picture one. Retinal pigment epithelial transplantation techniques are being investigated but are still experimental and not established as a means of improving vision in age-related macular degeneration, picture 2

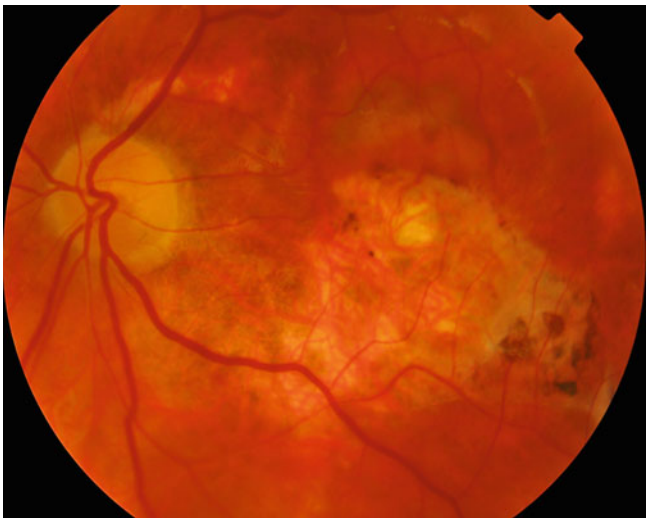


Fig. 11.21 Recurrences after 360 MT are common and usually occur on the foveal side of the scar, a colour and FFA images are shown (see Fig. 11.22)

11.1.6 Success Rates

The surgery does not significantly improve vision from preoperatively but does improve reading speed and quality of life scores (Fujikado et al. 2002; Cahill et al. 2005; Lai et al. 2002; Mruthyunjaya et al. 2004).

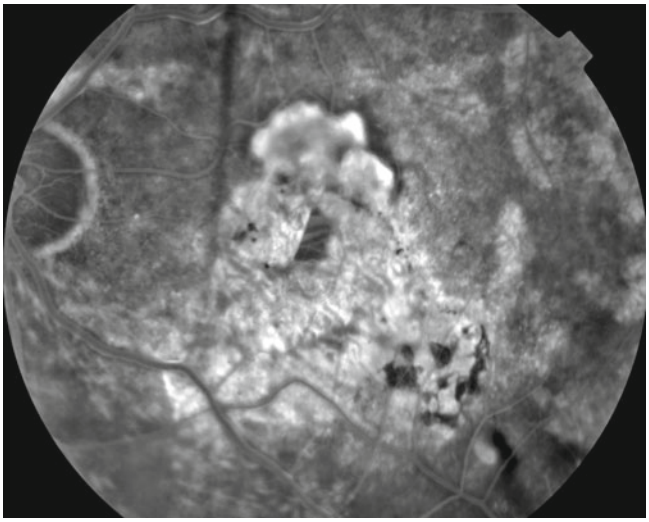


Fig. 11.22 See previous figure

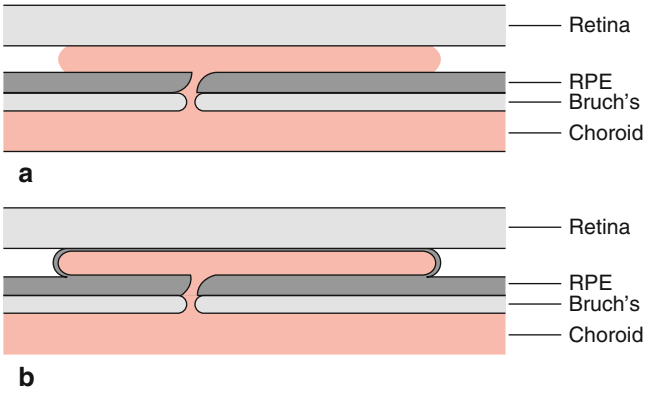


Fig. 11.24 Type 2 CNV typically penetrate the RPE and become surrounded by the RPE. Unlike type 1 CNV, the membranes can be removed with preservation of the RPE function

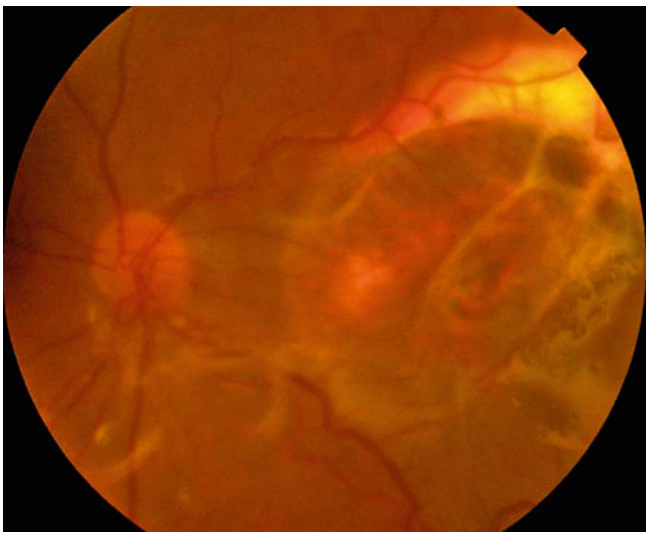


Fig. 11.23 The RPE has been cut and moved into the area of defect left by removal of a CNV

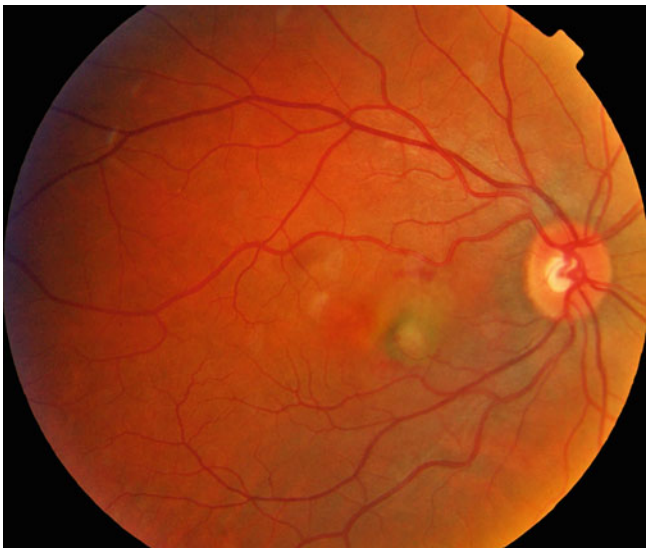


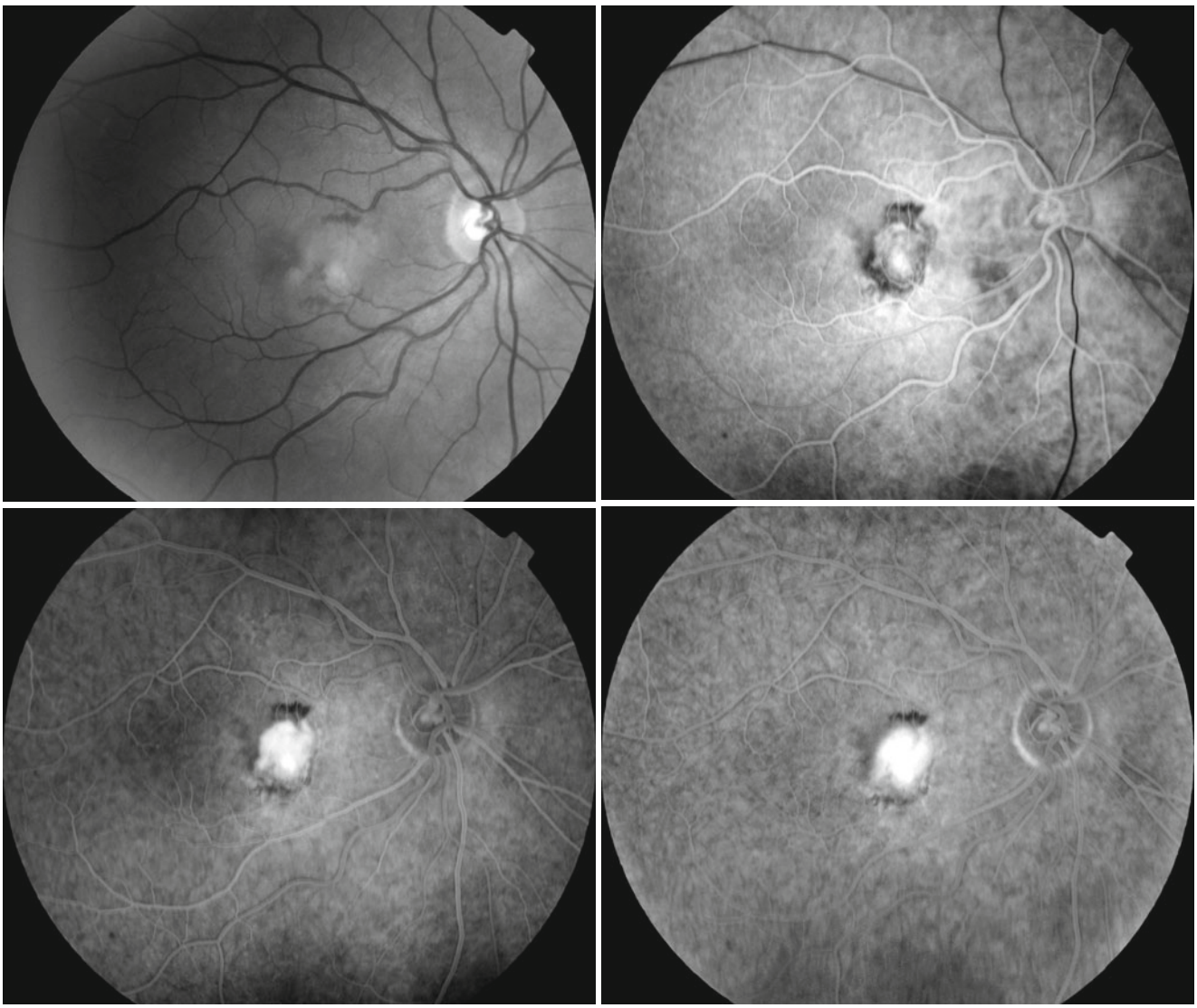
Fig. 11.25 Spontaneous idiopathic type 2 CNV can occur and can be treated with intravitreal anti-VEGF therapy although spontaneous resolution occurs in 50 %, FFA (see Fig. 11.26)

11.2 Choroidal Neovascular Membrane Not from ARMD

11.2.1 Introduction

These occur in a variety of conditions and most often have a more benign clinical course. The CNV are often smaller and self-limiting. Surgical removal is possible with immediate restoration of vision or reduction in distortion but with a high chance of recurrence of approximately 30 %.

Presumed ocular histoplasmosis (Atebara et al. 1998; Melberg et al. 1996; Lit et al. 2001) (also called punctate inner choroidopathy or multifocal inner choroidopathy in some countries), uveitis, choroidal rupture (Gross et al. 1996), juxtafoveolar telangiectasia (Berger et al. 1997), central serous chorioretinopathy (Cooper and Thomas 2000) or macular surgery (Ng et al. 2002) can all be associated with CNV which will respond to surgical removal. However, a randomised trial has shown no benefit of surgery over observation (Hawkins et al. 2004). Angioid streaks and myopia (Ruiz-Moreno and de la Vega 2001; Uemura and Thomas 2000a, b) may produce CNV, but surgical removal is less successful.



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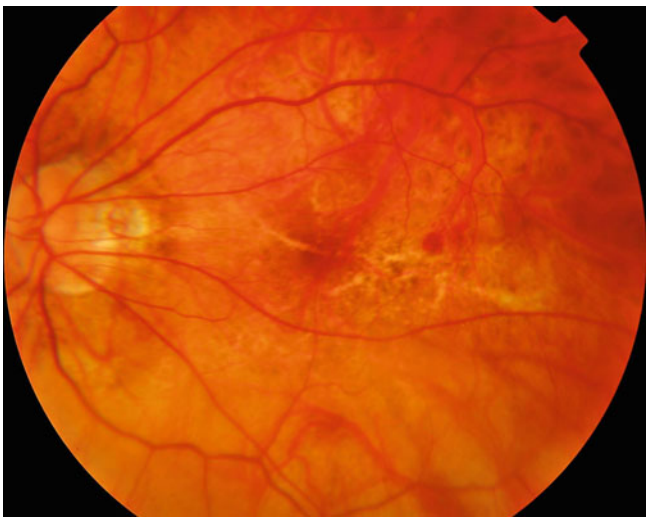

Fig. 11.27 There is a Foster–Fuch's spot temporal to the fovea in this high myope, signifying a subretinal bleed from a small type 2 CNV. Most of these resolve with maintenance of stable vision. Note the lacquer cracks (splits in Descemet's membrane) a risk factor for CNV

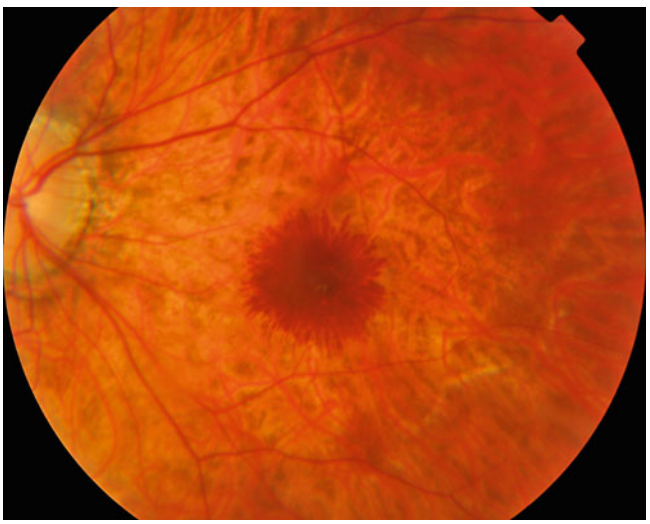

Fig. 11.28 Myopic CNV are often mixed type 1 and 2 and can produce subfoveal haemorrhage. Anti-VEGF therapy can be tried, but visual loss may persist

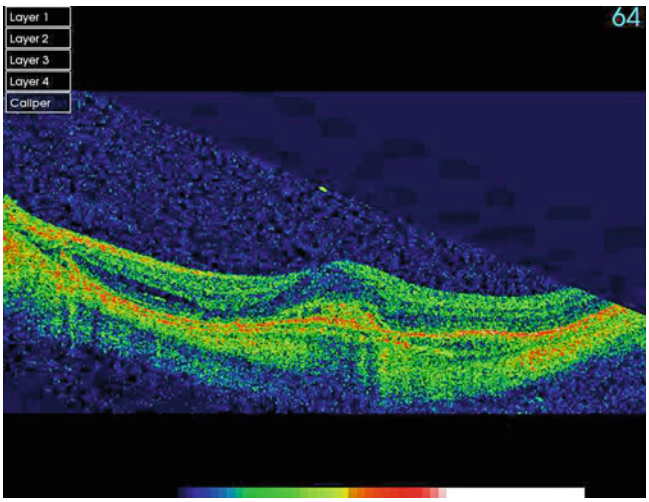

Fig. 11.29 CNV may appear in highly myopic eyes. These may regress spontaneously or be treated with intravitreal anti-VEGF therapy

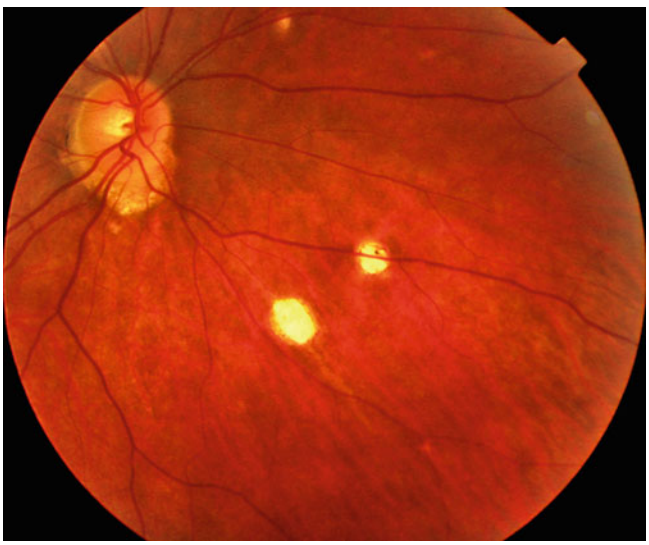

Fig. 11.30 PIC is often associated with neovascular membrane formation of type II. These can respond to surgery by removal, but recurrence is unfortunately common. Membranes vary in size, but the best for removal are small, well-circumscribed, pigmented lesions as opposed to more diffuse web-shaped lesions

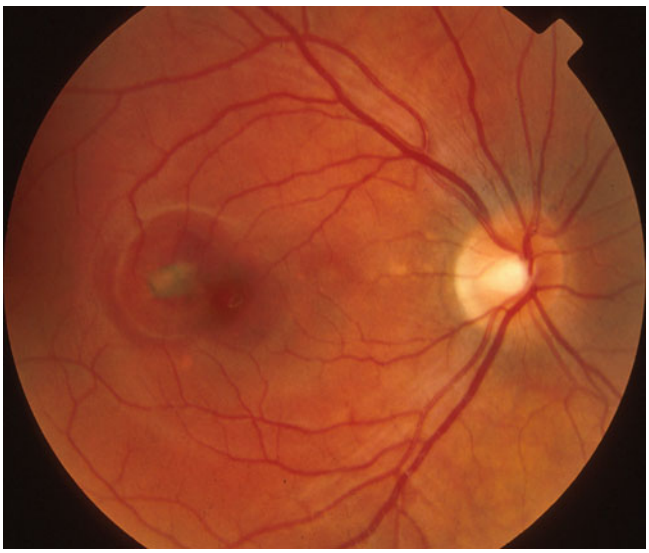

Fig. 11.31 Serous elevation around this small neovascular membrane distorts the fovea and reduces vision. Removal of the membrane will cause resolution of the serous elevation and improvement in the visual acuity

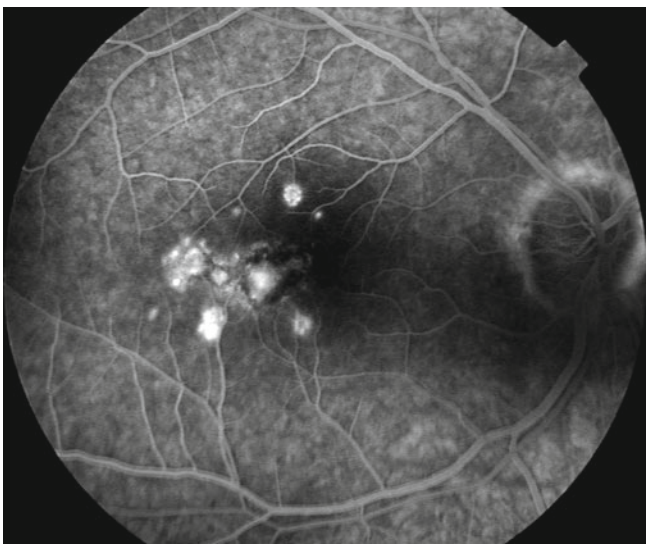

Fig. 11.32 A fluorescein angiogram of PIC

11.2.2 Surgery

Additional surgical steps

- Create a retinotomy in the macula, temporal to the fovea.
- Insert subretinal forceps.
- Loosen and grasp the CNV.

Table 11.3 Difficulty rating for PPV for type 2 CNV

Difficulty rating	Moderate
Success rates	Low
Complication rates	Low
When to use in training	Late

- Extract the CNV through the retinotomy.
- Access the retina via a PPV.

Usually the posterior hyaloid membrane requires detachment because these patients are young. With a bent MVR blade, incise the retina in the macula just temporal to the CNV to access the sub-neuroretinal space. Insert subretinal forceps (angled with delicate long prongs). With the forceps closed, sweep under and over the CNV to loosen attachments. With slightly open forceps, press down on the anterior surface of the CNV (this avoids grasping the retina whilst inserting the CNV tissue) and close the forceps. Extract the CNV through the retinotomy. Even quite large CNV will pass through the retinotomy, which has some inherent elasticity. The membranes can have retinal attachments. Care must be exercised during removal that the retina does not tear. Bleeding is usually slight because there is low blood flow in the CNV. Tamponade and laserpexy are not required and the PPV can be closed.

11.3 Summary

Vitrectomy surgery has uses in specific situations in AMD, but anti-VEGF therapy is the mainstay of therapy.

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