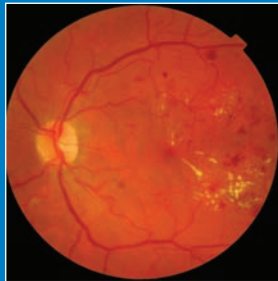


## MODULE 11 PART 5

## COURSE CODE: C-7983

# Optometric management of the posterior segment eye disease – vascular disorders of the retina



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In the field of medical retina, diagnosis is becoming more accurate with the introduction of new imaging techniques and better image resolution. However, despite all the advancements in ophthalmology, there is no substitute for a sound foundation of knowledge coupled with a careful patient history, detailed examination of the eye and referral to the appropriate ophthalmic speciality when needed.

The neurosensory retina begins at the retinal pigment epithelium (RPE) externally and extends to the internal limiting membrane internally. It is anatomically divided into 10 layers. Starting at the internal vitreous face, the layers are:

1. Inner limiting membrane
2. Nerve fibre layer
3. Ganglion cell layer
4. Inner plexiform layer
5. Inner nuclear layer
6. Outer plexiform layer
7. Outer nuclear layer
8. Outer limiting membrane
9. Photoreceptors
10. Retinal pigment epithelium

The RPE lies on Bruch's membrane of the choroid. Tight junctions between the RPE cells limit the transfer of substances from the underlying choroid capillaries to the outer neurosensory retina. This forms part of the blood retinal barrier. The internal neurosensory retina is supplied by branches of the central retinal artery and vein. The central retinal artery emerges from the centre of the optic

nerve, divides into four branches and supplies the four quadrants of the retina. The arterial branches run close to the internal limiting membrane in the nerve fibre layer. The branching arterioles then run through the different layers of the retina reaching the inner nuclear layer. The walls of the capillaries are non-fenestrated endothelial cells and this forms the second component of the blood retinal barrier.

There are no direct connections between arteries and veins in the retina and there is no lymphatic drainage. Veins follow the path of the retinal arteries and lie under the arteries that cross over them.

The veins drain into the central retinal vein and ultimately into the cavernous sinus or the superior ophthalmic vein.

The inner half of the retina derives its oxygen and nutrient supply from the central retinal artery. Diffusion from the choroid capillaries supplies the outer half of the retina. These basic concepts help us understand the basis behind vascular pathologies of the retina.

## Diabetic retinopathy

It is important to realise the overall impact of diabetes on the eye. Although this chapter concentrates on the retina, diabetics can suffer a myriad of signs and symptoms: cranial nerve palsies, pupillary abnormalities, neovascular glaucoma, cataracts and are more susceptible to vein and artery occlusions and ocular ischaemic syndromes.

Current management of diabetes and diabetic retinopathy is largely based on the evidence gained from key studies conducted in this field. These studies set the standard for current treatment and classification of the stages of diabetic retinopathy:

1. The United Kingdom Prospective Diabetes Study (UKPDS)
2. The Diabetic Retinopathy Study (DRS)
3. The Early Treatment Diabetic Retinopathy Study (ETDRS)
4. The Maculopathy Photocoagulation Study
5. The Diabetic Retinopathy Vitrectomy Study

Diabetes is generally classified as Type 1 or Type 2. Type 1 refers to patients with

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reduced insulin production who need insulin replacement. These patients tend to be younger. Type 2 diabetics develop insulin resistance and can be managed by diet, drugs and or insulin replacement. Although Type 2 diabetes tends to be a disease of the older population, we are now seeing a younger population diagnosed with this condition due to the increase in childhood obesity.

The UKPDS has shown that close monitoring of blood glucose and tight diabetic control, reduces the rate of developing diabetic retinopathy both in Type 1 and Type 2 diabetics.

Many theories exist on the pathogenesis of diabetic retinopathy. Retinal ischaemia is thought to be caused by factors such as altered platelet function and blood viscosity. Increased intravascular osmotic pressure due to high glucose levels also contributes to intracellular electrolyte imbalances and damage to the retinal vascular cells. It is the damage to the cells of the retinal vessels and their supporting cellular structures (pericytes) that lead to the signs associated with diabetic retinopathy.

Ischaemia leads to the production of vascular endothelial growth factors (VEGF) by retinal cells that subsequently lead to the development of retinal vascular abnormalities and new vessel formation.

The ocular manifestations of diabetes are summarised in table 1. These signs are listed in order of the severity of ischaemia and stages of diabetic retinopathy. In mild retinopathy, one may see only microaneurysms and as the severity of the retinopathy progresses, haemorrhages, cotton-wool spots and IRMA develop. Unchecked ischaemia ultimately leads to proliferative changes with new blood vessel formation.

### Examination of the diabetic retina should ideally be done addressing two questions:

**1. Is there diabetic maculopathy?** If yes, is it 'clinically significant' requiring treatment?

**2. What is the severity of the diabetic retinopathy?** Does the severity require close monitoring by an ophthalmologist or does the

retinopathy meet the criteria for treatment?

It is important to realise that significant diabetic maculopathy can exist in the absence of severe diabetic retinopathy and is potentially sight threatening (figure 1).

Clinically significant macular oedema (CSMO) should be referred promptly to an ophthalmologist to consider argon laser photocoagulation (table 2). This is either applied to focal areas of retinal thickening (focal laser) or as a grid to larger areas of diffuse

thickening (grid laser). The clinician may or may not perform a fundus fluorescein angiogram (FFA) prior to treatment.

The overall retina is evaluated, looking at signs to establish the degree of ischaemia and if 'high risk characteristics' are present. Non-proliferative diabetic retinopathy (NPDR) is now classified as mild, moderate and severe based on standard photographs from the ETDRS (table 3). These are available at: <http://eyephoto.opth.wisc.edu/Resear>

<b>Microaneurysms</b>	Seen as small red dots in the middle retinal layers. Weakening of the capillary wall causes dilatation and aneurismal changes.
<b>Exudates</b>	This is a collection of serum and breakdown products of neurones. They are seen as discrete yellow dots often surrounding areas of retinal thickening where fluid has leaked (e.g. from microaneurysms)
<b>Haemorrhages</b>	Rupture of weakened capillaries leads to haemorrhages. Deep haemorrhage (inner nuclear layer/outer plexiform layer) are round/oval, often called 'dot-blot haemorrhage'. Superficial haemorrhage (nerve fibre layer) is flame shaped.
<b>Cotton wool spots</b>	Local ischaemia causes swelling of the retinal nerve fibres due to obstructed axoplasmic flow. These are seen as white, fluffy spots.
<b>Venous beading and venous loops</b>	Sign of slow retinal circulation. Important indicator of ischaemia and areas of capillary non-perfusion.
<b>Intra retinal microvascular abnormalities (IRMA)</b>	Dilated capillaries representing collaterals that open up between the arterial and venous circulation.
<b>Neovascularisation of the disc (NVD)</b>	New vessels on or within one disc diameter of the optic nerve. New vessels appear as fine fronds that either lie flat on the surface of the disc or protrude into the vitreous gel. They tend to arise from retinal veins.
<b>Neovascularisation elsewhere (NVE)</b>	New vessels more than one disc diameter from the optic nerve. Fine vessels can lie flat on the retina or protrude into the vitreous gel.
<b>Vitreous haemorrhage</b>	Bleeding from NVE or NVD. May be subhyloid (between the vitreous face and the retina) or intravitreal.
<b>Fibrovascular change</b>	Proliferating NVE and NVD can develop fibrous changes. They appear as white bands that follow the NV.
<b>Tractional retinal detachment</b>	Posterior vitreous detachment and shrinkage can cause traction on NV and leads initially to vitreous haemorrhage and later to areas of tractional retinal detachment

➔ **Table 1**  
Ocular manifestations of diabetes

**Table 2 - Definition of CSMO**

1. Retinal thickening at or within 500µm of the centre of the macula
2. Hard exudates at or within 500µm of the centre of the macula associated with retinal thickening
3. An area of retinal thickening one disc area in size, at least one part of which is within one disc diameter of the centre of the macula

chAreas/Diabetes/DiabStds.htm

Once neovascularisation occurs (figure 2), this is called proliferative diabetic retinopathy (PDR). PDR can lead to vitreous haemorrhage and tractional retinal detachment. The Early Treatment of Diabetic Retinopathy Study (ETDRS) recommendation is to treat PDR with high risk characteristics (table 4), although each clinician should treat each patient as an individual, using the recommendations as a guideline.

Treatment for neovascularisation is argon laser pan-retinal photocoagulation (PRP) i.e. to all four quadrants of the retina. The treatment is given outside the retinal arcade. PRP does have complications: it can precipitate macular oedema which usually regresses after a few months; there is a reduction in colour vision sensitivity and the visual field is often moderately affected. Patients should be warned that this may affect their ability to drive in future. The aim of treatment is to preserve vision - not

**Table 4 - High risk characteristics of PDF**

1. NVD over 1/3 or more of the optic disc surface
2. NVE more than 1/2 of an optic disc area
3. Vitreous or preretinal haemorrhages

*The presence of these risk factors carries an increased risk of visual loss within two years.*

<b>Mild NPDR</b>	From at least one microaneurysm onwards but not as severe as 'moderate NPDR'
<b>Moderate NPDR</b>	Intraretinal haemorrhages and/or microaneurysm, and/or cotton wool spots, venous beading or IRMA present but not as severe as 'severe NPDR'.
<b>Severe NPDR</b>	Cotton wool spots, venous beading and IRMA all present in at least two quadrants; OR two features present in two quadrants with microaneurysms and haemorrhages present in all four quadrants; OR IRMA present in four quadrants, being severe in one quadrant, without proliferative changes. OR apply the 4-2-1 rule. Presence of one of the following: <ul style="list-style-type: none"> <li>• Intraretinal haemorrhages in four quadrants</li> <li>• Venous beading in two quadrants</li> <li>• Severe IRMA in one quadrant.</li> </ul>

➔ **Table 3**

Classification of diabetic retinopathy

necessarily to improve it.

Once treated, proliferative changes may regress completely or may stabilise leaving some new vessels that do not progress. Signs of ischaemia such as venous beading and haemorrhages resolve with time. There are however, patients who do not respond to PRP and other possible causes of ischaemia need to be addressed.

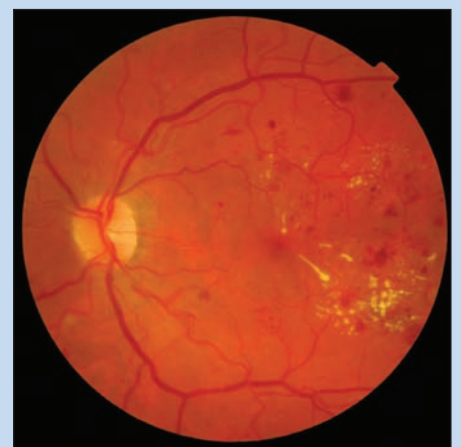
FFA is useful to determine the severity of diabetic retinopathy. It enables the ophthalmologist to determine areas of fluid leakage in macular oedema and shows areas of capillary non-perfusion in the retina. It can also help differentiate between IRMA and NV, as the latter leaks fluorescein dye.

Surgical intervention, in the form of pars plana vitrectomy, has proved useful in the management of diabetic retinopathy. If vitreous haemorrhage fails to clear spontaneously in a previously untreated eye, a vitrectomy is indicated to clear the view for both the patient and the ophthalmologist and enable retinal laser to be administered where appropriate. It is also indicated if recurrent haemorrhage fails to clear spontaneously after a period of observation in a previously treated eye. If the patient only has one good eye that develops a vitreous haemorrhage or bilateral vitreous haemorrhage occurs, a vitrectomy may

need to be performed to enable the patient to carry on with activities of daily living.

When tractional retinal detachment threatens the macular area, vitrectomy can be used to release traction from the vitreous. Delamination and segmentation of the overlying fibrous tissue can also be beneficial in releasing any horizontal tractional elements.

Management of the diabetic patient requires the patient to be treated as a whole. It is not uncommon to have patients present late in the disease and with already advanced diabetic retinopathy. As mentioned earlier, good diabetic blood sugar control is



➔ **Figure 1**

Non-proliferative diabetic retinopathy with clinically significant macular oedema



➔ **Figure 2**

Neovascularisation at the optic disc with corresponding fundus fluorescein angiogram

essential to control the progress of diabetic retinopathy. It is also important to realise that these patients can have other vascular pathology affecting their cardiovascular and renal systems. Many also suffer other systemic pathology and managing hypertension, hypercholesterolaemia and risk factors such as smoking are important adjuncts in managing retinal disease.

Finally, initial progression of diabetic retinopathy is seen when tight control of blood sugar is instituted in a poorly controlled diabetic. This does recover but may require close monitoring. Rapid deterioration of retinopathy is also recognised in pregnancy and should be monitored closely and treated as necessary.

### Hypertensive retinopathy

Hypertensive retinopathy is the result of systemic arterial hypertension. Malignant hypertension (Systolic > 200mmHg, diastolic >140mmHg) of rapid onset can result in dramatic retinal signs and can also involve the choroid and optic nerve. Chronic essential hypertension, found commonly in the population, is usually asymptomatic and tends to produce

more subtle signs that predominantly affect the retinal vasculature.

Retinal findings in chronic hypertension include 'silver wiring' where the light reflex overlying the arterioles is increased. A more specific finding is arteriovenous (AV) nicking. At sites where the artery crosses the vein they share the same adventitial sheath. In hypertension, the artery appears to 'nip' the vein and the vein becomes less visible under the artery. As more severe restriction to blood flow occurs, we see haemorrhages, exudates, cotton-wool spots and macular oedema.

In malignant hypertensive retinopathy, patients tend to be symptomatic describing alterations in acuity, photopsia or scotoma. Involvement of the retina, choroid and optic nerve are due to the breakdown of the blood retinal barrier. Patients develop arteriolar narrowing, exudates, macular oedema, cotton wool spots and linear retinal haemorrhages (flame shaped) and papilloedema. Choroidal filling is reduced and there is leakage into the subretinal space. Focal infarct of the RPE results in isolated yellow or red spots surrounded by pigment called Elschnig's spots.

The Keith-Wagner-Barker classification divides hypertensive retinopathy into four grades. General narrowing of the retinal arterioles is described as grade 1. Grade 2 includes grade 1 with focal arteriolar spasm, silver wiring and AV nicking. Grade 3 is Grade 2 plus haemorrhages, exudates cotton wool spots and retinal oedema. Grade 4 is all these changes plus optic disc swelling.

The differential diagnosis includes: central retinal venous occlusion, diabetic retinopathy, ocular ischaemic syndrome and hyperviscosity syndromes.

Treatment is managing the systemic condition and considering other organs that may also be involved. Management of malignant hypertension is a medical emergency and needs combined ophthalmic and medical input.

### Retinal arterial obstruction

Obstructions of the retinal arteries can occur either at the level of the central

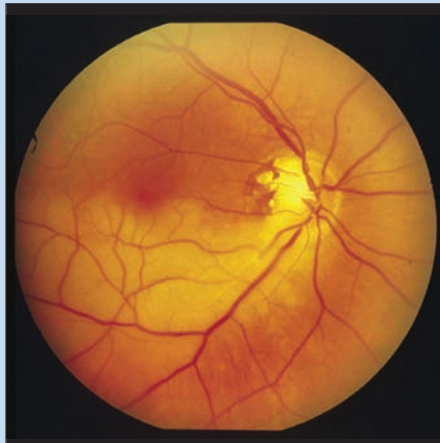
artery or one of its many branches. Obstructions can also occur further down the origin of the retinal artery and affect the ophthalmic or even the internal carotid artery. The obstruction may come from a distant source, called embolic obstruction, or due to local blockage referred to as arterial thrombosis. Because the outer retina receives its nutrients through diffusion from the choroidal circulation, it is affected to a lesser degree by obstructions of the retinal vasculature. Obstructions affecting the retinal circulation cause damage primarily to the inner neural retina. In 15 to 20% of people, a cilioretinal artery emerges from the ciliary circulation and supplies the area between the optic nerve and the macula. This area of retina is preserved in obstructions of the retinal circulation.

Branch retinal artery occlusions (BRAO) (figure 3) are mainly caused by embolic events and are rarer than central retinal artery occlusions (CRAO).

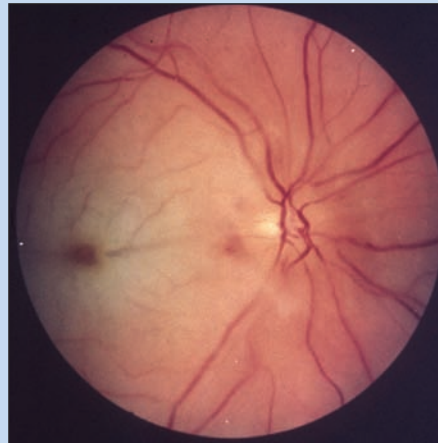
Embolic events are largely due to atherosclerotic disease. Atherosclerotic plaques in proximal arteries can break off (emboli) and cause obstruction more distally in the retinal arterial tree. The causes of atherosclerosis (hypertension, hyperlipidaemia, diabetes and smoking) need to be addressed in these circumstances. A carotid Doppler ultrasound can show plaques and narrowing of the carotid arteries and if a significant blockage is noted, the patient is referred to the vascular surgeons for possible surgery to clear the plaque.

Emboli are mainly cholesterol, calcium or platelet-fibrin in origin. Cholesterol plaques are yellowish and reflective in nature. Calcium is solid and white and platelet-fibrin plaques tend to be long and white lying within the artery involved. Calcium plaques often originate from calcified heart valves and require echocardiogram investigation.

Other causes of arterial obstruction are inflammatory vasculitis (including temporal arteritis), systemic coagulation problems (thrombotic events), optic neuritis, orbital trauma, radiation retinopathy, arterial spasm



➔ **Figure 3**  
Branch retinal artery occlusion



➔ **Figure 4**  
Central retinal artery occlusion with 'cherry red' macula

and raised intraocular pressure in an eye with already compromised perfusion.

In obstructions of the central retinal artery, the patient presents with painless loss of vision. Arterial spasm, on the other hand, manifestates itself as intermittent visual impairment. If pain is a feature, there may be generalised ischaemia of the globe. Vision is often significantly reduced and there is an afferent pupillary defect on the affected side. If the eye is examined a few hours after the event, the fundus may appear relatively normal. As time passes, the retina becomes pale and the macula

appears as a 'cherry red spot' (figure 4). The arteries and sometimes veins may show segmentation of the blood within them called 'box-caring'.

Unfortunately, no treatment to date is proven to make a significant difference to patients. The main aim of treatment is to reduce intraocular pressure in order to increase retinal artery flow. This can be done with glaucoma medication, ocular massage or a paracentesis.

About a month after the central retinal arterial obstruction occurs, the retinal pallor returns to normal although the retinal arteries may

remain attenuated. These patients need to be followed up by an ophthalmologist because of the risk of neovascularisation and neovascular glaucoma. The long-term visual prognosis is poor and treatment is aimed at addressing the cause of the initial obstruction and protecting the fellow eye.

## Venous obstructive disease of the retina

Obstructions of the venous circulation can occur either as central retinal vein occlusions (CRVO) (figure 5) or branch retinal vein occlusions (BRVO) (figure 6). CRVO are further classified as either ischaemic or non-ischaemic (table 5).

CRVO are most commonly associated with individuals with atherosclerotic disease, diabetes, hyperlipidaemia and hypertension. There is also an increased risk in patients with a history of glaucoma (chronic and acute). CRVO also occurs in patients with coagulation problems that lead to increased clotting. For example, an increase in blood viscosity, increased lupus anticoagulant, Protein C deficiency and malignant myeloma can lead to venous obstruction. These systemic associations should be considered especially in patients who present with bilateral disease.

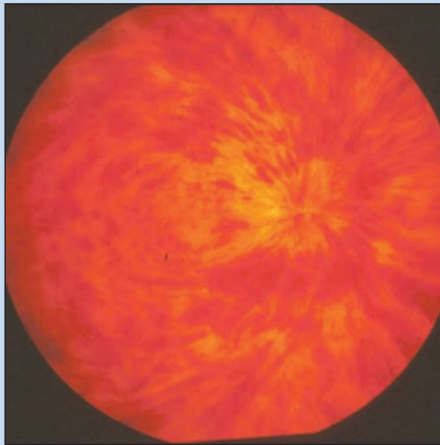
The pathogenesis of CRVO is due to obstruction of the central retinal vein at the level of the lamina cribrosa. Atherosclerosis of the accompanying retinal artery is thought to cause the damage to the neighbouring retinal vein. Raised intraocular pressure alters the structure of the lamina cribrosa and increases the risk of CRVO.

A patient with CRVO presents with variable degrees of reduced visual acuity that is painless. Some describe scotoma while others describe generalised visual loss. The presence of a relative afferent pupillary defect is often associated with more significant visual loss and ischaemia.

Examination of the fundus in the early stages shows tortuous retinal veins, retinal haemorrhages in all four quadrants and a variable number of cotton wool spots. Reduced visual acuity is usually due to macular oedema or macular haemorrhages.

	Non ischaemic CRVO	Ischaemic CRVO
<b>Decreased visual acuity</b>	Mild to moderate	Severe
<b>RAPD</b>	Absent or mild	Prominent
<b>Haemorrhages</b>	4 quadrants	4 quadrants and can be severe enough to cause vitreous haemorrhage.
<b>Cotton wool spots</b>	Absent or few	Present or numerous
<b>Optic nerve oedema</b>	Rare	Common
<b>Lipid exudates</b>	Absent	Can be extensive at macula
<b>Neovascularisation</b>	Rare	Over 2/3

➔ **Table 5**  
Clinical features of non-ischaemic and ischaemic CRVO



➔ **Figure 5**  
Central retinal vein occlusion

Macular oedema can be cystoid or diffuse in nature. Optic disc oedema has also been described in both ischemic and non-ischaemic CRVO.

The risk of neovascularisation is significant in ischaemic CRVO and these patients need to be followed up closely - it can occur within three months of the event (90 day glaucoma). Patients with initial signs of non-ischaemic CRVO have also been known to progress to an ischaemic picture after a few weeks. Clinical findings associated with neovascularisation may include raised intraocular pressure (sometimes leading to corneal oedema), anterior chamber flare, iris and angle neovascularisation, a fixed pupil and retinal neovascularisation.

Diagnosis and classification is aided by fundus fluorescein angiography (FFA). If more than 10 disc diameters of non-perfusion are found on FFA, there is an increased risk of neovascularisation and the eye is termed ischaemic. Often little information is gained if extensive haemorrhages are present. It is normal practice to wait till some of the haemorrhages clear before an FFA is performed.

All patients with CRVO need a full medical evaluation to address any outstanding risk factors: hypertension, hyperlipidaemia, diabetes, smoking.

There is currently no proven treatment to reverse the effects of CRVO. Systemic anticoagulation and anti-inflammatory treatments have been tried without any definitive effect. The surgical options include optic

nerve sheath decompression and attempts have been made to create an anastomosis between the arterial and venous circulation using lasers, all with variable results. Neovascularisation is treated with PRP. The aim of laser treatment is regression of the new vessels to prevent the long term problems associated with neovascular glaucoma. The patient needs to be aware that treatment is not aimed at restoring vision. Macular oedema may respond angiographically to grid laser treatment but this has not been shown to improve visual acuity.

Branch retinal vein occlusions (BRVO) are more common than CRVO. The obstruction occurs at the arteriovenous crossing where the artery and the vein share a common adventitial sheath. The current theory is that the arteriosclerotic artery causes



➔ **Figure 6**  
Branch retinal vein occlusion (left eye supratemporal branch)

compression of the retinal vein which leads to local venous thrombosis.

The patient may complain of a field defect or generally reduced visual acuity. The risk factors are similar to that of CRVO. Retinal findings include haemorrhages, tortuous veins and cotton wool spots confined to the area supplied by the blocked vein. The severity of the signs indicates the degree of obstruction and non-perfusion of the underlying retina. When the macular region is involved, macular oedema can develop, further reducing the visual acuity.

A fifth of patients will develop retinal neovascularisation, though anterior chamber neovascularisation is rare. This can lead to vitreous

haemorrhage that may require a vitrectomy to clear the view to enable sectoral argon laser photocoagulation. In patients with macular oedema and vision worse than 6/12, grid pattern laser photocoagulation can help reduce the oedema and improve vision. Because vision can improve spontaneously, patients are not treated until at least three months following the initial obstruction.

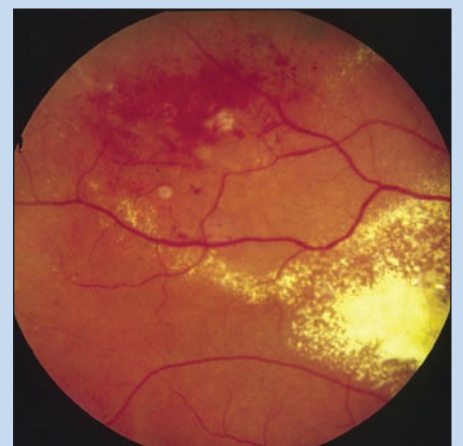
With time, the haemorrhages fade. There may be evidence of the BRVO in the form of sclerosed veins and vessels (especially at the optic disc and as microvascular abnormalities that drain the affected site). FFA shows leakage from new vessels but not from collaterals.

### Ocular ischaemic syndrome

The pathogenesis of ocular ischaemic syndrome is chronic ischaemia resulting from narrowing of the internal carotid artery. This is mainly due to atherosclerosis of the carotid artery but inflammatory arterial diseases can mimic the signs.

Patients present with variable, gradual loss of vision although a sudden drop in visual acuity is also described. Ischaemia of the globe or neovascular glaucoma can present with periorbital ache.

Clinical findings include: aqueous flare and anterior uveitis, neovascularisation of the anterior segment, neovascular glaucoma, narrowing of retinal arteries and dilatation of retinal veins, cotton wool spots and retinal neovascularisation. A



➔ **Figure 7**  
Coats' disease

'cherry red' macula is sometimes seen as is swelling of the optic nerve.

Diagnosis can be helped by FFA and electroretinography. Doppler ultrasound can be used to assess the retrobulbar circulation. Ultimately, the carotid arteries need to be assessed either by ultrasound or direct angiography to establish the source of ischaemia.

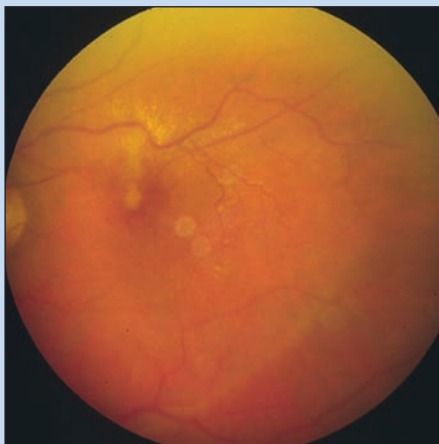
Treatment addresses the systemic risk factors for atherosclerosis and carotid narrowing of more than 70% can benefit from surgical carotid endarterectomy. This procedure however carries a risk of iatrogenic stroke and the patient needs to be evaluated by a vascular surgeon.

### Retinal telangiectasia

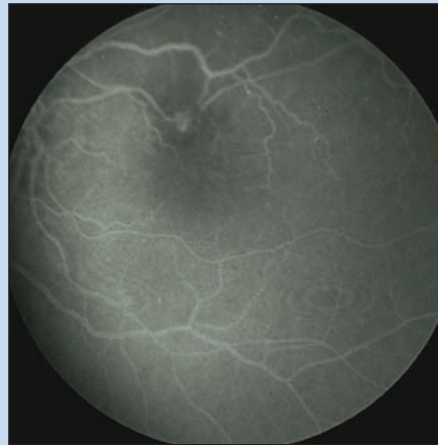
Primary retinal telangiectasia is described below and should be differentiated from secondary changes from conditions such as vein occlusions or diabetic retinopathy.

Coats' disease is a congenital form of retinal telangiectasia and is usually a unilateral exudative disease that ultimately leads to retinal detachment (figure 7). It is a disease found most commonly in young, male patients. Leber's miliary telangiectasia is an early form of Coats' disease. The pathology of the disease is aneurismal dilatation of both the retinal arterioles and venules which drain a dilated capillary bed. The dilatation of the capillary bed is referred to as telangiectasia and these vessels leak fluid.

Other forms of retinal telangiectasia



➔ **Figure 8**  
Macroaneurysm



➔ **Figure 9**  
Fluorescein angiogram of a macroaneurysm

are: idiopathic juxtafoveolar retinal telangiectasia, familial retinal telangiectasia and neural retinal angiomas.

Treatment is usually with laser photocoagulation or cryotherapy to the affected area of retina.

### Retinal macroaneurysms

Macroaneurysms are dilatations of the retinal arteries and arterioles and are larger than microaneurysms of the capillaries (figure 8). They are either congenital or acquired. Congenital forms are found in diseases such as retinal telangiectasia and angiomas. The acquired form is found predominantly in patients with atherosclerotic disease and/or hypertension.

Macroaneurysms can either involute spontaneously or result in retinal exudates and oedema. Retinal haemorrhage also occurs and in severe cases can lead to vitreous haemorrhage. The effect on visual acuity depends on the site of the macroaneurysm. If haemorrhages and exudates occur at the macula, vision can be significantly affected.

If significant bleeding is not present, a FFA can help diagnosis and evaluate leakage (figure 9). Treatment is often conservative as these lesions can resolve spontaneously. In some cases retinal laser, targeting the macroaneurysm can be attempted. Gentle grid laser to areas of macular oedema can also benefit the patient.

### Retinopathy of prematurity

Migration of the retinal vessels from the optic disc to the ora serrata begins at 16 weeks and usually reaches the nasal retina at 36 weeks and the temporal retina at 39 weeks. This process is interrupted by premature birth. Incomplete vascularisation of the retina in premature infants occurs due to closure of the retinal vessels when exposed to increased oxygen after birth. This then leads to hypoxia of the non-vascularised retina and drives the process of proliferative retinopathy.

Screening for retinopathy of prematurity (ROP) (figure 10) should be done on all babies weighing less than 1.501kg and born at 32 weeks gestation or below.

ROP is assessed in five stages of severity. The areas affected are further divided into three anatomical zones, centering on the optic disc. In addition, 'plus' disease' which may occur at any time describes dilated retinal vessels, engorged iris vessels with poor dilatation of the pupil and vitreous haze or haemorrhage. These classifications help determine the severity of ROP and the determination of 'threshold ROP'.

Threshold ROP is defined as disease that has a 50% likelihood of progressing to retinal detachment and this stage was defined as requiring treatment by the CRYO-ROP study. The early treatment for retinopathy of prematurity [ETROP] study advocates the treatment of pre-threshold ROP in



➔ **Figure 10**  
Retinopathy of prematurity

patients with high risk features. It showed a significant reduction in the unfavourable outcomes of ROP.

Treatment involves retinal laser photocoagulation or cryotherapy. Surgery is sometimes indicated to treat retinal detachments. Long-term follow up is indicated in patients with ROP as they can develop cataracts, retinal detachments, exudative retinopathy and significant refractive errors.

## Haemoglobinopathies

Red blood cells (RBC) contain haemoglobin. Mutations of the haemoglobin gene lead to formation of abnormal haemoglobin proteins. The abnormal proteins subsequently affect the morphology of the red blood cell and its response to oxygen binding. The globin proteins of haemoglobin are alpha-globin and beta-globin. Specific mutations of these proteins can lead to alpha-thalassaemia or beta-thalassaemia. Beta-thalassaemia is seen in people of Mediterranean, African or South East Asian origin.

Another specific mutation of the beta-globin chain leads to an alteration of the structure of the RBC and is referred to as sickle cell haemoglobin. Sickle cell disease is found largely in people of African ancestry. Although sickle cell retinopathy is described below, these changes can be seen in the other haemoglobinopathies.

Sickle cell disease can affect the whole of the eye. The abnormal haemoglobin causes the RBC to change into a 'sickle' shape which is much more rigid than normal RBC. This then leads to obstruction of small blood vessels by these sickle shaped RBC. Any pathology that potentially reduces blood oxygen can increase the number of cells that acquire a sickle shape.

Sickle cell retinopathy has five stages of classification. The arteriolar obstruction leads to chronic ischaemia of the retina which then drives neovascularisation and its sequelae. The clinical findings range from: arteriolar obstruction, arteriovenous anastomoses, neovascular proliferations (typical sea-fan anomaly) to vitreous haemorrhage and retinal detachments.

If the diagnosis is suspected from the clinical findings in a patient who is

unaware of having a haemoglobinopathy, laboratory blood analysis is indicated. Treatment involves cryotherapy, laser photocoagulation and surgery as indicated.

## Radiation retinopathy

Radiotherapy is administered to treat many different kinds of malignancies. When radiotherapy targets the head or eye region, the retina can be exposed to significant levels of radiation. This can lead to radiation retinopathy, maculopathy and optic disc swelling.

Radiation retinopathy is caused by occlusion of retinal capillaries that then leads to ischaemic changes. Telangiectasia and microaneurysms develop which can cause exudation and haemorrhages of the neurosensory retina. In severe cases, macular oedema develops and causes reduced visual acuity. Cotton wool spots, retinal haemorrhages and new vessels develop as a consequence of retinal ischaemia. These can later lead to vitreous haemorrhage, neovascular glaucoma and tractional retinal detachments. The choroid, retinal pigment epithelium and optic nerve can also be damaged by radiation.

Treatment is currently with laser photocoagulation (focal or grid laser to macular oedema and PRP to treat proliferative disease.) Surgery is used to treat retinal detachments and vitreous haemorrhage where appropriate.

## Conclusion

Vascular pathologies of the retina arise largely due to damage to the blood retinal barrier. This may be ischaemic, inflammatory, metabolic or a combination of these. When treating patients with retinal pathologies, it is important not to just consider the retina but the patient as a whole and any underlying systemic disease. These patients benefit greatly from the input of a medical retina team with a multi-disciplinary approach: medical, surgical and primary care.

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## References

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## Module questions

Course code: c-7983

Please note, there is only one correct answer. Enter online or by form provided

**An answer return form is included in this issue. It should be completed and returned to CET initiatives (c-7983) OT, Ten Alps plc, 9 Savoy Street, London WC2E 7HR by May 28 2008.****1. Which one of the following is correct? The blood retinal barrier:**

- a. allows free diffusion of minerals from the retinal circulation into the neurosensory retina
- b. is formed by the retinal pigment epithelium and the walls of the retinal blood vessels
- c. is formed by connection between arteries and veins in the retina
- d. consists of fenestrated epithelial cells

**2. Which one of the following is NOT usually a feature of proliferative diabetic retinopathy?**

- a. tractional retinal detachment
- b. vitreous haemorrhage
- c. cherry-red spot at the macula
- d. new vessels at the disc

**3. Which one of the following is NOT a feature of moderate non-proliferative diabetic retinopathy?**

- a. cotton wool spots
- b. microaneurisms
- c. intraretinal microvascular abnormalities (IRMA)
- d. new vessels at the disc

**4. Argon laser photocoagulation treatment is NOT indicated in which one of the following?**

- a. proliferative diabetic retinopathy with high risk features
- b. branch retinal vein occlusion with macular oedema and visual acuity of 6/6
- c. central retinal vein occlusion with macular oedema and neovascularisation
- d. radiation retinopathy

**5. Which one of the following features is a characteristic of hypertensive retinopathy rather than diabetic retinopathy?**

- a. Elschnig's spots
- b. cotton wool spots
- c. flame shaped haemorrhages
- d. macular oedema

**6. Which one of the following features is characteristic of a central retinal artery occlusion?**

- a. flame shaped haemorrhages
- b. cotton wool spots

- c. cherry-red macula
- d. microaneurisms

**7. All of the following are risk factors for retinal vein occlusions EXCEPT:**

- a. glaucoma
- b. hypertension
- c. hyperlipidaemia
- d. retinoschisis

**8. Which one of the following is correct regarding retinal telangiectasia?**

- a. Coats' disease is an acquired form of retinal telangiectasia
- b. Leber's millary telangiectasia is the end stage of Coats' disease
- c. the main pathology is leakage from dilated retinal capillaries
- d. Coats' disease is usually bilateral

**9. Which one of the following is incorrect regarding retinal macroaneurysms?**

- a. they may cause macular oedema and exudates
- b. they are dilatations of the retinal arteries and arterioles
- c. they may be congenital or acquired
- d. all lesions require treatment

**10. Which one of the following lesions leak fluorescein dye during a fluorescein angiogram of the fundus?**

- a. intraretinal microvascular abnormalities
- b. new vessels at the disc in diabetic retinopathy
- c. collaterals at the disc following central retinal vein occlusions
- d. cotton wool spots in hypertensive retinopathy

**11. Which one of the following is incorrect regarding retinopathy of prematurity?**

- a. retinal vessels reach the temporal retina at 29 weeks gestation
- b. in premature babies, retinal vessels close when exposed to increased oxygen after birth
- c. treatment may involve retinal laser photocoagulation or cryotherapy
- d. long term follow up is required

**12. Which one of the following is incorrect regarding Sickle cell disease?**

- a. it is largely found in people of Chinese ancestry
- b. clinical findings include arteriolar obstruction
- c. a 'sickle' shaped red blood cell is more rigid than a normal red blood cell
- d. clinical findings include neovascular proliferations

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