Patient Information Brochure

Retinal Vascular Occlusions

Q: What is retina?

A: The eye is a spherical structure with the lens of the eye that focuses light in the front. In the back of the eye is the retina, which converts the images on the retina into electrical impulses and sends them along the optic nerve to the brain.

The retina has both arteries and veins (blood vessels). In most patients, there is a single artery or vein that enters the eye through the optic nerve. These are called the central retinal artery and central retinal vein.

These arteries and veins spread out to the periphery of the retina and the arteries and veins cross each other. These crossing points can cause problems as you get older because if the arteries become thickened, they can compress the vein.

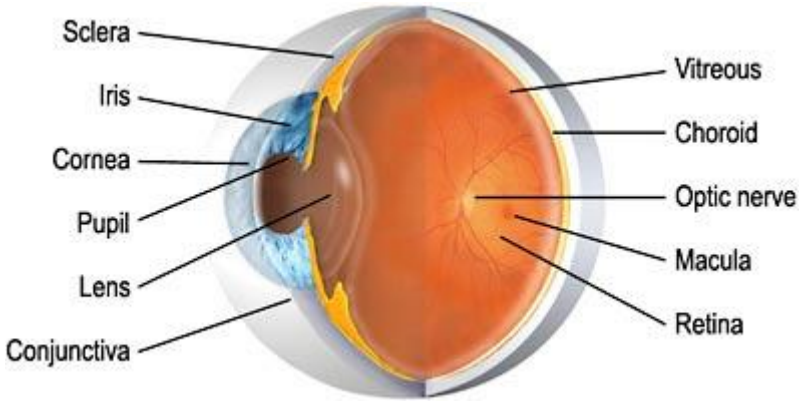


Fig 1. Retina and its blood vessels

Q: What are Retinal Vascular Occlusions (RVOs)?

A: A retinal vascular occlusion is blockage of the retinal vessels, either the arteries or the veins, in the back of the eye. If these blockages took place in the brain they would be called a "stroke". As a result, we often call these problems "stroke in the eye".

These blockages have different causes usually relating to a systemic disease like hypertension (blood pressure), diabetes mellitus, dyslipidemia (cholesterol problem), homocystinemia, anaemia, renal failure, liver problems, autoimmune disorders etc. and habits like smoking, tobacco and alcoholism.

Q: How do Retinal Vein Occlusions cause loss of vision?

A: Retinal Vein Occlusions cause vision loss in the following two ways

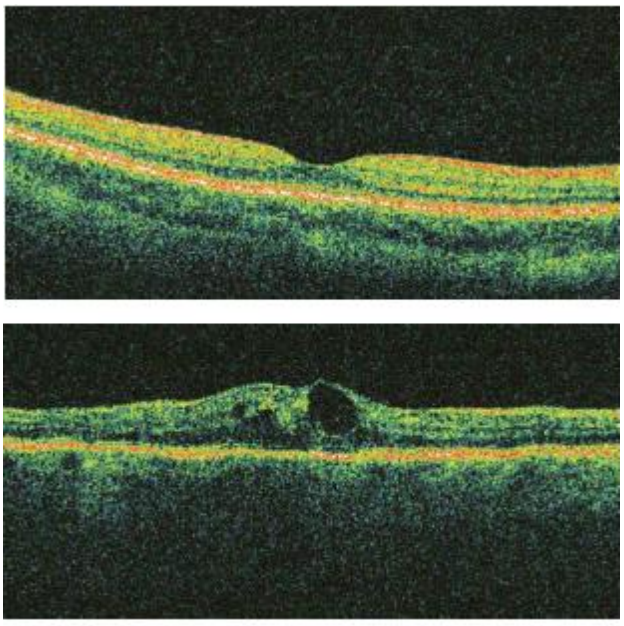
a) <u>Macula edema</u>

The major cause of vision loss in retinal vein occlusion is macular edema. The macula is the central retina and is responsible for fine detail vision for reading, recognising faces and driving. It is an intricate and delicate structure that needs to have proper connections and needs to be free of swelling with fluid (edema).

In retinal vein occlusion, the blockage of the veins results in leakage of fluid and blood through the blood vessel walls. This is much like what happens when a garden hose is plugged and water leaks through the wall of the hose due to the increased pressure and damage to the rubber wall.

We are able to diagnose and monitor this complication with a test called Optical Coherence Tomography (OCT) scan. The OCT scan provides a cross section of the macula to evaluate its thickness and structure. In a normal OCT scan, the central macula has a thickness of between 150 and 250 microns (one fourth of a millimetre). A central depression call the fovea is what gives one the fine detailed 6/6 vision.

In macular edema, fluid accumulates and causes the macula to swell like a sponge. As a result, vision can be distorted or blurred, and the images may be magnified or minified much as when looking through a glass of water.



OCT scan of normal retina (top) with central depression or foveal pit. OCT scan of retina with macular edema characterized by thickening and cysts.

b) <u>Neovascularisation and vitreous haemorrhage</u>

This normally occurs around 3 months after the initial blockage if necessary treatment is not taken and in some cases in spite of treatment. The lack of blood supply to the area where the blood vessel is blocked, causes the retina to release many chemicals (VEGF etc.). These chemicals cause the formation of new, abnormal blood vessels,

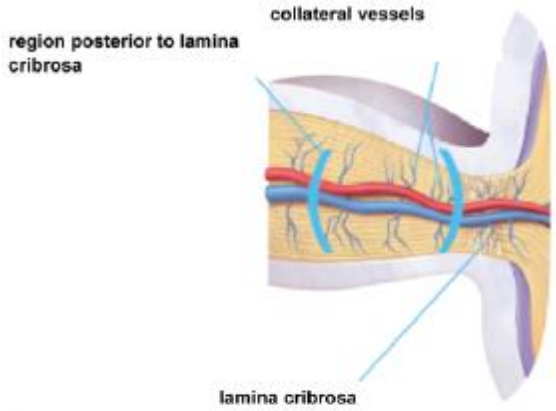
supposedly to supply blood to the affected area. These abnormal blood vessels are very fragile and can bleed on trivial jerks like coughing, sneezing, rubbing etc., causing bleeding inside the eye called vitreous haemorrhage.

This generally indicates poor prognosis and if left untreated causes rise in intraocular pressure (neovascular glaucoma) and painful blind eye.

Q: What are Central Retinal Vein Occlusion (CRVO) and Hemi-Central Vein Occlusion (HCRVO)?

A: A blockage of the main vein in the eye is called a central retinal vein occlusion. The blockage of the vein takes place in the optic nerve behind the retina. Because the blockage takes place outside the eye in the optic nerve, it usually affects the entire eye and vision may be severely affected.

In some patients there are two or more central retinal veins. These patients can have occlusion of only one of these veins and have what is called hemi-central vein occlusion. These often cause less damage than a full central vein occlusion.



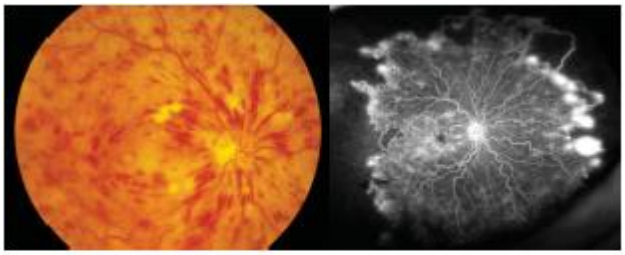
Schematic of central retinal vein occlusion (CRVO) with blockage at the level of the optic nerve.

Most patients who have this problem have risk factors for vascular disease. This may be diabetes, high blood pressure, arteriosclerosis, open angle glaucoma or a condition called thrombophilia. In younger patients, usually under age 40, we check for clotting disorders. We may find an important abnormality that needs to be treated. If there is a family history of strokes or miscarriages or if the patient has autoimmune problems, then the tests are particularly important. Since these problems are stroke-type events, we request that you check with your primary care doctor for a review of your medical condition.

The blockage causes blood to back up in the eye, which causes hemorrhages, swollen retinal veins, and edema or swelling. This often leads to visual loss.

If the occlusion is severe, there can also be marked ischemia or closure of the capillaries (small blood vessels). This can lead to abnormal blood vessels in the eye (neovascularisation),

haemorrhage into the vitreous and even abnormal blood vessels in the front of the eye that can lead to high intraocular pressures and glaucoma (rubeosis).

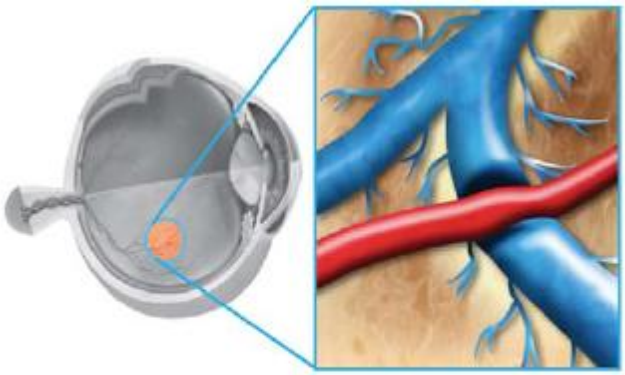


Central retinal vein occlusion: Photograph (left) and fluorescein angiogram (right). Note accumulation of dye in the center of the retina (leakage), and the loss of blood vessels in the peripheral retina.

It has been noted for forty years that some central vein occlusions are severe, leading to blindness and complications and others are less severe with some visual loss but maintenance of some vision. Those eyes with severe vein occlusion have blood vessel closure (ischemia) and are more likely to have problems.

Q: What is Branch Retinal Vein Occlusion (BRVO)?

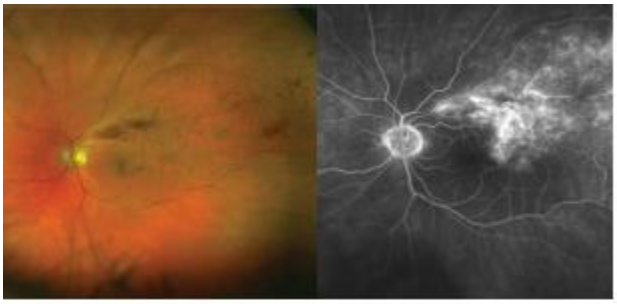
A: A more localised blockage of the retinal venous system may occur and this is called a branch vein occlusion. The arteries and veins in the back of the eye cross each other like highways on a map. At the places where arteries cross veins, there can be a blockage of the vein. The artery and vein share a common sheath and as the artery thickens with age and hypertension, the vein can be blocked by the thickened artery.



Schematic of branch retinal vein occlusion (BRVO) with compression and blockage of the vein (blue) by a thickened, stiff artery (red).

Most patients who have this problem have risk factors for vascular disease. This may be diabetes, high blood pressure, arteriosclerosis, open angle glaucoma or a condition called thrombophilia. In younger patients, usually under age 40, we check for clotting disorders. Sometimes we find an important abnormality that needs to be treated. If there is a family history of strokes or miscarriages or if the patient has autoimmune problems, then the tests are particularly important. Since these problems are stroke-type events, we request that you check with your primary care doctor for a review of your medical condition.

These blockages may not have any symptoms if the occlusion does not involve the macula. If the macula is involved, then there can be swelling of the retinal tissue that can lead to visual loss (macular edema).



Branch retinal vein occlusion: Photograph (left) and fluorescein angiogram (right). Note accumulation of dye in the center of the retina (leakage).

Laser treatment for BRVO has been shown to improve vision compared to the natural course without any treatment. The Lucentis study compared a control group that was treated like the vein occlusion study with a combination of untreated patients if the vision got better and laser treatment if the vision did not get better. In the Lucentis treated group, 61.1 % got better and in the control group (including laser) only 28.8 % improved three lines or more. The percentage of patients seeing 6/9 or better was 64.9 percent for the Lucentis group and 41.7 percent in the sham group. This difference, while significant was not large.

Because the Lucentis shots often require monthly injections, we usually treat with both approaches with the hope of being able to stop the monthly injections.

The most common systemic cause for BRVO is hypertension (blood pressure). It can also be seen in arteriosclerosis and diabetes. Sometimes there is no associated problem.

Q: What treatments are available for Retinal Vein Occlusions (RVOs)?

A: The treatment options are enlisted below

I. <u>Treatment with Lucentis</u>

There is a new treatment that is effective in improving vision and clearing macular edema in central retinal vein occlusion. It is injection of Lucentis into the eye once a month for at least six months. Lucentis is an antibody against the molecule that causes macular edema and the growth of abnormal vessels (Vascular Endothelial Growth Factor or VEGF)

Vision improvement is rapid and seen on average, by seven days. Patients were treated with six monthly injections. After six months it may be possible to stop the treatment, but this varies from patient to patient. If the vision is down, we usually restart treatment immediately. If vision is good and there is no macular edema, observation may be continued.

In CRVO, about 50 % of the patients got significantly better (3 lines improvement in vision) compared to 17 % in people who underwent no treatment.

In BRVO, about 60 % patients improved by at least three lines compared to 30 % of patients who underwent laser only

II. Treatment with Avastin

This is another Anti –VEGF drug, which is FDA approved for treatment of cancers and has also been shown to work for macular edema. Research has proven it to be equally effective and safe as Lucentis.

We prefer to use Lucentis when possible and patient permitting, because it is the drug that has been shown to work in large clinical trials and is prepared under strict and specific FDA guidelines for use inside the eye.

III. Treatment with Steroids

Intraocular steroid injections like triamcinolone (IVTA) and Ozurdex are another treatment option. The SCORE trial was a large multicentre trial that showed a **benefit in CRVO but not in BRVO.**

The duration of action is much longer and so the need for less frequent injections. In some cases like recurrences or long standing vein occlusions, they are more effective than anti-VEGF injections.

However there is a significantly higher risk of glaucoma and cataracts in patients given steroid injections, especially if they are repeated.

Ozurdex is a long acting steroid implant, which contains a different steroid, dexamethasone. The duration of action is for about 4 months. The risk of cataract and glaucoma is marginally less than triamcinolone (IVTA).

While Lucentis is a better, safer option for most cases, sometimes steroid treatment by itself or in combination with Lucentis may be warranted.

IV. Treatment with Laser

In two large, multicentre clinical trials conducted in the 1990's (the Central Vein Occlusion Study, or CVOS and the Collaborative Branch Vein Occlusion Study, or BVOS) demonstrated that laser treatment to the macula (center of vision) demonstrated a **benefit in BRVO but not in CRVO.**

However, laser treatment outside the macula (peripheral or scatter laser) was demonstated to be effective when abnormal blood vessels grow in the retina or iris (neovascularisation). This is a rare but serious complication that can result in bleeding inside the eye (vitreous haemorrhage) and increased eye pressure (neovascular glaucoma).

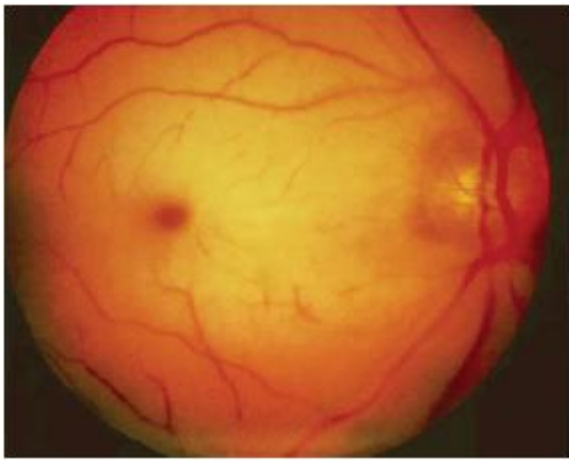
Recent evidence shows the benefit of scatter laser in long term reduction of VEGF levels and indirectly reducing macular edema in all vein occlusions.

Q: What are occlusions of the retinal and optic nerve arterioles?

A:

i. Central Retinal Artery Occlusion

The arterial circulation of the eye can become occluded just like the venous system. What you see inside the eye is completely different. In a vein occlusion there is edema and haemorrhage. In retinal artery occlusion, the retina turns white.



Central Retinal Artery Occlusion with Cherry Red Spot at Macula

Patients with central retinal artery occlusion lose vision suddenly. Unfortunately, the visual loss in central retinal artery occlusion is usually irreversible, although there may be some improvement over time.

There is no good treatment of central retinal artery occlusion. Lowering the eye pressure by drugs, paracentesis or ocular massage or breathing into a bag have been suggested, but they don't seem to help.

Treating the artery occlusion aggressively like you would treat a stroke in the brain with TPA (tissue plasminogen activator) has also been tried, but without success.

If you have a central retinal artery occlusion, it is important to figure out why.

Sometimes these problems are caused by emboli (small piece of cholesterol or other matter) from the heart or the carotid artery. Sometimes the blockage is a thrombus (clot) that forms in the artery itself with an aggregation of platelets. Patients with artery occlusion need to be checked by their doctor and usually have a carotid ultrasound to rule out disease there and an echocardiogram to rule out a clot in the heart. In younger patients there may be a heart condition called foramen ovale where there is a hole between the right heart and the left heart and emboli can cross into the arterial circulation. Patients also need to control their cholesterol and high blood pressure if elevated. Usually such patients are treated with aspirin or clopilet.

ii. Branch Retinal Artery Occlusion

Like in vein occlusions, sometimes only a part of retina is involved and this is a branch retinal artery occlusion. The same risk factors related to central artery occlusions also apply to branch artery occlusions. Medical evaluation should be undertaken.

There is a unique subset of retinal emboli where the ophthalmologist can actually see flecks of cholesterol in the eye. Sometimes they block the artery and sometimes not. Patients with plaques in the retina called Hollenhorst plaques need to be evaluated to rule out carotid disease and hypercholesterolemia.

iii. Ischemic Optic Neuropathy

It is the occlusion of the choroidal vessels around the optic nerve. This can lead to sudden visual loss and usually affects the upper or lower field of vision. There are currently no proven treatments although steroids and anti-VEGF drus like Lucentis have been tried with mixed results.

Ischemic optic neuropathy may be caused by hypertension or arteriosclerosis. It is also asscociated with temporal arteritis, an inflammatory disease of the arteries of the head. Additional symptoms with temporal arteritis are headaches. Difficulty chewing, feeling tired, difficulty getting hands above the head, scalp tenderness and weight loss. Patients suspected of this condition need blood tests, ESR and c-reactive protein. Often a biopsy of their temporal artery is needed to confirm the diagnosis. The treatment for temporal arteritis is high dose steroids so it is important to be sure of the diagnosis if treatment is going to be continued for a long time.

Ischemic optic neuritis has also been associated with drugs to treat erectile dysfunction like Viagra. If you are taking these drugs it is important to stop and be evaluated.