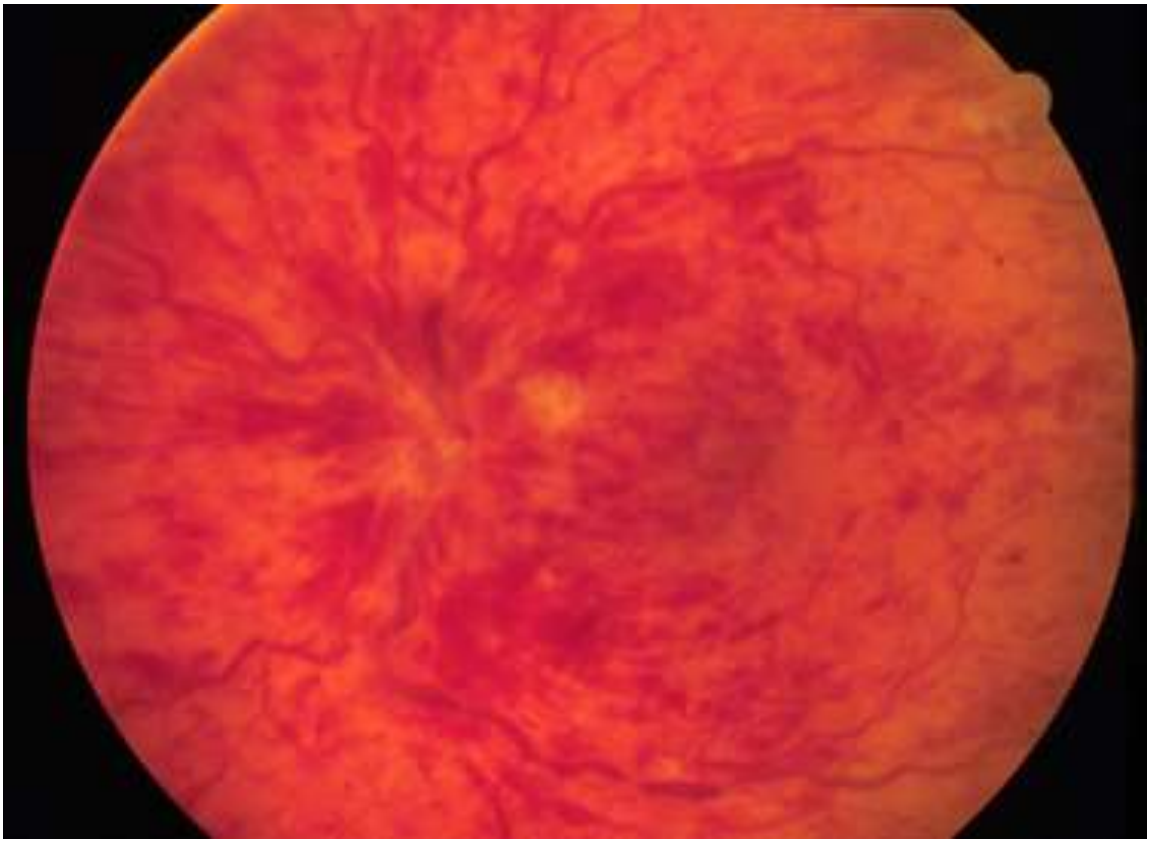
THE NORTHERN HOSPITAL

RETINAL VEIN OCCLUSION



Typical appearance of a Central Retinal Vein Occlusion, showing the *widespread hemorrhagic "blood and thunder" fundus.*

Introduction

Retinal Vein Occlusion (RVO) is an uncommon condition that presents with sudden painless loss of vision.

When venous stasis is severe, **infarction** may occur due to slowed retinal blood flow on the arterial side.

Until recently this could be a disastrous condition, e.g. in cases of **CRVO**, as there was no treatment for it.

Recently, however **anti-VEGF therapy** has become available. Anti-VEGF drugs are one of the **most significant advances** in ophthalmology in the last decade.

This is an antibody based treatment which blocks **vascular endothelial growth factor (VEGF)** a protein that stimulates the formation of new abnormal blood vessels that can occur in response to various retinal diseases, amoung them **RVO**.

Although these agents cannot reopen occluded veins they can limit the significant amount of visual loss caused by secondary damaging edema and neo-vascularization that occurs in patients with RVO.

Epidemiology

Retinal vein occlusion is an important cause of visual loss among older adults throughout the world.

It is the second most common cause of vision loss from retinal vascular disease, following diabetic retinopathy .

Classification

Anatomical classification:

Retinal vein occlusion (RVO) is classified into 3 main groups depending on the exact location of the venous occlusion as follows:

1. Central Retinal Vein Occlusion (CRVO):

    - CRVO occurs due to thrombus within the central retinal vein at the level of the lamina cribrosa of the optic nerve, leading to involvement of the **entire retina**.

      The lamina cribrosa is the connective tissue "sieve" consisting of holes through which retinal nerve fibers pass from the retina to the optic nerve.

2. Branch Retinal Vein Occlusion, (BRVO):

    - This is when a branch vein in the **peripheral retinal venous system** is occluded, leading to hemorrhage along the distribution of that branch

3. Hemiretinal Vein Occlusion (HRVO) (less commonly):

    - This is a blockage is in a vein that drains the **superior or inferior hemi-retina**, leading to involvement of one half of the retina

See Appendix 1 below

Pathological classification:

Pathologically, there are essentially two types:

1. Ischemic/ atheromatous disease.

2. Non-ischemic disease:

    Other causes are non-ischemic in nature and are rare, but may include:

- Vasculitis
- Coagulopathies
- Chronic glaucoma.

Pathology

Branch retinal vein occlusion (BRVO) appears to be related to compression of the branch vein by sclerotic retinal arterioles at the arteriovenous crossing points.

Central retinal vein occlusion (CRVO) is usually associated with primary thrombus formation.

Complications

These are:

1. Vision loss:
    - When venous stasis is severe, **infarction** may occur due to slowed retinal blood flow on the arterial side.
    - Vision loss can also be due to abnormal neo-vascularization
2. Secondary glaucoma:
    - Neovascularization of the iris and/or neo-vascularization of the anterior chamber angle can lead to the development of neo-vascular glaucoma.

      In addition to decreased vision, these patients may complain of a red, painful eye secondary to elevated intraocular pressure.

      Beware of "90 day glaucoma" - i.e neovascular glaucoma occurs in approximately 50% of ischemic CRVO cases after 3 months. [3]

Natural history:

Whether visual loss progresses depends largely on the **type** and **location** of the retinal vein occlusion

Patients with **non-macular branch** retinal vein occlusion (BRVO) may be asymptomatic and may not experience any loss of visual acuity.

Patients with **macular edema** from BRVO may experience spontaneous vision improvement in the first three months after onset of symptoms. After three months, the likelihood of spontaneous improvement in visual acuity diminishes.

Patients with **central retinal vein occlusion (CRVO)** have much worse outcomes, with final visual acuity dependent largely upon **visual acuity at presentation**.

Ocular neo-vascularization:

Neovascularization of the iris (NVI), neo-vascularization of the anterior chamber angle (NVA), and retina are common complications of both CRVO and BRVO, although NVI/NVA occur more commonly in CRVO.

Neovascularization of the retina can lead to:

- Vitreous hemorrhage
- Traction retinal detachment
- Neovascular glaucoma.

It remains unclear if RVO is associated with cardiovascular disease.

Risk factors:

Recognized risk factors for RVO include:

1. Increasing age
2. Hypertension
3. Diabetes
4. Smoking
5. Obesity
6. Hypercoagulable states:
    - Particularly factor V Leiden and activated protein C resistance
7. Glaucoma:
    - This can prevent retinal vein outflow and leads to stasis
8. Retinal arteriolar abnormalities

Among patients with hypertension or diabetes, the risk of BRVO is increased in the presence of end - organ damage. There is no increased risk for patients with diabetes and no end- organ damage.

Clinical Features

Important points of History:

1. The typical history is a **uni-ocular** reduction in vision

- Monocular loss of a portion of peripheral vision suggests or branch retinal vascular occlusion (either arterial or venous) but could also represent subtotal retinal detachment, or an ischemic optic neuropathy,

  Patients will describe blurred or greyish vision corresponding to the area of retinal vein occlusion

  This may be:

  - ♥ A scotoma
  - ♥ A visual field deficit (e.g. HRVO)
  - ♥ Loss of central vision if the macula is involved.
  - ♥ A global loss of vision in cases of CRVO

2. The loss of vision is **painless**.

3. The loss of vision is **acute**:

   - While vision loss may be severe, the onset is typically more **subacute** in contrast to the *very sudden* visual loss typical of a retinal artery occlusion, and may be as gradual as a few days.

4. Extent of visual loss:

   - Visual loss can be **severe** in cases of **central retinal vein occlusion** with only some residual vision such as light/dark perception remaining.
   - Loss is less severe in cases of *branch* venous occlusions.

     With minor peripheral branch retinal vein occlusion some patients may in fact be asymptomatic and are only diagnosed on routine ophthalmologic examination.

Important points of Examination:

1. Visual acuity:

   Record the visual acuity of both eyes.

   - When loss is profound then the degree of impairment can be roughly quantified in terms of no light perception, hand movement only perceived, or by the counting of fingers.

2. Pupils:

   - Test for a relative afferent pupillary defect (RAPD) (in ischaemic **CRVO**)

3. Fundoscopy:

    - The anatomy of the optic nerve head is unique and allows for occlusion of the central retinal vein in the context of a normally functioning artery giving rise to a striking appearance of the fundus often called the "**blood and thunder**" fundus

      Fundoscopy shows:

      ♥ **Prominent congestion of veins**

      ♥ **Flame shaped hemorrhages**

      ♥♥ The classical description is *wedge-shaped*, with the *apex situated at the offending arteriovenous crossing*

      ♥ Cotton wool spots (exudates)

      Clinical signs suggestive of ischaemic CRVO include: poor presenting visual acuity, RAPD, significant retinal haemorrhages, cotton wool spots and presence of neo-vascularisation.

4. Check for hypertension.

5. Intra-ocular Pressure Measurement:

    - Acute glaucoma can lead to venous congestion and ultimately to total obstruction.

      Note that in *the absence of pre-existing glaucoma*, intraocular pressure is unaffected in the acute phase, of a RVO. IOP may rise later as a *secondary* complication of neo-vascularization.

Investigations

Blood tests:

1 FBE

2. CRP/ ESR:

    - If a vasculitis is suspected.

3. U&Es / glucose:

    - Check in particular for diabetes.

4. A procoagulation screen

5. Fasting blood lipid profile

ECG

For evidence of associated ischemic heart disease or hypertension

Other specialist Investigations:

Other **specialist Ophthalmological** testing can be done in order to:

- Confirm the diagnosis
- Assess retinal capillary non-perfusion.
- Follow disease progression and/or response to treatment.

These specialist investigations may include:

1. Fluorescein angiography:
    - Fluorescein angiography may be useful if photocoagulation therapy is being considered.

      The fluorescein angiogram allows for quantification of the surface area of capillary non-perfusion.
2. Optical Coherence tomography:
    - Macular optical coherence tomography (OCT) allows high-resolution cross sectional imaging of the retina.

      Its main use in RVO is in quantifying retinal thickening from intra-retinal fluid in cases of macular edema
3. Colour fundus photographs to document retinal findings

Management

There are no treatments proven to reopen occluded retinal veins.

Management is therefore directed at preventing the secondary complications of RVO that affect vision, including:

1. Macular edema
2. Neo-vascularization, including:
    - Retinal neo-vascularization
    - Anterior segment neo-vascularization

Patients with BRVO or CRVO *without* macular edema or neo-vascularization may be treated conservatively

Treatment is indicated in patients with RVO for:

1. Macular edema

2. Retinal and anterior segment neo-vascularization

The goals of treatment include:

1. Maintaining central visual acuity by minimizing the effects of chronic macular edema.

2. Reducing the risk of bleeding into the vitreous cavity by inducing regression of retinal neo-vascularisation

3. Preventing neovascular glaucoma that can occur with severe disease.

4. Management of predisposing risk factors, such as diabetes and hypertension.

Macular edema:

Pharmacologic treatment with intravitreal anti-vascular endothelial growth factor (VEGF) agents is now first-line therapy for macular edema from BRVO or CRVO that has caused visual loss

VEGF inhibitors in patients with RVO are thought to limit macular edema and improve vision by decreasing vascular permeability.

Anti-VEGF intravitreal agents currently available for clinical use in Australia include:

- **Bevacizumab**
- **Ranibizumab**
- **Aflibercept**

Intravitreal glucocorticoid therapy is considered an alternative for patients with edema refractory to anti-VEGF monotherapy.

Grid laser photocoagulation therapy is another distant alternative for treatment of BRVO but has limited, if any, benefit in patients with CRVO.

There is no established role for prophylactic therapy for macular edema with either anti-VEGF therapy or laser therapy.

Retinal neo-vascularization:

Scatter laser photocoagulation is recommended to reduce the risk of visual impairment from vitreous hemorrhage (secondary bleeding into the vitreous cavity) for established neo-vascularization of the retina or optic disc due to RVO.

In BRVO, scatter laser photocoagulation is usually applied to the portion of the retina in the distribution of the occluded vein where retinal capillary non-perfusion most likely exists.

The laser application is often guided by fluorescein angiography.

In CRVO, the scatter laser treatment is applied throughout the fundus periphery, known as panretinal scatter laser retinal photocoagulation.

Anterior segment neo-vascularization:

Patients with *established* anterior segment neo-vascularization are at risk of neovascular glaucoma due to neo-vascularization that obstructs the trabecular meshwork and produces synechial angle closure glaucoma.

Prophylactic scatter retinal photocoagulation is recommended to reduce this risk.

In addition, **intravitreal anti-VEGF therapy** may be used as an adjunct to laser treatment.

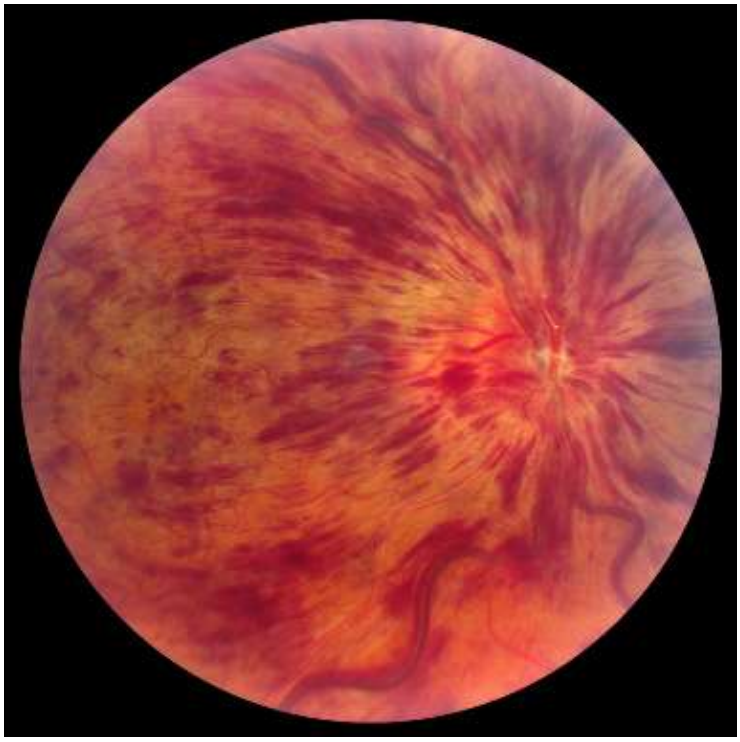
Anti-VEGF therapy may be used as a temporizing measure because the effects of laser take two to four weeks to develop.

Additionally, in some patients laser cannot be performed initially because of anterior segment bleeding, elevated intraocular pressure, corneal edema, miosis, or extensive retinal hemorrhage preventing laser uptake.

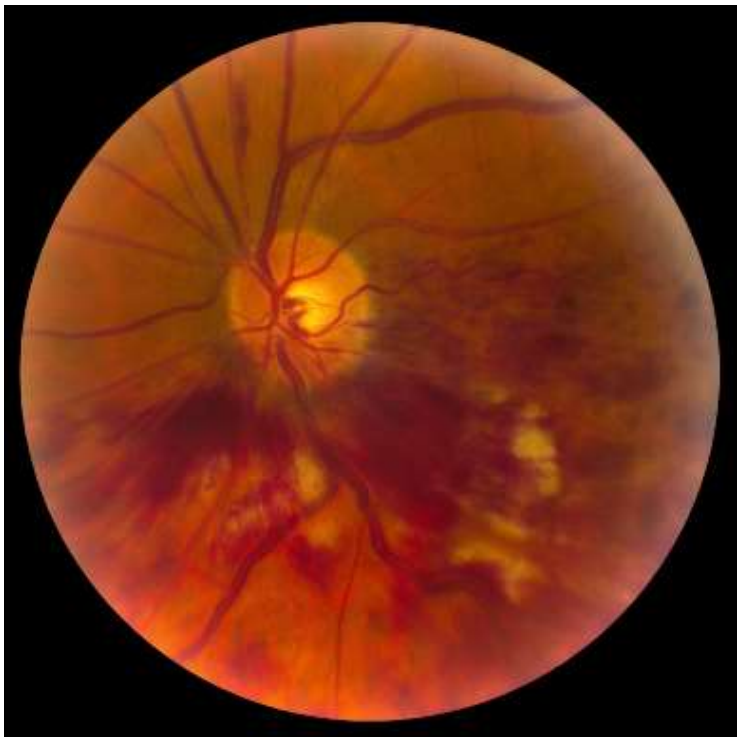
Disposition

As for *any* sudden loss of vision, there should be urgent consultation with an Ophthalmologist.

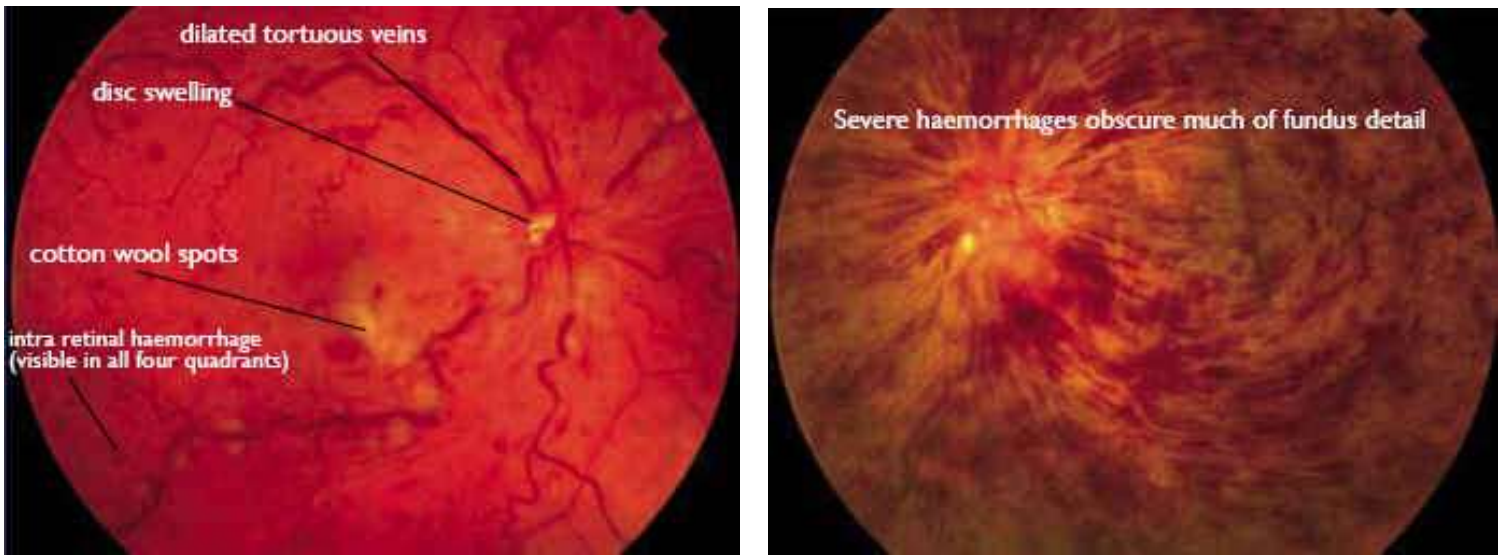
Appendix 1



Left: A central retinal vein occlusion. Right: A branch retinal vein occlusion - in this case, an occlusion of the supero-temporal branch of the retinal vein.



Left: A Hemiretinal vein occlusion.



Left: Non-ischemic CRVO (less severe). Right: Ischemic CRVO (more severe). [1]

References

1. The Eye Emergency Manual, an illustrated guide. NSW Department of Health, 2nd ed 2009.

2. Douglas J Covert. Retinal vein occlusion in Up to Date Website, September 2018.

3. Royal Victorian Eye and Ear Hospital - Central Retinal Vein Occlusion (CRVO) Clinical Practice Guideline, February 2016.

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Reviewed October 2018.