# 5. EYE COMPLICATIONS

## Principles

- To rapidly assess and treat patients with new vision changes or eye trauma.
- To use appropriate screening tests for patients at increased risk of eye disease.
- To identify proliferative sickle retinopathy early.
- To initiate appropriate monitoring and treatment as soon as eye complications have been identified.

## Recommendations

***Investigation***

- Any patient with SCD who develops new changes in vision should be referred to an ophthalmologist immediately.
- Any patient with SCD who sustains eye trauma should be referred to an ophthalmologist immediately to rule out hyphema.
- By the age of 10, all patients with sickle cell disease should have had a full ophthalmologic examination, which should include:
  - Assessment of visual acuity
  - Intraocular pressure
  - Evaluation of anterior structures with slit-lamp biomicroscopy
  - Examination of posterior and peripheral retina, with fluorescein angiography when indicated

  If eye examination is normal, routine follow-up should take place every 1 to 2 years.
- If proliferative or other eye complications are identified, the patient should have more frequent follow-up with an ophthalmologist.
- Patients with eye complications should ideally be followed by a retinal specialist who has experience with sickle cell disease.

***Treatment***

- All patients with proliferative retinopathy should be followed by an ophthalmologist who has experience with SCD, and who will determine the appropriate timing and modality of therapy.

## Background

### *a. Proliferative Sickle Retinopathy*

While many ocular complications of sickle cell disease can occur, the most recognized complication is proliferative retinal vascular disease. Occlusion of the peripheral retinal pre-capillary arterioles produces local retinal ischemia, which triggers neovascularization and formation of fibrovascular lesions referred to as "sea fans."[1] Only arterioles and capillaries are occluded in children, whereas both arteries and veins occlude in adults, possibly because sickled red blood cells are the only insult in children, but leukocyte and endothelial activation over time with cumulative damage to the vascular system causes additional occlusion in adults.[1] The new, fragile vessels are prone to vitreous hemorrhage, and fibrovascular lesions can cause traction on the retina and subsequent retinal detachment and visual loss. The Goldberg staging system (stages I to V) reflects this spectrum of disease progression.[2] Another classification system has also been proposed.[3] *See table 1* for a summary of ocular complications of sickle cell disease.

Proliferative sickle retinopathy (PSR) is more prevalent in patients with hemoglobin SC disease (HbSC)[4] than in patients with sickle cell anemia (HbSS).[5] The typical age of onset is earlier in men with HbSC (ages 15 to 24) than in women with HbSC (ages 20 to 39) and than HbSS patients of both genders (ages 25 to 39).[6] There can be evidence of PSR as early as 8 to 10 years of age in patients with HbSC[7-9] and as early as 13 years of age in patients with HbSS.[9] The risk factors for closure in HbSS disease are a low total hemoglobin, low fetal hemoglobin (HbF), and high

irreversibly sickled cell count.[1] Autoinfarction of a sea fan causes spontaneous regression, and is more common in patients with HbSS.[10]

PSR is usually asymptomatic, unless the patient develops complications, such as vitreous hemorrhage or retinal detachment, in which case he or she may complain of floaters or visual field loss. If macular ischemia occurs, vision loss can arise from a single macular infarct or cumulative insult to the small vessels surrounding the fovea, causing enlargement of the foveal avascular zone and reduced visual acuity over time.

Eye examinations, therefore, should be performed in response to new symptoms, and as part of a routine screening program. Examination should include: assessment of visual acuity, intraocular pressure, evaluation of anterior structures with slit-lamp biomicroscopy, and examination of posterior and peripheral retina, including fluorescein angiography, when indicated.[9] Diagnosis of PSR is suspected on funduscopy by the characteristic appearance of the retinal vasculature, and is confirmed by documenting retinal ischemia on fluorescein angiography. There is no known method of preventing PSR, although hydroxyurea and other inducers of HbF, theoretically, could be protective.

Laser photocoagulation is the established treatment of PSR. Intravitreal anti-vascular endothelial growth factor agents may complement laser treatment, but their use is not yet supported in the literature. Current evidence indicates that no active interventions are required for new vessels that are asymptomatic or do not threaten the macula. Sectoral or circumferential retinal photocoagulation destroys the ischemic retina, which is responsible for the proliferative retinopathy. Patients are usually treated if there is bilateral disease, spontaneous hemorrhage, a high degree of neovascularization, or if they have already lost vision in one eye due to proliferative retinopathy.[9]

In patients with early disease, prophylactic photocoagulation may prevent visible progression.[11] One study, however, showed no absolute difference in visual acuity between eyes that had undergone photocoagulation and those that had not.[12] This may be due in part to the relative rarity of visual loss as a result of PSR. In a natural history study of a cohort of 59 patients with sickle cell disease (SCD) and PSR, vitreous hemorrhage was rare with no longstanding visual sequelae, and prolonged vision loss due to retinal detachment only occurred in 2 patients.[8] Further study is required.

Chronic phlebotomy to a target hemoglobin (Hb) of 90 to 100g/L has been suggested as a means of preventing progression, but this has not been tested in a prospective, randomized fashion.

### *b) Central Retinal Artery Occlusion*

Central retinal artery occlusion (CRAO) can cause sudden, painless onset of blindness. CRAO is rare, with only 17 cases reports identified in a recent systematic review of the literature, mostly in patients with HbSS.[13] Patients were 5 to 32 years of age. About one-third of events occurred during a vaso-occlusive crisis, supporting the hypothesis that CRAO is caused by acute thrombus formation.

There is no proven treatment for CRAO in SCD. As with other severe complications of vaso-occlusion, simple or exchange red blood cell (RBC) transfusion may help ameliorate symptoms by decreasing sickle hemoglobin (HbS) cells. Thirteen of the patients in this series had at least partial recovery. There was no clear association between those patients who received exchange transfusion and those whose vision improved. Other treatments included: oxygen, chronic transfusion, acetylsalicylic acid, heparin, and/or nifedipine.

### *c) Hyphema*

Trauma to the eye can cause bleeding into the anterior chamber, known as hyphema. In a patient with SCD, or even sickle-cell trait, sickled RBCs can block drainage of the anterior chamber, increasing the risk of elevated intraocular pressure and subsequent retinal or optic-nerve ischemia. Because of this risk, it is prudent for all patients and carriers with SCD to have an ophthalmologic evaluation after any ocular trauma.

## Table 1. Ocular Complications of Sickle Cell Disease

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| Retrobulbar and Orbit | Orbital compartment syndrome with inflammation: orbital cellulitis, orbital wall infarction |
| | Recurrent bilateral lacrimal gland enlargement |
| Anterior Segment | Conjunctival vessel dilation |
| | Ischemia associated with retinal surgery or extensive panretinal photocoagulation |
| | Iris ischemia resulting in iris atrophy, pupillary abnormality, and, rarely, iris neovascularization |
| | Traumatic or post-surgical hyphema with induced glaucoma |
| Posterior Segment | Vascular occlusion (arterial and or venous) |
| | Central or branch retinal artery occlusion (spontaneous or following trauma or surgery with elevated intraocular pressure) |
| | Branch retinal artery occlusion |
| | Submacular choroidal infarction |
| | Macular infarction or enlargement of the foveal avascular zone |
| | Epiretinal membrane |
| | Macular hole |
| | Retinal schisis and/or holes |
| | Retinal neovascularization |
| | Choroidal ischemia, neovascularization |
| | Optic disc neovascularization |
| | Angioid streaks |

## References


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