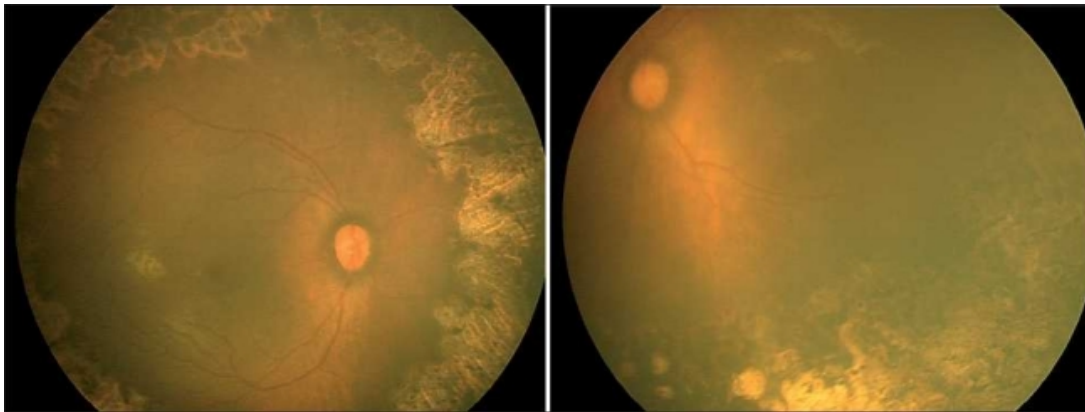


Retinopathy of Prematurity (ROP) — Diagnosis and Treatment

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Retinopathy of prematurity (ROP) is a condition that is characterized by progressive nature and is only seen in premature infants of low birth weight. The condition is caused by the formation of fibrous tissue behind the lens, hence the old term “retrolental fibroplasia”. Infants affected by ROP develop severe visual impairment or can become blind.



Overview of Retinopathy of Prematurity

Retinopathy of Prematurity (ROP) refers to the abnormal development of retinal blood vessels in premature infants. Left untreated, the condition can lead to blindness. It was considered rare when it was first described **by Theodore Terry in 1942 (it is also known as Terry syndrome)**. Today, premature infants of low birth weight are more likely to survive due to advances in medical care. Accordingly, the incidence of children affected by ROP has increased.

Epidemiology of Retinopathy of Prematurity

The incidence of the disease is directly proportional to the patient’s gestational age and inversely proportional to the birth weight. A 2018 study indicated that approximately 12.5% of premature infants whose birth weight is lower than 1251 grams have ROP. The risk is higher in infants who are born before the 31st week of gestation.

Risk factors

- Low birth weight
- Low gestational age
- Supplemental oxygen therapy

- Genetic predisposition
- Infections
- Cardiac defects

Pathogenesis of Retinopathy of Prematurity

Premature infants of low birth weight are at risk of developing [hyperoxia](#) during their care. At term, retinal vascularization is complete on the nasal half of the retina; the temporal half vascularizes after birth. Thus, premature infants may have a poorly developing retinal vascular system.

The disease progresses in some patients despite timely intervention while rarely progresses to severe states in others, thus suggesting some genetic influence on the pathogenesis.

Two schools of thought have been put forward to explain the disease pathophysiology:

Upon birth, the neonate is exposed to a relative hyperoxic state compared to a hypoxic in utero state. This damages the mesenchymal spindle cells behind the retina that develop gap junctions, leading to abnormal vascularization.

The two-phase theory, as put forward by Ashton, states that, upon birth, the initial event occurs upon exposure to a hyperoxic environment and instead of vascularization. The vessels undergo vasoconstriction to cause irreversible capillary cell destruction. This triggers the release of mediators, such as vascular endothelial growth factor (VEGF), that induces disorganized vascularization and thus does not respond well to proper regulation.

These changes are also associated with the formation of fibrous tissue.

Classification of Retinopathy of Prematurity

In 1984, an international classification of ROP was established. The retina was divided into three zones, and ROP was classified according to the extent of involvement of these three zones. The zones start from the most posterior part of the retina to the most anterior part. Retinal imaging, which has improved significantly in the last few years, allows clinicians to describe the extent of ROP accurately.

Zones of the Retina in ROP

The retina is classified into three concentric zones:

| | |
|-----------------|---|
| Zone I | Optic disc at the center and spans twice the distance from the disc to the fovea |
| Zone II | Starts from the edge of zone I and extends to the ora serrata nasally and a similar imaginary boundary temporally |
| Zone III | Remaining most-anterior part of the retina |

The extent of involvement of the retina in ROP needs to be documented for prognostic figures. This is routinely expressed in the number of clock hours involved. Therefore, the retina can also be classified into clock-hour segments “12 segments.”

Stages of ROP

In addition to the extent of the anatomical involvement in ROP, the degree of vascular changes also needs to be documented.

Stage 1 ROP

Stage 1 is characterized by a demarcation line between the vascular and avascular retina. This is a thin structure that lies in the plane of the retina.

Stage 2 ROP

The previously described demarcation line grows to occupy a volume, and forms a ridge above the plane of the retina. Popcorn small vessels, "due to the formation of small tufts of new vessels," are seen on the posterior aspect of the ridge.

Stage 3 ROP

In addition to the formation of a retinal ridge, there is retinal fibrovascular proliferation. The fibrovascular tissue is seen to extend from the abnormal retinal ridge into the vitreous.

Stage 4 ROP

Stage 4 is characterized by partial or subtotal retinal detachment. Subtotal retinal detachment in ROP can be exudative or tractional. Partial retinal detachment can be without the involvement of the fovea (stage 4A) or can involve the fovea (stage 4B).

Stage 5 ROP

Here, there is a total retinal detachment. The patient presents with leukocoria (white pupillary reflex).

Plus disease

This is a severe form of ROP that is characterized by venous dilation and arterial tortuosity of the posterior retinal vessels. Infants with aggressive posterior ROP are at the highest risk of progression to stage 5 ROP.

Screening for ROP

Premature infants of low birth weight should receive regular screening for ROP starting four weeks after birth. In the developing world, screening for ROP should be started two weeks after birth because of the higher risk of early aggressive posterior ROP.

The pupils are dilated and indirect ophthalmoscopy with a 28D lens is used to examine the retina in the screening process. Pupil dilation should be performed 45 minutes before the ophthalmoscopic examination. A mixture of cyclopentolate and phenylephrine drops can be used to dilate the pupils.

ROP screening is also possible with the RetCam digital camera system which uses a wide-angle lens and allows experts to share high-resolution retinal images.

In infants with ROP, it is important to determine the risk of progression. Postnatal weight gain, elevated levels of serum insulin-like growth factor 1, and early aggressive ROP are indicators of early disease progression.

Using the weight, insulin-like growth factor 1 levels, and weekly weight from

birth until 36 weeks can help classify the patients into two categories:

- Infants with low-risk ROP
- Infants with proliferative ROP who require laser treatments

Treatment of ROP

The ROP threshold is defined as the ROP stage that requires active treatment. Infants with stage 3 ROP involving zones I or II of the retina require treatment.

Infants with pre-threshold ROP might also need treatment to prevent disease progression. However, there has been a debate over which infants with pre-threshold ROP require early treatment.

The early treatment for ROP (ETROP) study answered this important question with the following recommendations:

Type 1 ROP is known as high-risk pre-threshold ROP. Type 1 ROP is defined as any stage of ROP in zone I with plus disease, stage 3 in zone I without plus disease, or stage 2 or 3 in zone II with plus disease. Type 1 ROP requires active treatment.

Type 2 ROP is known as an observational pre-threshold ROP. Type 2 ROP is defined as stages 1 or 2 in the zone I without plus or stage 3 in zone II without plus. Patients with type 2 ROP should be given weekly follow-ups without any active treatment.

The currently available active treatments for ROP include [cryotherapy](#), indirect laser photocoagulation, and anti-vascular endothelial growth factor drugs, such as **intravitreal bevacizumab**. These three treatment modalities share one common mechanism: they stop the growth and formation of new retinal vessels. Cryotherapy and laser photocoagulation can destroy the retina and result in visual field loss. Thus, pharmacological treatments are gaining more acceptance in the current era.

Cryotherapy is stressful for babies and requires general anesthesia. Moreover, cryotherapy can also cause periocular inflammation. Accordingly, if indirect laser photocoagulation or anti-vascular endothelial growth factor drugs are available, cryotherapy should not be considered as an option for active treatment of ROP.

References

Quinn GE, Gui-shang Y, Bell EF. Incidence and Early Course of Retinopathy of Prematurity: Secondary Analysis of the Postnatal Growth and Retinopathy of Prematurity (G-ROP) Study. *JAMA Ophthalmology*, 2018;136(12):1383-1389. doi:10.1001/jamaophthalmol.2018.4290

Shah PK, Prabhu V, Karandikar SS, Ranjan R, Narendran V, Kalpana N. Retinopathy of prematurity: Past, present and future. *World Journal of Clinical Pediatrics*. 2016;5(1):35-46. doi:10.5409/wjcp.v5.i1.35.

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