RETINOPATHY OF PREMATURITY

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Introduction

Retinopathy of prematurity (ROP) is a vasoproliferativedisorder of the retina among premature babies. In almost all terminfants, the retina and retinal vasculature is fully developed, and ROPcannot occur; however, inpreterm infants, the development of the retina, which proceeds from the optic nerve head anteriorly during the course of gestation, is incomplete, with the extent of the immaturity of the retina depending mainly on the degree of prematurity at birth.

ROP begins to develop between 32 and 34 week after conception, regardless of gestational age at delivery and has two distinct phases

[1]. During the acute first phase, the normal vasculogenesis of the retina is disturbed by the relative hyperoxia of the extrauterine environment. This causes vaso-obliteration and non-vascularization of some areas of the anterior retina

[2]. The subsequent hypoxia causes a second chronic phase, characterized by the proliferation of vascular and glial cells, arteriovenous shunt formation, occasionally leading to involution or permanent cicatricial changes and visual impairment.

In its more severe forms, it results in severe visual impairment or blindness, both of which carry a high financial cost for the community but also a high individual cost by affecting the normal motor, language, conceptual, and social development of the child.

Staging of ROP is described based on the

1) location of retinal involvement by zone

2) extent of retinal involvement by clock hour, and

3) stage of the disease at the junction of the avascular and vascular retina.

Location of the disease-

Zones are centered around the optic disc and not the macula.

Zone I (innermost) is a circle, the radius of which extends from the center of the optic disc to twice the distance from the center of the optic disc to the center of the macula.

Zone II extends centrifugally from the edge of zone 1 to the nasal ora serrata.

Zone III is the residual crescent of retina temporal to zone 2.

Extent of the disease-

The extent of the retinal involvement is recorded as hours of the clock or as 30 degrees sectors.

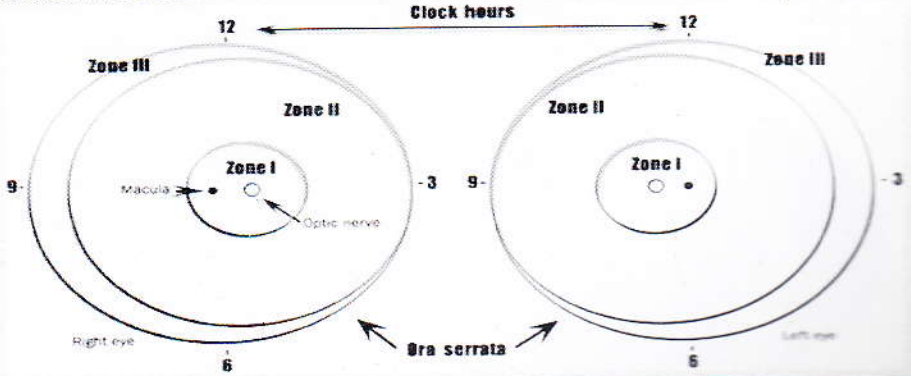

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FIGURE 1

Scheme of retina of the right and left eyes showing zone borders and clock hours used to describe the location and extent of ROP. Diagrammatic representation of the potential total area of the premature retina, with zone I (the most posterior) symmetrically surrounding the optic nerve head (the earliest to develop). A larger retinal area is present temporally (laterally) rather than nasally (medially)

(zone III). Only zones I and II are present nasally. The retinal changes discussed in recommendation 4 are usually recorded on a diagram such as this one.

Stage of the disease-

The clinical appearance of the stages of ROP is related to the appearance of the retinal vessels at the avascular-vascular junction. More than one stage may be present in the same eye; staging then is determined by the most severe manifestation present. Immature or incompletely vascularized retina: this is seen prior to the development of ROP and is characterized by dichotomously branching retinal vessels of normal caliber.

Stage 1- A flat demarcating line is seen delimiting vascularized retina from the anterior avascular retina. Abnormal branching or arcading of vessels is seen leading up to the demarcation line.

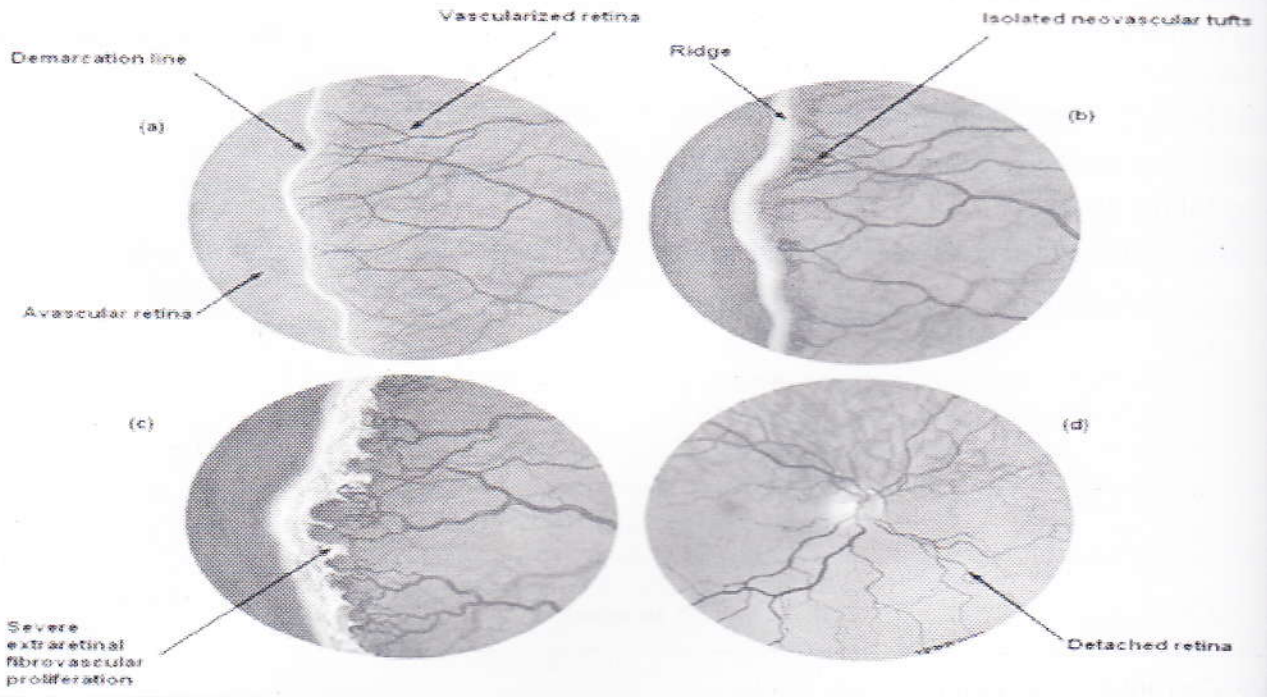
Stage 2-The demarcation line develops into a ridge. This ridge is raised and has volume.

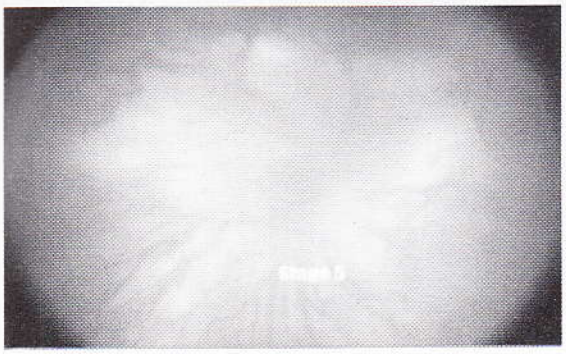
Stage 3- Extra-retinal neovascularization into the vitreous is seen with the development of abnormal shunt vessels at the ridge.

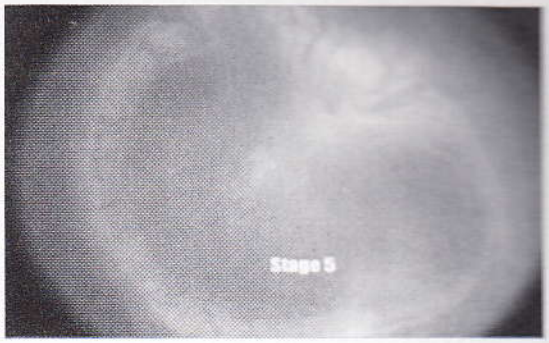
Stage 4- ROP associated with retinal detachments are classified into

stage 4A (partial retinal detachment, not involving the macula) and stage 4B (involving the macula).

Stage 5- Total retinal detachment is usually tractional and funnel shaped and presents as a leucocoria or white pupillary reflex.

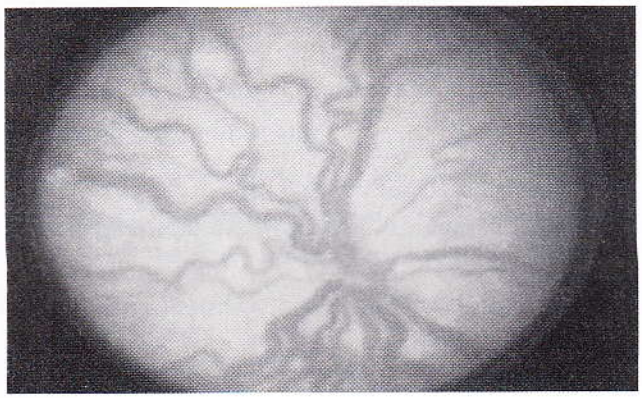




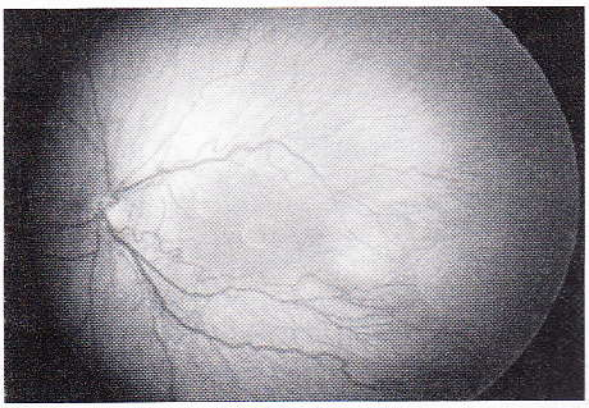


Special Conditions:

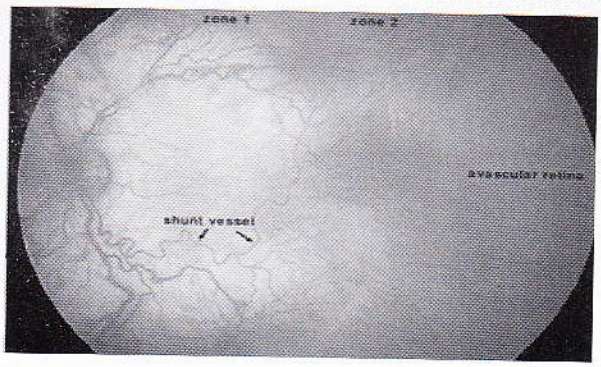
Plus disease: refers to venous dilatation and arteriolar tortuosity of the posterior retinal vessels in at least two quadrants of the eye. Engorgement of iris vessels, pupillary rigidity and vitreous haze may also be seen. A plus symbol is added to the ROP stage number to designate the presence of plus disease.



Pre-plus: is the term used to denote vascular abnormalities of the posterior retina that are insufficient for the diagnosis of plus disease, but that cannot be considered normal.



Aggressive-posterior ROP (AP-ROP): (previously called type II ROP and "rush disease"): is a rapidly progressing, severe form of ROP which if untreated progresses to stage 5 ROP. The features include posterior location (zone I and sometimes posterior zone II), prominence of plus disease, ill-defined nature of the retinopathy, flat network of neovascularization and hemorrhages. The earliest phase of this disease shows abnormal closed-loop vessels (and not the normal dichotomous branching pattern) with mild tortuosity that can develop into the full-blown picture in less than a week. The disease does not proceed from the classical stages of 1 through 3. Diagnosis can be made on a single visit and does not require evaluation over time.



SCREENING GUIDELINES

Recommendations based on review of data from the CRYO-ROP and LIGHT-ROP studies

— **Whom to screen**

1. BW < 1500 g or
2. Gestational age < 30 weeks or
3. Infants with an unstable clinical course who are at high risk (as determined by paediatrician)

Initial screening should be performed by 31 wks PCA or 4 wks CA, whichever is later.

In Indian Scenario

— BW < 2000 g

— GA < 34-35 weeks

— Initial screening recommended between 20-30 days of life.

— Early screening (i.e. < 20 days of life) is strongly recommended for babies < 30 weeks of GA.

Treatment

The goal of treatment in ROP is prevention of retinal detachment and any scarring with optimization of visual outcome.

Indication of treatment

Ablation treatment should be considered for

Type I ROP

- Zone I, any stage ROP with plus disease or
- Zone I, stage 3, with or without plus disease or
- Zone II, stage 2 or 3 ROP, with plus disease

Continued serial examination should be considered for

Type II ROP

- Zone I, stage 1 or 2 with no plus disease or
- Zone II, stage 3 with no plus disease

Table 2: treatment guidelines for ROP adapted from the current ETROP guidelines[1]

Zone I	NO PLUS	Stage 1	Follow	Zone II	NO PLUS	Stage1	Follow
		Stage 2	Follow			Stage2	Follow
		Stage 3	Treat			Stage3	Follow
	PLUS	Stage 1	Treat		PLUS	Stage1	Follow
		Stage 2	Treat			Stage2	Treat
		Stage3	Treat			Stage3	Treat

Available treatment modalities

Treatment involves ablation of the peripheral avascular retina.

Diode laser therapy has largely replaced cryotherapy[2,3] although it is indicated[3] in cases where there is poor fundus visibility, unavailability of laser and physician's unfamiliarity with indirect laser photocoagulation.

Laser photocoagulation

At present the standard of care in ROP is diode laser (810nm). It can be done under local or general anesthesia or sedation. Laser treatment has supplanted cryotherapy as it has better structural[4] and visual outcomes[1]. Its advantages over cryotherapy are its ease of treatment, portability, less postoperative pain, less damage to the adjacent tissues, lesser chances of exudative retinal detachment, vitreoretinal traction and vitreous hemorrhage due to reduced breakdown of blood retinal barrier. It minimizes the risk of missing areas, as laser spots are visible during the treatment. Treatment includes ablation of the entire avascular retina from the ora serrate up to the ridge with near confluent burns spaced one to half burn width.

Materials and preparation for laser treatment

Materials required for laser ablation are- pediatric (alphonso's speculum), pediatric scleral depressor, sterile cotton tipped applicator, topical anesthetic eye drops and dilating[5] along with sterile Ringer Lactate in a syringe. Preparation requires pupils should be dilated and autoclaved instruments should be used. If topical anesthesia is used the child should be fed and burped at least 30 minutes prior to the treatment. The treatment should be carried out in a Neonatal intensive care unit (NICU) or in a setting where suction and resuscitation equipment are readily available.

Postoperative care

The child should be after 30 minutes of the procedure and should be under the care of a neonatologist. Postoperative hypothermia and hypoglycemia should be prevented. Counseling should be done regarding postoperative chemosis and conjunctival hyperemia to avoid alarm. Topical steroids should be started thrice a day to manage postoperative inflammation and prevent formation of post laser posterior synechiae.

Follow up after laser

In patients with zone II disease, re-evaluation should be done within 7 days and signs of regression should be looked for. If adequate regression has not occurred laser treatment is done to the skipped areas and around the active areas. With zone I or APROP cases, one session is usually inadequate for regression, hence, re-evaluation and complete ablation should be done every 3-4 days until complete regression is seen.

Table 1: Follow up schedule for screening/treatment[5]

How frequently to examine	
1. Mature retina	Follow-up 3 months – 1year
2. Immature retina	Follow-up bi-weekly
3. Immature Zone I retina	Follow-up weekly
5. Prethreshold ROP	Follow-up 3-7 days
6. Threshold ROP	Early treatment within 72 hours
7. Retinal Detachment in ROP	Early surgical treatment

Treatment of Retinal detachment associated with ROP

Stage 4 or 5 ROP is a high risk of irreversible blindness. It requires vitreoretinal surgical intervention with lens sparing vitrectomy. It has shown promising results in stages 4A and 4B[6]. The results of surgical intervention are poor in stage 5 ROP[7].

Role of anti-VEGF

Anti VEGF have been used in severe forms of ROP, however its role is controversial. According to BEAT ROP Bevacizumab showed promising results in zone I stage 3+ ROP but not in zone II[8]. In zone I, recurrence rates after laser treatment is higher when compared to Bevacizumab. Since systemic absorption may cause delayed vascular development in other organs, it is not recommended as the first line therapy[9].

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