CME SERIES (No. 12)

Retinopathy of Prematurity

ALL INDIA OPHTHALMOLOGICAL SOCIETY
CME SERIES (No. 12)

Retinopathy of Prematurity
CME Series

Prof. Raj Vardhan Azad, MD, FRCS Ed.
Head, Vitreoretina Services
Dr. Rajendra Prasad Centre for Ophthalmic Sciences,
All India Institute of Medical Sciences
New Delhi 110029 India

Dr. Nikhil Pal MD,
Senior Resident, Vitreoretina Services,
Dr. Rajendra Prasad Centre for Ophthalmic Sciences,
All India Institute of Medical Sciences
New Delhi 110029 India

ALL INDIA OPHTHALMOLOGICAL SOCIETY

Printed by:
Syntho Pharmaceuticals Pvt. Ltd.
This CME Material has been supported by the funds of the AIOS, but the views expressed therein do not reflect the official opinion of the AIOS.

(As part of the CME Programme)

For any suggestion, please write to:

Prof. Raj Vardhan Azad
Hony. General Secretary

Published by:

ALL INDIA OPHTHALMOLOGICAL SOCIETY
Dr. Rajendra Prasad Centre for Ophthalmic Sciences,
All India Institute of Medical Sciences,
Ansari Nagar, New Delhi-110029
Ph.: 011-26593187 Fax: 011-26588919
email: rajvardhanazad@hotmail.com

Society’s Secretariat Phone: 011-26588327, Email: aiossecretariate@yahoo.co.in
CME Series

Retinopathy of Prematurity

Prof Raj Vardhan Azad MD FRCS Ed; Dr Nikhil Pal MD

Retinopathy of prematurity (ROP) is a disease affecting the retina of premature infants. Its key pathologic change, retinal neovascularization, has several features in common with the other proliferative retinopathies such as diabetic and sickle cell retinopathy. Each of these proliferative retinal vascular disorders appears to be associated with local ischemia and the subsequent development of neovascularization.

ROP is unique in that the vascular disease is found only in infants with an immature, incompletely vascularized retina; hence its connection with premature infants. The spectrum of outcome findings in ROP extends from the most minimal sequelae without affecting vision in the mild cases to bilateral, irreversible, and total blindness in more advanced cases. Contemporary neonatology practices in the premature infant nursery have improved the survival rate of the smallest premature infants, who are at the highest risk of developing ROP. This disorder is a major challenge to all physicians dealing with premature infants.

Historical Perspective

Retinopathy of prematurity, first identified by Terry\(^1\) in 1942, within a decade became the largest cause of child blindness in the United States and a major cause of blindness throughout the developed world. In the United States in the early 1950s, ROP exceeded all other causes of child blindness combined. Terry’s original reports designated the condition *retrolental fibroplasia* based on his impression that the primary change involved a proliferation of the embryonic hyaloid system which incorporated the retina. As the pathogenesis became better understood, the term retinopathy of prematurity was generally adopted. The term ROP was coined by Heath in 1951. He was much more precise in his descriptions and his histopathological studies offered rare insight into the disease processes as it was then understood.

The incrimination of oxygen as the principal cause of ROP in the 1950s\(^2,3\) led to the practice of rigid curtailment of oxygen in the nursery, and a dramatic decrease in the incidence of ROP followed. With the de-
velopment of neonatology, more of the high risk premature infants, those with extremely low birth weights, are now surviving. It is these infants, with the greatest immaturity of the retinal vasculature, who have the highest risk of ROP. In 1981, Phelps estimated the incidence of ROP associated with an increase in survival rates of infants with birth weights less than 1000 gms. Eight percent of these low-birth-weight infants survived in 1950, whereas in 1980, 35% survived. Infants weighing 700 to 799 g born in 1983 and 1984 survived at a rate of 57% compared with 68% for those born in 1986 and 1987. Clearly, infants are surviving today who would not have survived to develop ROP in earlier years; these very-low-birth-weight survivors account for the significant number of new cases of ROP occurring in recent years. As a result, there is renewed interest in the pathogenesis and therapy of ROP.

Before 1984 it was difficult for ophthalmologists to interpret and communicate to each other about the development of ROP because there was no universally accepted classification system available. This issue was finally decided in 1983 when a universally accepted classification system called as the International Classification of Retinopathy of Prematurity was devised under the leadership of John Flynn.

In 1970s the Japanese physicians treated the ridge and the adjacent avascular retina. Hindle and Leyton, in Canada, treated the ridge, and the retina anterior and posterior to it. McPherson, Hittner, and Kretzner advocated the cryo of the ridge and adjacent posterior avascular zone to destroy the spindle cells, the presumed source of angiogenic factor.

With the advent of the portable diode laser systems, most of the advanced countries have switched over to laser photocoagulation because of its precision and fewer side effects, but in a vast majority of the developing nations, cryotherapy still remains the only option for treating threshold ROP.

Management of stage 4 and 5 ROP by advanced surgical techniques is being carried out by limited centers around the world and though the process of refining these techniques is continuing, the present status gives little cheer to an infant with an advanced stage of ROP.

ROP Classification

Reese, King and Owens classified Retrolental Fibroplasia in 1953. They divided the classification into the active and the cicatricial groups. 

Rush disease was characterized by engorgement of the posterior pole vessels whose most anterior development was still in the posterior pole and it was associated with broad anterior avascular retina.

Plus Disease: Schaffer, Quinn and Jonson recognized this feature when they noted that posterior polar dilation and tortuosity constituted an important sign related to the severity of the disease. Associated with it was the iris vessel dilation and engorgement, which resulted in poor pharmacological dilation of the pupil. This was called the plus disease.
A symposium was held in Calgary in 1982, attended by 22 ophthalmologists and one ocular pathologist from eleven countries across the globe. They agreed upon a classification and worked upon this for a year. They met again at Baltimore to refine the classification and give it the present form known as the International Classification of Retinopathy of Prematurity.  

Zone I (Posterior pole or inner zone): The limits of zone I are defined as twice the disc fovea distance in all directions from the optic disc [Also defined as a circle, the radius of which subtends an angle of 30’ and extends from the disc to twice the distance from the disc to the center of the macula].

Zone II: Extends from the edge of Zone I peripherally to a point tangential to the nasal ora serrata (at 3 O’clock in the right eye, 9 O’clock in the left eye).

Zone III: Is a residual temporal crescent of retina anterior to Zone 2. This is the Zone, which is last vascularized, in the premature eye.

In routine usage zones 1 & 2 are often sub-divided into an anterior and a posterior zone to give a better idea of the exact location within the zone.

Extent: The extent of the disease is coded by the number of clock hours with ROP. The extent of the disease is further described as contiguous clock hours of ROP or noncontiguous clock hours. Since their can be more than

![CLOCK HOURS](image)

**Fig 2:** Depicts the zones in the fundus as described in the ICROP Classification.
one zone involved in an eye at a particular exam in various clock hours, it is standard better to classify the disease in that eye by the most posterior zone.

Staging the Disease (As defined by the ICROP)

ICROP Staging

<table>
<thead>
<tr>
<th>Rop: Stages</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Demarcation Line</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Ridge</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Ridge with Extra Retinal</td>
</tr>
<tr>
<td>Mild / Moderate / Severe</td>
<td>Fibrovascular Proliferation</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Subtotal Retinal Detachment</td>
</tr>
<tr>
<td>A</td>
<td>A. Not Involving Macula</td>
</tr>
<tr>
<td>B</td>
<td>B. Involving Macula</td>
</tr>
<tr>
<td>Stage 5</td>
<td>Total Retinal Detachment</td>
</tr>
</tbody>
</table>

*Stage 1 (Demarcation Line):* This line is a thin but definite structure that separates the avascular retina anteriorly from the vascularized retina
posteriorly. There are recognizable abnormal branching or arcing of vessels leading up to it. It is relatively flat, lies within the plane of the retina and is white in color.

Stage 2 (Ridge): The line of stage I now has grown, has height and width, occupies a volume, and extends up out of the plane of the retina. The ridge may change in color from white to pink and describe location and extent of retinopathy of prematurity.

Stage 3 (Ridge with Extraretinal Fibrovascular Proliferation): To the ridge of stage 2 is added the presence of extraretinal, fibrovascular proliferative tissue.

Stage 4 (Retinal Detachment): It may be caused by an exudative effusion of fluid, traction, or both, even in this early stage

Stage 4a. Subtotal retinal detachment not involving the Macula:

Stage 4b. Subtotal retinal detachment involving the macula

Stage 5: Total tractional retinal detachment is always funnel shaped and is based on configuration of the funnel.

<table>
<thead>
<tr>
<th>Funnel</th>
<th>Anterior</th>
<th>Posterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i)</td>
<td>Open</td>
<td>Open</td>
</tr>
<tr>
<td>(ii)</td>
<td>Narrow</td>
<td>Narrow</td>
</tr>
<tr>
<td>(iii)</td>
<td>Open</td>
<td>Narrow</td>
</tr>
<tr>
<td>(iv)</td>
<td>Narrow</td>
<td>Open</td>
</tr>
</tbody>
</table>

Prethreshold ROP

Prethreshold ROP is defined as:
1) Any stage of ROP in zone I with plus disease
2) ROP stage 3 with plus disease with 3 contiguous or 5 interrupted clock hours of involvement of retina in Zone II with plus disease but less than threshold

ROP Sequelae

Fig 7: Stage 1: ROP Stage 5: ROP

Fig. 8: Regressed ROP
Threshold ROP Treated with Laser

Fig. 9: Pre Laser  
Fig. 10: Post Laser

It is important to understand this situation since it can rapidly progress to disease, which requires treatment. As the timeframe for therapy is narrow, once prethreshold ROP is detected, one is obliged to make frequent examinations to detect progression to threshold disease.

Threshold Disease
This is defined as:

Zone I or II: ROP stage 3 more than 5 contiguous or 8 cumulative clock hours with plus disease present

This is the stage in which the treatment is mandatory since the chances of progression to retinal detachment are 50% if left untreated.

Regressed ROP
A significant number of patients with active ROP undergo partial regression. The residual changes have been divided in the classification into those affecting the retinal periphery and those affecting the posterior fundus. Each location has been further subdivided to describe separately the vascular alterations and the residual retinal changes.

Peripheral Changes

Vascular
- Failure to vascularize peripheral retina
- Abnormal, nondichotomous branching of retinal vessels
- Vascular arcades with circumferential interconnection
- Telangiectatic vessels

Retinal
- Pigmentary changes
- Vitreoretinal interface changes
- Thin retina
Peripheral folds
Vitreous membranes with or without attachment to retina
Latticelike degeneration
Retinal breaks
Traction or rhegmatogenous retinal detachment

Posterior Changes

Vascular
- Vascular tortuosity
- Straightening of blood vessels in temporal arcade
- Decrease in angle of insertion of major temporal arcade

Retinal

Pigmentary changes
- Distortion and ectopia of macula
- Stretching and folding of retina in macular region leading to periphery
- Vitreoretinal interface changes
- Vitreous membrane
- Dragging of retina over disc
- Other ocular findings of regressed ROP:

Myopia
In the very low-birth-weight infants who are born weighing less than 1251 g, 20% develop myopia in the first 2 years of life. The lower the birth weight, the higher the chance of myopia. In addition, among the infants with ROP the incidence of myopia increases in direct relationship to the severity of ROP, e.g., in patients who develop zone II, stage 3 ROP (without plus disease), 44% to 45% are myopic at 12 and 24 months post term. In contrast, infants of this same birth weight group who never develop ROP have a 13% incidence of myopia. The exact mechanism of the myopia is still not understood. Fletcher and Brandon suggested that it may be due to an elongation of the globe, alteration of the lens or the corneal curvature, or a combination of these factors.

Other refractive and muscle defects
Amblyopia, nystagmus, and strabismus
Lens and corneal changes-Cataract keratoconus, irregularities of corneal curvature, band keratopathy, and acute hydrops
Glaucoma is a serious complication of ROP in both the acute and regressed phases of the disease.
Pathogenesis of ROP

Concept of Retinopathy of Prematurity has dramatically changed ever since Terry first described it in 1942. Supplemental oxygen administration which was for a long time considered as the most important causative factor is now considered as only a risk factor. Low birth weight and decreased gestational age are now considered primary causative factors.

Two important hypotheses described are:

(i) The classical theory
(ii) Spindle Cell theory

(i) The Classical Theory

Arhton and Patz proposed the classical pathogenesis of ROP.9 According to this theory which was once widely accepted, supplemental oxygen administration was considered as the main causative factor. Elevated arterial P02 causes retinal vasoconstriction, leading to vascular closure and if vasoconstriction is sustained, subsequent permanent vascular occlusion occurs. Endothelial cell proliferation adjacent to closed capillaries is followed when neonate returns to room air thus leading to neovascularization. Subsequent extension of this neovascularization may reach vitreous, producing hemorrhage leading to fibrosis and causing vitreous traction and Retinal Detachment.

(ii) Spindle Cell Theory

This theory which was proposed by Kretzer et al10, postulates the induction of retinal and vitreal neovascularization by spindle cell insult. In premature newborn, the peripheral retina is avascular and thin. After birth the spindle cells are exposed to hyperoxic environment because of increased oxygen diffusion through this retina from choroidal vasculature. Oxygen free radical: a cytotoxic agent attacks compromised spindle cells, which has deficient anti-oxidative defense mechanism. This abnormal spindle cells stop migration and canalization.

Growth Factors in ROP

Vasoformative factors play a vital role in the normal development of Retinal Vasculature.11 Many vasoformative factors have been described but vascular endothelial growth factor (VEGF) was among first to be identified and cloned. VEGF is produced anterior to the vascular area. Adequate amount of VEGF is required for retinal growth. If the avascular zone is larger, and when this is exposed to the hyperoxic state, VEGF expression is decreased leading to vasobliteration. This causes hypoxia and ischemia in nonperfused area if insult is sustained. This again stimulates VEGF production and thus neovascularization. Over the time if VEGF production decreases, ROP will regress. If VEGF production increase or
persist, ROP will progress. The manipulation of these factors could be beneficial therapeutically.

**Incidence and Natural Course of ROP**

A review of literature reveals that the incidence and severity of ROP increases with decreasing birth weight and gestational age. Thus, nine out of ten infants with birth weight less than 750 grams or less will develop ROP while only 4.7 out of the ten in a birth weight group of 1000-1250 grams will develop ROP.\(^{12}\) Similarly, the incidence of ROP reported in infants of gestational age groups of 24-27, 28-31, 32-35 and above 36 weeks is 89, 63, 26 and 19% respectively.\(^{12,13}\) A study from the Indian subcontinent quotes an incidence of 38% for a birth weight less than 1500 grams criteria.\(^{14}\) The CRYO ROP study has examined the natural history on a cohort of 4099 infants & reports the occurrence of events in the history. Stage 1 ROP occurred at a median age of 34.3 wk. PCA (Post Conceptional Age). Stage 2 was seen at a median age of 35.4 wk. PCA (range 32-40.3 wks.). Similarly stage 3 was noticed at median age of 36.6 wk. PCA (range 32.9 to 42.4 wks.) Stage 3+ was seen at a median age of 36.3 wk. PCA (range 32.6-42.9 wks.) Prethreshold ROP occurs at median age of 36.1 wk. PCA (range 32.4-41.5 wk.). Threshold ROP occurred at median age of 36.9 wk. PCA (range 33.6 - 42.0 wks.)

**ROP Screening Examination**

1. Screen all premature infants less than 1500 gram birth weight
2. Screen all babies born at less than or equal to 32 weeks of post-conceptional age or 4 weeks from birth whichever is earlier.
3. Special Criteria: Neonatologist is to be cautioned to include all babies for screening who they consider most sickly survivors because of sepsis, multiple blood transfusions, RDS, pneumonitis, extra ordinary oxygen support. Obviously the previous criteria will cover the vast majority of sick babies.

**How to perform the Screening Examination for ROP**

Before embarking upon the screening exam for ROP one has to keep in mind that the children to be screened are premature infants and thus are susceptible to a particular set of problems. It is these problems that the ophthalmologist has to be aware of and tailor the examination to prevent them. Many of the babies will still be in the nursery at the scheduled time of 1st exam either requiring oxygen therapy or other critical care. The following points if kept in mind will ensure that the child neither develops vision threatening ROP nor any systemic complications as a result of the screening examination.

(a) **Place:** The ideal place for the screening examination is a temperature controlled room, since premature neonates are susceptible to hypothermia. The screening should be done in the presence of a neonatologist

*Retinopathy of Prematurity CME Series*
in a pediatric ward so that any systemic complication can be handled easily. Those babies in incubators or on oxygen therapy may be examined in the nursery with the ophthalmologist taking care to prevent contamination. The usual complications are bradycardia or a decrease in the oxygen saturation which is easily reversible.

(b) Preparation of the child: The pupils are dilated with a mixture of phenylephrine 2.5% & Tropicamide 0.5% instilled 3 times at 10 mins interval about 1 hour before the scheduled exam. Alternatively a combination of 0.2% cyclopentolate & 2.5% phenylephrine may be instilled twice at 5 minutes interval. Care should be taken that the baby has not had a feed immediately before the exam as the child might vomit or aspirate especially if cyclopentolate has been used as the mydriatic. The parents should be explained the nature of the examination.

(c) Instruments: Screening for ROP involves a carefully done indirect ophthalmoscopic examination of the peripheral retina. Since the infants’ eyes are small, a pediatric wire speculum is helpful in keeping the eyelids apart. Though Indirect Ophthalmoscopy may be performed with a 20D lens, a 28D lens is helpful in examining the periphery especially in mid-dilated pupil. Gentle indentation with a wire vectis or a pediatric depressor helps stabilize the globe and visualise the periphery. The instruments should be washed thoroughly after each examination.

(d) Procedure: After decreasing the room illumination, first the posterior pole is visualised for plus disease. Then the periphery is examined to look for the extent of changes. The head may be turned towards the side being examined to increase visualisation of temporal periphery. Care should be taken not to put too much pressure on the globe. Globe indentation may give an erroneous impression of plus disease so plus disease should be looked for without indentation. The findings are carefully noted in the ROP file. After each examination the child is given a mild topical antibiotic for a couple of days.

Now, Retcam 120; a real time wide angle digital imaging system is also performed in all babies for proper documentation and follow up of ROP as well as for telemedicine purposes.

Fig 11: Indirect Ophthalmology Screening
Pupillary Dilatation

A number of drugs can be used for this purpose, including Tropicamide, Phenylephrine, and Cyclopentolate eye drops.

The Cryo ROP study has used Cyclopentolate 0.2% and Phenylephrine 1.0%, 1 drop to each eye twice, separated by 2-5 minutes. Whenever this was not adequate, 1-2 drops of Cyclopentolate 0.5% were permitted as an alternative mydriatic. We have finally settled for the combination of Tropicamide 1.0% and Phenylephrine 2.5% eye drops, used twice at 15-minute intervals. Tropicamide is preferred because of its lack of systemic side effects, where as GIT & central nervous system disturbances are common with Cyclopentolate. The GIT disturbance can be presence of ileus, abdominal distension and vomiting.

1. Inform Neonatology unit nurse regarding time when you will examine all children in nursery, which meet your screening criteria.
2. Nurse will administer eye drops as desired by doctor to dilate the pupil (instruct nurse to check whether pupil is properly dilated, so that extra medication can be used if required).
3. Feeding the infants is to be avoided until 60 minutes after eye exam.
4. Neonatologist is to be in attendance, especially in cases, which are unstable.
5. Wash hands with Betadine sponge or other such disinfectants, and rinse with water.
6. Always wear gloves.
7. Apply speculum optional for experienced physicians (choice of using local anesthetic is personal). Look for anterior segment anomaly, tunic vasculosa lentis and remnants of hyaloid artery.
8. Keep intensity of indirect ophthalmoscope light on low and look for plus disease. Use +20 diopter lens for comparing to standard photographs.
10. Use scleral depressor to screen entire periphery until ora going in each clock hour.
11. Draw retinal chart.
12. Fix time for next exam.
13. Explain disease status to neonatologist and parents.

Follow-up Examination schedule

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Zone 1</th>
<th>Zone 2 posterior border</th>
<th>Zone 2 – mid and anterior</th>
<th>Zone 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immature</td>
<td>1 week</td>
<td>1 week</td>
<td>2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Stage 1</td>
<td>1 week</td>
<td>1 week</td>
<td>2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Stage 1+</td>
<td>1 week</td>
<td>1 week</td>
<td>1 week</td>
<td>2nd opinion³</td>
</tr>
<tr>
<td>Stage 2</td>
<td>1 week</td>
<td>1 week</td>
<td>2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Stage 2+</td>
<td>1 week</td>
<td>1 week</td>
<td>1 week</td>
<td>2nd opinion</td>
</tr>
<tr>
<td>Stage 3</td>
<td>1 week</td>
<td>1 week</td>
<td>1 week</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Stage 3+</td>
<td>3 days</td>
<td>1 week</td>
<td>1 week</td>
<td>2nd opinion</td>
</tr>
</tbody>
</table>

The overall status of the eye will read either

I) Mature  II) Immature  III) ROP

II) Mature: Signifies that the vessels have now reached at our within one disc diameter of both nasal and temporal ora serrata. This child does not require further follow up.

II) Immature: signifies that though there is no ROP, yet the vasculature has not matured fully, Immature vasculature is defined as vessels which are short of 1 dd of the nasal or temporal ora. Thus they could terminate in zones I/II/III and are designated accordingly immature I,II or III. A potential for developing ROP exists till the vessels are still immature. Therefore an exact record of the zone in which the tip of these immature vessels have reached must be kept in seqal examinations. They are then followed up till maturity as given in the screening protocol.

III) ROP: Presence of ROP is to be recorded meticulously in relation to:

a. Zone and stage of ROP in each clock hour.
b. Presence or absence of plus disease.

Most of the proformas for recording ROP (as given in the appendices) are self explanatory and would help the examiner record all relevant findings.
For recording of findings in an universally acceptable way, we recommend the use of graphic representations and standard notations of the STOP-ROP study which have been provided at the end of the chapter. These help to depict various stages of ROP along with ancillary findings.

**Selection of Eyes for Ablative Management**

*How does Peripheral Retinal Ablation helps in Treating ROP?*

Vasoformative factors are produced anterior to the vascular area, which causes neovascularization at junction of avascular and vascular area. The larger the avascular area, more is the production of vasoformative factors and more is the neovascularization. So the aim is to eliminate the source of vasoproliferative response i.e., avascular area by ablation.

**Cryo ROP Study**

The most detailed and comprehensive data regarding the safety and efficacy of ROP was made available by the multicenter trial of Cryotherapy

<table>
<thead>
<tr>
<th></th>
<th>Cryotherapy</th>
<th>Laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy in treating ROP</td>
<td>Well Proven</td>
<td>Now well Proven</td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Availability &amp; Usage</td>
<td>Common &amp; Easy</td>
<td>Less commonly available in developing word</td>
</tr>
<tr>
<td><strong>During Procedure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Need of Anesthesia/</td>
<td>High</td>
<td>Easy under local/sedation on</td>
</tr>
<tr>
<td>Ease of reaching Posteriorly</td>
<td>Difficult in zone I &amp; Posterior</td>
<td>Easy zone II</td>
</tr>
<tr>
<td>In small pupil/Tunica vasculosa lentis Cataract/iris damage during procedure</td>
<td>Easy/None</td>
<td>Difficult/Possible</td>
</tr>
<tr>
<td>Post operative swelling of lids &amp; chemosis</td>
<td>+++</td>
<td>—</td>
</tr>
<tr>
<td>Exudative detachment</td>
<td>Possible with heavy treatment</td>
<td>Rare</td>
</tr>
<tr>
<td>Treatment</td>
<td>Diffuse shorter</td>
<td>More precise, takes longer time</td>
</tr>
</tbody>
</table>
for Retinopathy of Prematurity. This study was carried out in 23 centers across USA.

We find that the CRYO ROP results indicated an unfavorable outcome in 25.7% of the eyes that received cryotherapy compared with 47.4% of the control eyes. Though this data signifies a definite advantage of treatment over no treatment but the rate of 25% blindness is still very high.

Checklist for Cryotherapy

1. Obtain informed consent from the parents
2. Inform Neonatologist and pediatric anesthetist well in advance
3. Neonatal intensive care unit (NICU) nurse informed to:
   - Keep infant fasting for 4-6 hours before procedure
   - I.V. drip to be installed
   - Admit outpatient infants
   - Keep ventilators and monitors in readiness
   - Dilatation should be complete half an hour before the procedure time.
4. ROP fundus drawings are put up at a convenient place where surgeon can visualize them easily during the procedure.
5. Check the cryo trolley
   - Cylinder of gas is full (800-1000 psi)
   - Probe frosts and defrosts quickly
   - Probe size and shaft thin and curved
   - Probe shaft covered if not a special tip freeze probe only
   - Speculum, desmarres retractor, lid sutures, kelgie swab or a shoket depressor, serrated forceps scissors, needle holder, sterilized drape and cleaning material and 6-0 vicryl sutures in case need to convert to open cryo
   - Vial of topical anesthetic, saline and antibiotic drops and ointment
   - If chances of shifting to operation room then get that room preheated
6. Even with general Anesthesia, always supplement with topical drops
7. Recheck the charts previously drawn.
   - Note the distance of ridge from limbus in 4 quadrants
   - Note the time taken for first few cryo spots
   - Cryo the easily accessible areas first
   - Do cryo in the avascular area covering entire region from anterior of ridge to ora for the clock hours where the ridge exists.
   - Then cryo more posteriorly in areas with greater neovascularization
• In-between 2 cryo spots always irrigate eye copiously
• If retina is not visualized due to corneal edema then try only probe to lift lid or try desmarres/lid sutures
• If probe not reaching the areas near the ridge then do a peritomy
• Always let the probe defrost completely
• Examine the eye after 48 to 72 hours

How to do cryotherapy
Cryotherapy spots are applied in a contiguous manner anterior to the ridge and then to the entire avascular retina with the end point as a creamy white intensity spot and an. average number 21 spots ranging from 15 to 30.

Photocoagulation Treatment for Retinopathy of Prematurity
Photocoagulation has largely supplanted cryoablation established as standard treatment by the CRYO-ROP trial.16,17 The following are necessary special personnel and equipment when performing photocoagulation:
1) The Surgeon.
2) The neonatologist or anesthesiologists.
3) An assistant. This can be a fellow, resident, or nurse, if another investigator is not available.
4) Sterile equipment including lid speculum (i.e., Sauer, Alfonzo, Cook), scleral depressor (i.e., Storz SP725466-2), Calgi swabs, cotton swabs, balanced salt solution or saline drops, proparacaine eyedrops.
5) Binocular indirect ophthalmoscope with 28 or 30 and 20 diopter lenses.
6) Monitoring equipment.
7) Photocoagulation unit and safety goggles.

Before beginning treatment the operating surgeon must examine both fundi to confirm the presence of criteria for treatment and rule out exclusionary indications which may have developed since the previous examination.

Diode laser with an indirect ophthalmoscopic delivery system (Nidek DC 3000, Gamagori, Japan) is used to deliver an average number of 1500-1800 spots of 100m size placed one-half burn width apart and the end point for laser burns is a grade II gray burn, and is applied to the entire avascular retina, up to the ora serrata, avoiding the mesenchymal ridge.

Surgery for Retinal Detachment
The surgical options for treatment of eyes that develop partial retinal detachment (stage 4) and total retinal detachment (stage 5) include scleral buckle, combined lensectomy and vitrectomy, vitrectomy with lens conservation, and observation. No single approach can be applied to all patients.

Retinopathy of Prematurity CME Series 15
Each procedure has distinct advantages and disadvantages.

Since in general the retina surgeon’s goal seems to be simply focused on retinal reattachment, it is worth stating that the goal for the treatment of ROP retinal detachments is maximizing both the likelihood and quality of vision for each patient. Since complete attachment may come at a very high risk of surgical complications the analysis of surgical risks and benefits with this objective is different from the analysis that is directed towards maximizing retinal reattachment. Moreover, this goal may result in a different recommendation for each eye. Generally, the surgeon performs surgery either to achieve the minimum visual goal, ambulatory vision, or the maximum objective, macular vision.

Scleral buckling is done for progressive stage IV A and stage IVB. Vitreoretinal surgery is reserved for cases that further progress to stage IV a and stage V. All these infants are operated under general anesthesia. In cases planned for scleral buckling, conjunctival peritomy and anchoring of all the four recti by sutures is done. A 2.5 mm encircling band is passed underneath these four recti with one anchoring mattress suture (4-0 ethibond) in all quadrants. The final knot is tied in the temporal quadrant so that it is easy to remove after 3-6 months depending upon retinal reattachment period in each case. In cases planned for closed vitrectomy, a limited conjunctival peritomy is done. The infusion cannula is put within 1-1.5 mm from the limbus. Standard three-port vitrectomy is performed to achieve pars ciliaris entry to avoid subretinal entry of instruments. Although it is difficult to
access the periphery with lens in situ, associated lensectomy enables approach to the periphery satisfactorily. Lenscortexy is performed via the pars plana route with enlargement of the pupillary aperture. This is also necessary to avoid future closure of pupillary area due to reproliferation of membranes. A cleavage plane is obtained in the retrolental membrane tissue using two bent needles in a cruciate fashion. These membranes are then dissected with pediatric curved scissors from the center to the periphery with minimal traction on the retina. An effort is made to relieve traction as much as possible and settle the posterior pole of the retina as an end point. The vitrectomy probe removes the very peripheral membranes after extending the membrane flaps to the periphery. Viscoelastic materials like HPMC 2% is used in some cases to facilitate in the dissection and separation of the membranes. Although it is possible in the early or open funnel cases to achieve a satisfactory operative result, those with closed funnel are difficult to settle and surgery may have to be abandoned after a considerable effort. Coaxial illumination is used for funnel dissection. No attempt is made to drain the subretinal fluid. Associated abnormalities like conical opacities, shallow anterior chamber, posterior synechiae with/without closure pupillae, microcornea, hypotony are observed in many cases and contribute to the difficulty in surgery.

Surgical Results in Advanced Stage of ROP

Anatomical success in ROP surgery is defined as a successful attachment of the posterior pole. In an ongoing series, we have observed surgical success rates as defined by an attached posterior pole after surgery in 40% (16/40) eyes. Gopal L observed an anatomical success rate (defined as attached posterior pole) in 22.9% cases with 10.4% with total reattachment and 12.5% with posterior pole reattachment with better results in cases of open funnel as compared to closed funnel. They identified indicators of poor postoperative visual prognosis as late disease identification, lack of prior treatment in the form of cryo or laser and narrow-narrow configuration of the RD. Zilis JD et al. achieved macular attachment in 9/14 (64%) eyes with stage 4 and in stage 5 eyes, partial posterior attachment was obtained in 38/121 (31%) eyes and complete posterior attachment in 11 eyes (9%). The funnel type, which was wide anteriorly and posteriorly, had the best anatomic (63%) and visual (19%) success, Choi WC reported anatomical success in 11 eyes (29.0%) and open-funnel type showed better results than closed-funnel type (44.4% compared to 15.0%).

In cases of advanced ROP, surgery is essential but surgical results are disappointing. With the increasing awareness about ROP, improved neonatal setups, development of modern surgical techniques and early screening and ROP detection programs, the outlook for a child suffering from advanced ROP maybe brighter.
Differential Diagnosis of ROP

Differential Diagnosis

<table>
<thead>
<tr>
<th>Bilateral</th>
<th>Unilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinoblastoma</td>
<td>(PHPV) Persistent Hyperplastic</td>
</tr>
<tr>
<td>Retinal dysplasia</td>
<td>Primary Vitreous</td>
</tr>
<tr>
<td>Norrie’s disease</td>
<td>Coats’ disease</td>
</tr>
<tr>
<td>Walker Warburg syndrome</td>
<td>Retinal vascular anomalies</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>Parasitic endophthalmitis</td>
</tr>
<tr>
<td>Fundus coloboma</td>
<td>Prenatal infantile trauma</td>
</tr>
<tr>
<td>X-linked retinoschisis</td>
<td>Trauma (child abuse syndromes)</td>
</tr>
<tr>
<td>Falciform folds</td>
<td></td>
</tr>
<tr>
<td>Incontinentia pigmenti</td>
<td></td>
</tr>
<tr>
<td>Intrauterine catastrophes</td>
<td></td>
</tr>
<tr>
<td>Anterior encephaloceles in Asians</td>
<td></td>
</tr>
<tr>
<td>Cataracts</td>
<td></td>
</tr>
</tbody>
</table>

Stages 1 to 3

In stages, 1, 2, and 3 the principal condition to be considered in the differential diagnosis is familial exudative vitreoretinopathy. Indeed, in older children it is impossible to make the correct diagnosis without a careful family history.

Familial exudative vitreoretinopathy is an autosomal dominant disease, which, in its acute form, is characterized by peripheral areas of avascularity in the temporal retina. The neovascularization that is associated with the disease is almost indistinguishable from that seen in acute ROP. The changes in familial exudative vitreoretinopathy may progress, as in ROP, to dragging of the retina temporally, subretinal exudation, cicatization, and retinal detachment. The severe changes are usually asymmetric and generally detected anywhere from birth to 10 years of age. Asymptomatic affected older family members often exhibit only avascularity of the peripheral temporal retina. In contrast to its usual course in ROP, neovascular growth may occur several years after birth in familial exudative vitreoretinopathy.

A history of prematurity with a negative family history helps to rule out the diagnosis of familial exudative vitreoretinopathy.

We have noted that atypical cases of Coats’ disease, Eales disease, and sometimes retinoschisis will occasionally resemble ROP. The absence of the history of prematurity usually eliminates these cases from consideration as ROP.
Stages 4 and 5 ROP
Those conditions associated with leukocoria, most importantly retinoblastoma, must be differentiated from the advanced stages of ROP. Other conditions include persistent hyperplastic vitreous, congenital cataracts, and Norrie’s disease.

Retinoblastoma

History
In general, patients with retinoblastoma have a history of term birth, whereas ROP is virtually always associated with prematurity. The exceptions of retinoblastoma occurring in a premature infant and of ROP occurring in a term or near-term infant are extremely rare.

Family history
Another important clue in the differential diagnosis is the positive family history of retinoblastoma in approximately one third to one fourth of the cases. The family history for ROP is negative unless there have been siblings or other family members with a history of prematurity.

Clinical features
Retinoblastoma is usually more advanced in one eye, in contrast to ROP, which is usually bilateral and fairly symmetric. However, the examiner should recognize that the stage of retinal detachment in ROP can sometimes be asymmetric, and retinoblastoma may be advanced in both eyes at diagnosis. The small retinoblastoma which presents as a localized white nodule is not a problem in differential diagnosis. Large retinoblastomas with tumor in the vitreous may require further study.

Ultrasonography
Ultrasonography examinations can be helpful in differentiating the mass or tumefaction of a large retinoblastoma from the complex retinal detachment with vitreoretinal membranes in advanced ROP. Retinoblastomas are frequently posterior mass lesions and often demonstrate calcium. In ROP, common examination findings are multiple echoes and complex ultrasound patterns that are usually located just behind the lens or in the retinal periphery.

Computed tomographic scans
Computed tomographic (CT) scans in retinoblastoma will show a tumor mass, as opposed to retina and membranes. Calcium is frequently present.

Persistent hyperplastic primary vitreous
Persistent hyperplastic vitreous is a congenital anomaly, usually unilateral and occurring in the term infant. Microcornea is usually present and
the ciliary processes appear to be dragged by traction toward the center of the pupil. The membrane behind the lens in hyperplastic primary vitreous has a grayish white color, but usually no retinal vessels are visible. A history of prematurity will reduce the likelihood of this diagnosis.

**Congenital cataracts**

The diagnosis of congenital cataracts is easily made by slit-lamp examination. When the cataracts are not dense, some areas of normal retina can be visualized posteriorly and peripherally.

**Norrie’s disease**

Norrie’s disease is a congenital retinal dysplasia that can exactly mimic the clinical appearance of advanced ROP. It is an X-linked recessive syndrome. There is an absence of prematurity, which may be the crucial factor in making a distinction. An examination at 4 to 6 weeks of age would be a great aid in making the differential diagnosis. Patients with Norrie’s disease demonstrate leukocoria considerably earlier than those with ROP. Norrie’s disease is generally associated with, deafness and mental retardation.

**Key message—Neonatologists View**

**Prevention of ROP**

1. **Definite and well accepted**
   1. Prematurity / Gestational Age / Birth Weight
   2. Oxygen Supplementation

2. **Associated Factors:**
   1. Light
   2. Vitamin E Deficiency
   3. Apnea with bag / mask ventilation
   4. Methyl xanthine administration
   5. Respiratory distress syndrome
   6. Asphyxia / Hypoxia
   7. Shock
   8. Hypercarbia / Hypocarbia
   9. Acidosis / Alkalosis
   10. Sepsis
   11. Patent ductus arteriosus / Indomethacin
   12. Blood transfusions / Exchange transfusions
   13. Intraventricular hemorrhage
   14. Chronic in utero hypoxia

   **Light:** Retinal damage because of exposure to bright light has been demonstrated in animal studies and this could be exaggerated by elevated
body temperature and hyperoxia. Glass et al reported a lower incidence of ROP in infants protected from high levels of light but no statistically significant difference in the prevalence of severe ROP, but Ackerman et al reported no difference in shielded and light exposed groups of babies less than 1500 gms. Lack of convincing evidence on the association between light exposure and ROP has failed to resolve the issue, however there is evidence that reduced ambient light may improve the neurobehavioural developmental outcome of these infants. In our nursery we routinely shield the baby’s isolette and diminish the ambient light.

Bauer implicated hypercarbia because of its ability to inhibit the vasospasm induced by oxygen but a subsequent study did not confirm this finding. Interestingly hypocarbia and alkalosis have also been associated with ROP, possibly by the resultant vasoconstriction of cerebral vasculature causing retinal ischemia. Hypercarbia, acidosis and blood transfusions can also increase the release of oxygen from hemoglobin by inducing the Bohr effect resulting in a hyperoxic environment for the retina. Gunn et al implicated sepsis in the causation of ROP and suggested a role for endotoxin on the retinal tissue. The presence of patent ductus arteriosus may result in a hyperoxic retina, with post ductal oxygen monitoring. Yeh compared the effect of indomethacin treatment of a symptomatic patent ductus arteriosus on ROP with placebo and found no difference in the incidence of severe ROP.

Vitamin E: Vitamin E is an important antioxidant, which mops up oxygen free radicals, reduce auto-oxidation resulting from ischemic injury and also prevents gap junction formation in the spindle cells. It is present in low concentrations in the premature infants and has been shown to have a protective effect on oxygen induced retinopathy. Owens and Owens reported the reduction in the risk of ROP with vitamin-E supplementation as early as 1949. There have been numerous trials involving vitamin-E supplementation and results have failed to show any significant beneficial effect. In addition concerns regarding Necrotizing enterocolitis (NEC) and an increased incidence of sepsis have been raised. To date there is, no evidence that vitamin-C supplementation reduces the overall incidence of ROP.

Prenatal steroids reduce the incidence and severity of respiratory distress syndrome and other morbidities such as patent ductus arteriosus, intraventricular hemorrhage and necrotizing enterocolitis, hence could affect the incidence of ROP indirectly.

B. All NICU providing care to <1500g, <32wk, gestation babies must have protocol for ROP screening.

C. Often introduction of screening programme results in introduction of rational management practices for VLBW babies.
D. Practices which result in lower incidence and less severity of ROP include
  - Maintain of p02 50-70 mm of Hg
  - Oxygen saturation 90-93% (alarm 88-95)
  - Periodic monitoring and documentation of oxygen flow, Fi02 (oxygen analyser), oxygen saturation (pulse oximeter) combined with arterial blood gas.
  - Judicious use of blood transfusion
  - Calibration of pulse oximeter, blender of ventilators.

E. Introduction of maintenance oral dose of vitamin E in a close 15-25 unit/ day is recommended

Prevention and management of ROP can’t be done by Neonatologist alone. Full cooperation of house staff and nurses in monitoring babies is required. The ophthalmologist need to be involved at right time for screening and management of ROP. Communication with parents is an integral part of management. They should be told about potential complications and explained the need for close follow up.

STOP-ROP STUDY (Supplemental therapeutic Oxygen for prethreshold ROP)

It concluded that use of supplemental oxygen at pulse oxymetry saturations of 96% to 99% did not cause additional progression of prethreshold ROP but also did not significantly reduce the number of infants requiring peripheral ablative surgery.

Supplemental oxygen increased the risk of adverse pulmonary events including pneumonia and exacerbations of chronic lung disease and the need for oxygen, diuretics and hospitalisation at 3 months corrected age.

The relative risk/benefit of supplemental 02 is to be weighed by the treating physician; they need not worry that supplementary oxygen could exacerbate the prethreshold disease.

Light ROP study

Light Reduction in ROP study showed no benefit to preterm infants from a reduction in light exposure from birth to postmenstrual age 32 weeks.

ETROP (Early Treatment of Retinopathy of Prematurity)

This project has been initiated to prove scientifically the benefit of treatment in ROP, earlier than as recommended by the CRYO-ROP Study.\textsuperscript{20,21} It was indeed the high failure rate in even the treatment group of the Cryo ROP study, which has resulted in initiation of such a study.

Results: Grating acuity results showed a reduction in unfavourable visual acuity outcomes with earlier treatment from 19.5% to 14.5 % (p=0.01) and unfavourable structural outcome were reduced from 15.6% to 9.1 % (p<0.00 1) at 9 months. Further analysis supported retinal ablative therapy
for eyes with *type 1 ROP* defined as zone 1 ROP, any stage ROP with plus disease; zone 1, stage 3 ROP without plus disease; or zone 2, stage 2 or 3 ROP with plus disease. The analysis supported a wait and watch approach to *type 2 ROP*, defined as zone I stage 1 or 2 ROP without plus disease or zone 2, stage 3 ROP without plus disease. These eyes should be considered for treatment only if they progress to type 1 or threshold ROP.

**Psychosocial factors**

Infants and children who are blind or visually impaired from ROP have unique developmental needs, often complicated by other health and medical problems. Their orientation to the world around them is different from that of sighted children. This factor can affect their development in all areas, including cognitive, motor, language, social, affective and exploratory learning. Natural curiosity must be encouraged and developed. A mediated environment in which parents and family members facilitate learning opportunities seems to be the optimal approach.

Having a baby with a visual impairment will have an immediate and lasting effect on the family. Coping strategies must be developed, often requiring support and services from professionals. Educational and medical service providers must recognize that the family is the most influential factor in the young child’s growth and development.

As parents acquire techniques and assume a growing responsibility for effective parenting and teaching strategies in relation to the needs of their disabled child, they can enhance the cognitive, social, physical and affective development of their child and become “empowered” in their own eyes.

**Medicolegal issues**

Although claims against hospitals, neonatologists or ophthalmologists for alleged mismanagement of ROP are relatively infrequent, indemnity payments for judgments in such cases may be very high because of the severity of the visual loss and the life expectancy of the young blind plaintiff. Malpractice exposure is a constant threat for physicians who examine preterm babies for ROP. A number of lawsuits pertaining to complaints related to ROP blindness are now pending in Indian courts. Unfortunately a large population of ophthalmologists and pediatricians still remain unaware of the importance of screening for ROP highlighting the importance of CME programs.

**Genetics in ROP**

ROP, Norrie’s disease, Familial exudative vitreoretinopathy and primary vitreoretinal dysplasia have very similar clinical manifestations. This led to the supposition that a common gene might predispose to this condition. Detection of such a gene can help in, prognostication as to which baby is at a high risk for developing severe ROP.
Norrie's disease gene (Norrin) was found to have mutations in severe ROP patients in a study from US. Of the 16 ROP cases, 4 cases had missense mutation in exon of the ND gene, 3 patients had R121W mutation (C to T transition at codon 121 of ND gene) and one had L108P mutation. In another study in Kuwaiti Arab population, PCR-RFLP technique was used to study the ND gene in ROP. The ND gene missense mutations -A105T and val6Oglu were not significantly associated with risk of severe ROP. Another report from same population found no significant association between mutation in exon 3 of ND gene, R121W mutation and L108P mutation in ROP patients & normal patients.

**ROP: Indian Scenario**

Childhood blindness is a curse more so if it occurs immediately after birth. It is important not only in terms of economic burden but its severe social implication, which is very long in terms of blind years. Among the preventable causes of blindness in children, which is 57%, Retinopathy of Prematurity (ROP) figures very high in the agenda. Since 22% of all blind children have retinal causes, ROP is amongst the first few in high and middle income group countries. Nevertheless occurrences of ROP in low income group has been largely unnoticed and attributable to a so called ‘first epidemic’ which resulted due to insufficient oxygen administration i.e. unmonitored oxygen levels in the absence of better life supporting systems. In the context of our country we are sitting on the summit of two volcanoes - one where all latest state of art health care is, available i.e. mainly in metropolis and the other where even minimal basic health care is unavailable. ROP is known to grow in both these conditions and therefore to have any estimate regarding

ROP will be an underestimate. Available figures for blinding and statistics are depressive and yet challenging varying from 2.3 % to 3.5 % of all premature children. Coming on to risk factors, low birth weight and low gestational age are the two important vectors which govern which child will develop ROP and which will not. In terms of birth weight, children less than 1500 gms have almost 20 to 50% chance of developing any stage of ROP and 7 to 16% chance of developing threshold ROP or blinding ROP. These figures are from three major centers in India i.e. Delhi, Bangalore and Chennai. A very low gestational age(<28 weeks) again compounds the risk of developing threshold ROP or blinding ROP of a very severe grade. Low incidence of ROP in India is basically due to (a) low or no survival rate of children < 1,200 gm in rural / semiurban settings (b) cases of IUGR presenting commonly in view of low nutrition and anaemia amongst Indian mothers, (c) unawareness amongst ophthalmologists & neonatologists and (d) lack of experience and infrastructure for ROP screening.

In our country clinical presentation is very late because of nonawareness amongst ophthalmologists as well as neonatologists. These
cases are often missed and even if detected there are very few centers in our country where it can be tackled. In a tertiary care centre i.e. R.P. Centre at least 50 cases of stage IV and stage V ROP have been seen in the last two years. Out of these 50 cases, at least, 35 of them have been operated. I would prefer doing surgery rather than to abandon these cases, in view of preserving partial vision and providing home navigation.

An early and prompt management offers very high success rates in ROP. Not only is blindness prevented but the structural and functional outcome is excellent. Trend towards treating ROP cases even before threshold have shown zero unfavourable outcome, not even disc drag or macular drag. The argument that early treatment of ROP carries the risk of over treatment is untenable in view of its greater social and visual after effects when the child grows and attends school. As regards modality of treatment, laser emerges as the treatment of choice today; nevertheless it does not take away the right of performing cryotherapy especially in a country like ours due to economic reasons. Intervention programs in India are limited to very few tertiary care centers. Recent initiative by the Ministry of Health, Govt. of India has helped initiating ophthalmologists and neonatologists in ROP training program/workshop.

References
ROP Screening Form
Dr. R.P. Centre, A.I.I.M.S, New Delhi India

Mother’s Name __________________________ Neonatal No. __________________________
Address __________________________ Date of Birth __________ __________
Phone No. __________________________ Birth Weight ________ Grams
Sex M F Gestational Age ________ Weeks
Date of Examination __________ __________ Post Conceptional Age at Exams
(G.A.+Post Natal Age) ________ Wks

RIGHT EYE
Immature ________ Zone 2 3
Worst Stage of ROP 1 2 3 4 5
Clock Hours Involved 1 2 3 4 5 6 7 8 9 10 11 12
Plus Disease Yes No.
Regressing ROP Stage 1 2 3 Th 4a 4b
Mature Yes No.
Follow up After 1 2 3 4 5 6 Weeks

LEFT EYE
Immature ________ Zone 1 2 3
Worst Stage of ROP 1 2 3 4 5
Clock Hours Involved 1 2 3 4 5 6 7 8 9 10 11 12
Plus Disease Yes No.
Regressing ROP Stage 1 2 3 Th 4a 4b
Mature Yes No.
Date on __________ __________

Lost to Follow up

Comments: ____________________________________________

Examined by: Dr. __________________________

Diagram of retinal zones and disc locations.
Follow Up Sheet

Mother’s Name ____________________ Follow up No. ____________________
Age of Examination ________ Weeks
Post Conceptional Age at Exams (G.A.+Post Natal Age) ________ Wks
Date of Examination ________ / ________ / ________

RIGHT EYE
Immature ____________________
Zone ____________________
Worst Stage of ROP

1 2 3 4 5
Clock Hours Involved

1 2 3 4 5 6 7 8 9 10 11 12
Plus Disease ____________________ Yes No.
Regressing ROP Stage

1 2 3 Th 4a 4b
Mature ____________________ Yes No.
Follow up After ________ 1 2 3 4 5 6 Weeks
Lost to Follow up ____________________

LEFT EYE
Immature ____________________
Zone ____________________
Worst Stage of ROP

1 2 3 4 5
Clock Hours Involved

1 2 3 4 5 6 7 8 9 10 11 12
Plus Disease ____________________ Yes No.
Regressing ROP Stage

1 2 3 Th 4a 4b
Mature ____________________ Yes No.
Date on ________ 1 2 3 4 5 6 ________

Comments:
Examined by: Dr. ____________________

[Diagram of retinal zones and disc]
<table>
<thead>
<tr>
<th>Risk Factors During First 6 Weeks of Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apgar at 1 minute: Unknown=00 [ ]</td>
</tr>
<tr>
<td>RDS:</td>
</tr>
<tr>
<td>Yes [1]</td>
</tr>
<tr>
<td>Apgne A tacks:</td>
</tr>
<tr>
<td>Yes [1]</td>
</tr>
<tr>
<td>&gt; 20 seconds (or any duration)</td>
</tr>
<tr>
<td>Bradycardia:</td>
</tr>
<tr>
<td>Blood Components:</td>
</tr>
<tr>
<td>Yes [1]</td>
</tr>
<tr>
<td>No. [2]</td>
</tr>
<tr>
<td>Sepsis:</td>
</tr>
<tr>
<td>Yes [1]</td>
</tr>
<tr>
<td>Oxygen given:</td>
</tr>
<tr>
<td>Yes [1]</td>
</tr>
<tr>
<td>No. [2]</td>
</tr>
<tr>
<td>Oxygen admin</td>
</tr>
<tr>
<td>Ventilator [ ]</td>
</tr>
<tr>
<td>CPAP [ ]</td>
</tr>
<tr>
<td>Nasal Catheter [ ]</td>
</tr>
<tr>
<td>Hood [ ]</td>
</tr>
<tr>
<td>Highest pO2 recorded (mmHg) [ ]</td>
</tr>
<tr>
<td>Higest SO2 recorded (%) [ ]</td>
</tr>
<tr>
<td>pH [ ]</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Comments