In The Name of God

دکتر بهزاد برکتین

فوق تخصص نوزادان

دانشیار و عضو هیات علمی دانشگاه علوم پزشکی اصفهان

رتینوپاتی نارسی بیماری عروق شبکیه در نوزادان نارس است و می تواند به طیف وسیعی از اختلالات بینایی از نقائص جزئی قابل اصلاح در حدت بینائی تا جدا شدن شبکیه و کوری منجر گردد.

این بیماری در اغلب موارد قابل پیشگیری و در صورت تشخیص به موقع قابل درمان است و در صورت عدم تشخیص به موقع بیماری پیشرونده بوده و به سرعت منجر به نابینایی می گردد .

اقدامات درمانی در مراحل اولیه بیماری اثر بخش تر است. در مراحل انتهایی بیماری درمان بسیار مشکل و در بعضی موارد غیر ممکن می باشد و در درمان های موجود برای مراحل پیشرفته بیماری به هیچ عنوان بینایی قابل قبولی را به کودک برنمی گرداند.

با افزایش چشمگیر میزان بقای نوزادان نارس که در چهل سال اخیر از حدود 5% به بیش از 55 % برای نوزادان با وزن کمتر از 1000 گرم افزایش یافته است، تعداد نوزادان مبتلا به رتینوپاتی نارسی افزایش خواهد یافت مگر آنکه در زمینه پیشگیری از بیماری اقدامات جدی صورت گیرد.

شیوع و شدت رتینوپاتی نارسی با کاهش سن حاملگی و وزن هنگام تولد نوزاد افزایش می یابد.

حدود 30 تا 60 درصد نوزادان با وزن تولد کمتر از 1500گرم دچار درجاتی از رتینوپاتی نارسی می شوند و حدود 10 % به درجات شدید پیشرفت می کنند. نوزادان با وزن کمتر از 750 گرم ممکن است تا 90 درصد درجاتی از بیماری را نشان می دهند.

با توجه به گسترش بخش های مراقبت ویژه نوزادان لزوم تدوین برنامه مدون غربالگری رتینوپاتی نارسی واضح و مسلم است.

در حال حاضر بیش از 100 بخش مراقبت ویژه فعال در سطو کشور وجود دارد .

مطالعه منطقه ای در استان های مختلف کشور بین سال های 1380تا 1390 در خصوص شیوع رتینوپاتی نارسی صورت گرفته ا ست که بر پایه آن شیوع کشوری 27.48 درصد است.

First described in the early 1940s, Retro Lental Fibroplasia (RLF), as it was first named, almost disappeared between 1954 and 1970, when oxygen use for preterms was severely restrictedbut it returned in a second epidemic in the 1970s to plague neonatal intensive care units (NICUs) as one of the major causes of disability in surviving infants with extremely low gestation.

Effective interventions have reduced its toll of vision loss in developed countries, but worldwide, ROP now appears as a third epidemic in developing countries as they begin to provide neonatal intensive care.

About 400-600 children per year may be blinded by ROP, representing 20% of blindness in preschool children.

Pathogenesis:

Normal vascularization :

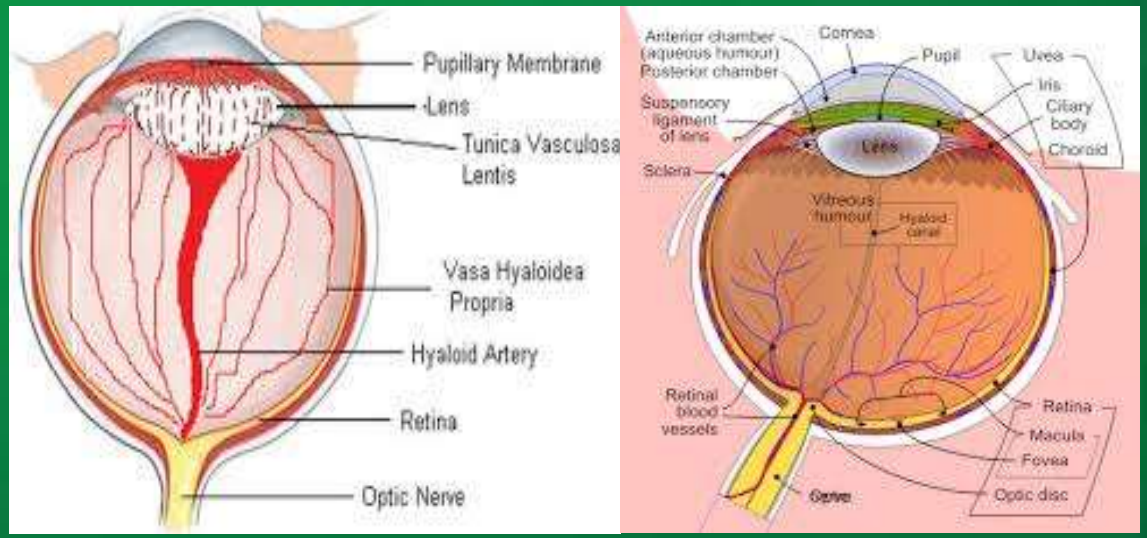
The sequence of vascularization of the eye is important in understanding the pathogenesis of ROP.

No blood vessels are present in the retina before approximately 16 weeks' gestation.

From approximately the sixth week, the anterior segment of the eye receives its vascular supply from the hyaloid artery.

This artery originates from the optic nerve, passes through the vitreous, and supplies vessels to both surfaces of the lens and iris.

These vessels usually are resorbed by 34 weeks of gestation.

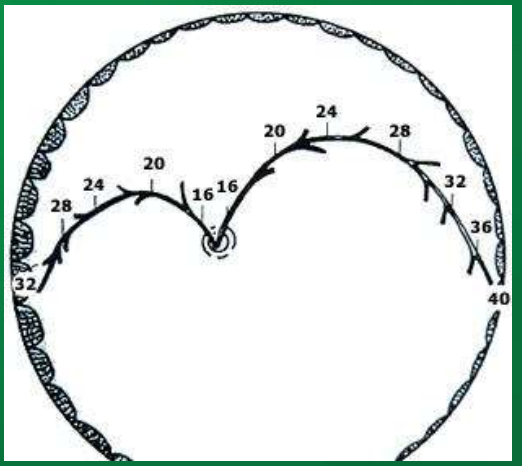


Retinal vascularization begins at 15 to 18 weeks' gestation.

Retinal blood vessels extend out from the optic disc (where the optic nerve enters the eye) and grow peripherally.

Vascularization in the nasal retina is complete at approximately 36 weeks.

Vascular development usually is complete in the temporal retina by 40 weeks, although maturation may be delayed until 48 to 52 weeks' postmenstrual age in premature infants.

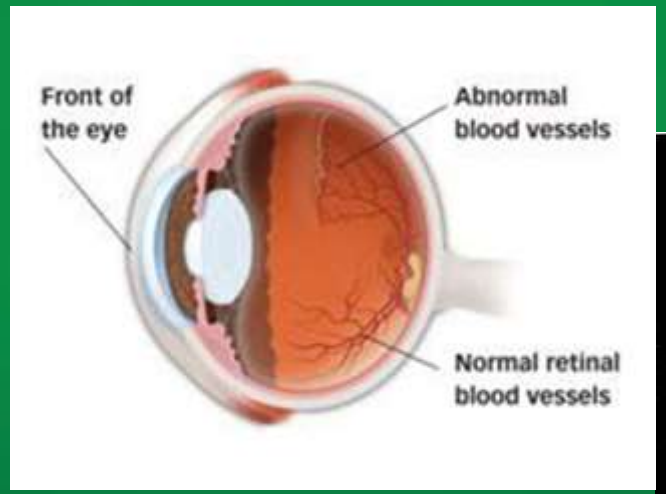


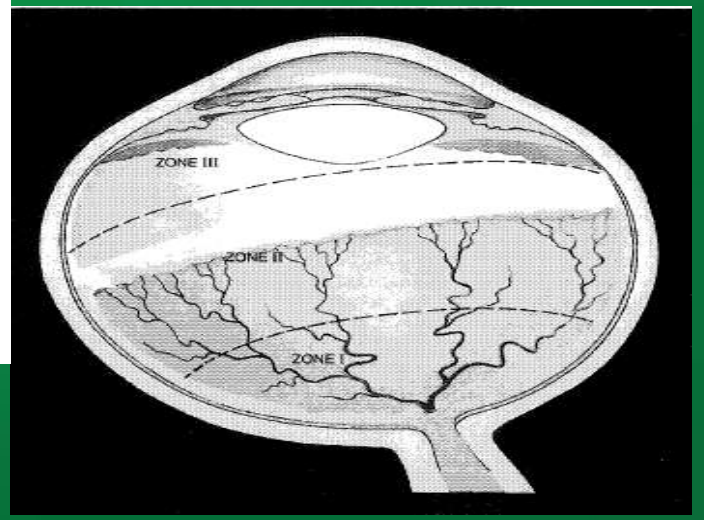
Vascularization in ROP :

ROP begins to develop between 32 and 34 weeks 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 *vasoobliteration* and *non-vascularization* of some areas of the anterior retina.

2.The subsequent hypoxia causes a second chronic phase by producing of VEGF (vascular endothelial growth factor) , characterized by the *proliferation of vascular (neo vascularization) and glial cells , arteriovenous shunt formation,* occasionally leading to involution or permanent cicatricial changes and visual impairment.





Insulin-like growth factor-1 (IGF-1) supports normal retinal vascular growth.

The possible role of IGF-1 in ROP has been evaluated in several series of preterm infants who had serial blood samples and retinal examinations.

In each of these series, decreased serum concentrations of IGF-1 were associated with the development of ROP.

Risk factor:

Low gestational age and low birth weight have always been the strongest predictors of ROP.

After controlling for these parameters in regression analyses, the strongest additional risk factors for severe stages of ROP are prolonged administration of oxygen, duration of mechanical ventilation, and other indicators of a complicated hospital course, such as hypotension (e.g., hypovolemic shock, pneumothorax, severe intraventricular hemorrhage, septic shock), number of transfusions, multiple birth, nonblack race for the more severe stages of ROP, and small for gestational age status at birth.

Other Risk factors of ROP in various studies include vitamin A deficiency, inositol deficiency, indomethacin therapy for prevention of patent ductus arteriosus, vitamin E deficiency, exposure to light, intravenous lipid administration, apneic episodes, elevated or depressed Paco2,Septicemia, bronchopulmonary dysplasia, systemic fungal infection, and early administration of erythropoietin for the treatment of anemia of prematurity.

None of these factors has been identified as a direct cause of ROP.

Classification:

A serious impediment to identification of disease is posed by an inability to communicate.

Such a critical foundation was lacking in ROP for many years. However, the International Classification of Retinopathy of Prematurity (IC-ROP) changed all that .

This system of consistently describing the salient clinical characteristics of acute ROP was rapidly adopted worldwide.

Additional terminology has also become generally accepted, usually arising from the large, NIH funded multicenter trials,

STOP-ROP (supplemental therapeutic oxygen for prethreshold ROP)

CRYO-ROP (cryotherapy for ROP)

LIGHT-ROP (light reduction in ROP)

ET-ROP (early treatment for ROP)

The system of applying the

severity (stages) and zones

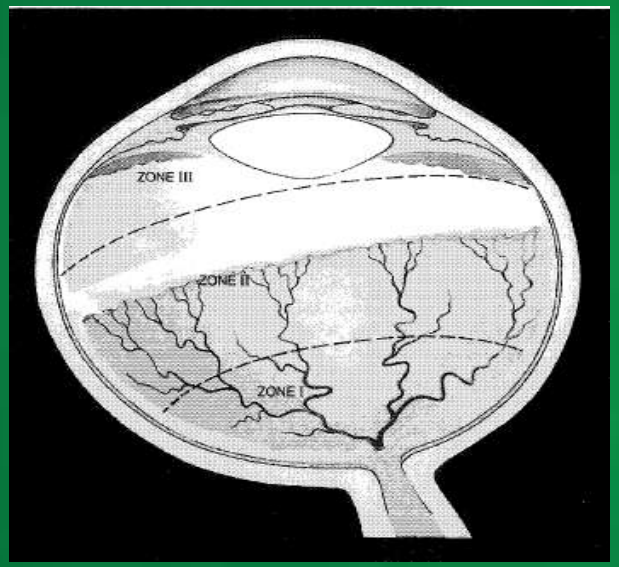
is to classify ROP according to the highest stage present in any part of the retina and the most posterior zone touched by disease in any part of the retina.

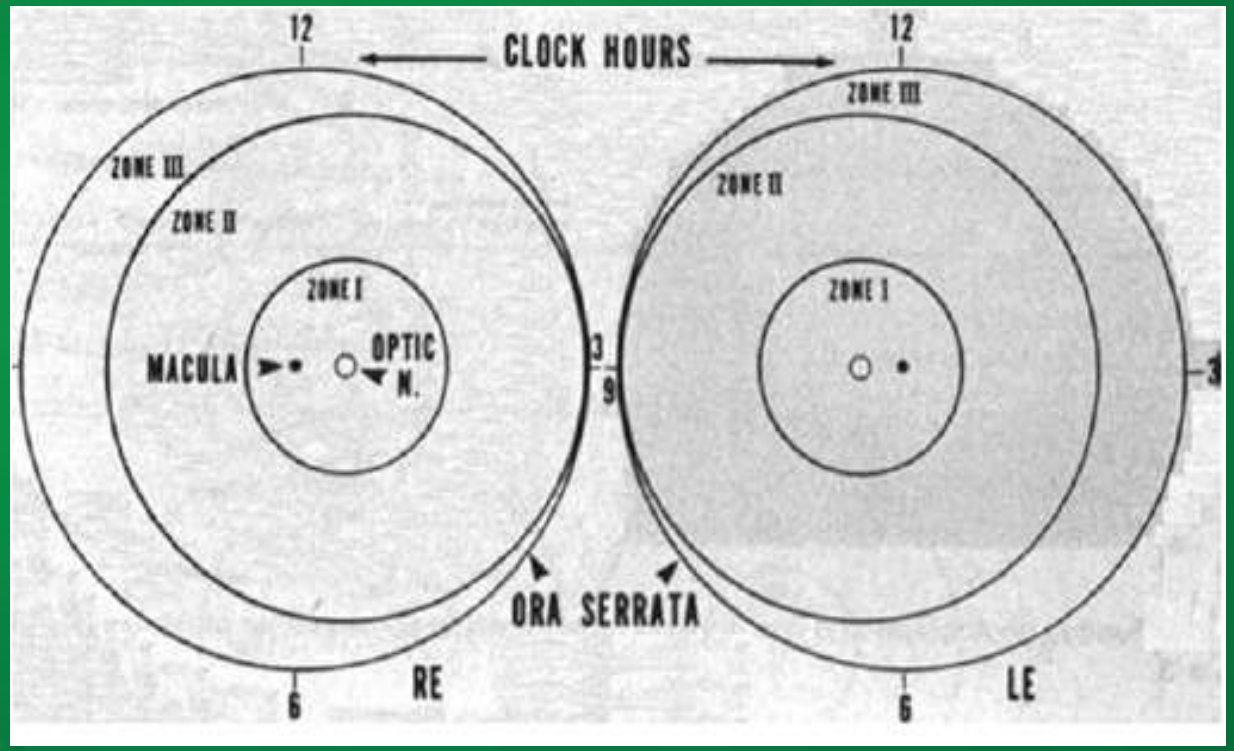
The ***zone (location)*** of disease is critical to the potential severity.

The retina was divided into concentric zones

Zone I	Concentric circle, centered on the optic nerve, with a radius of 2 times the distance from the center of the nerve to the center of the fovea
Zone II	Diagrammatically a concentric annular area arising from the outer border of zone I and ending at the ora nasally and just beyond the equator temporally
Zone III	A large temporal crescent arising from the outer border of zone II and terminating at the temporal ora serrata. (Fig. 4.17)

Schematic representation of the retinas divided into three zones, with the relevant anatomic landmarks. (printed from American Medical Association)





Dr B Barekatain

The ***severity*** of acute disease is classified in stages

As in previous classifications, the degree of vasculopathy at the vascular-avascular transition is divided into stages 1 through 5.

Stages 1 through 3 are increasing degrees of abnormal blood vessel growth (neovascularization) at this transition, with vessels actually leaving the retina and growing in the vitreous in stage 3.

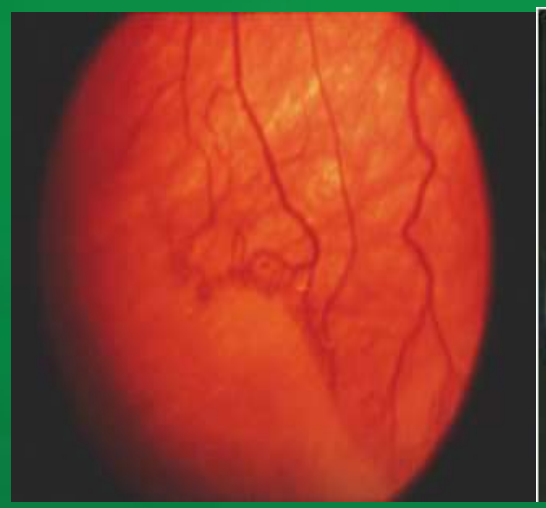
Stage 4 is partial retinal detachment, and stage 5 is complete retinal detachment, both of which carry a grim prognosis for normal vision.

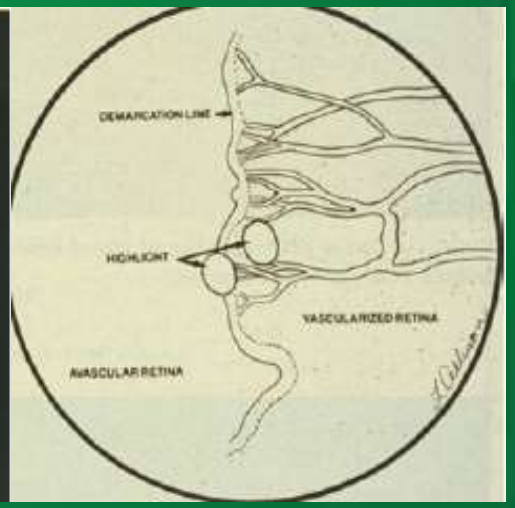
Table 4.1 Severity of acute ROP	
Stage 1	Line of demarcation (Figs. 4.1 and 4.2)
Stage 2	Ridge of elevated tissue (Figs. 4.3 and 4.4)
Stage 3	Extra retinal fibrovascular proliferation (neovascularization) (Figs. 4.5–4.11)
Stage 4	Partial retinal detachment (Figs. 4.12–4.14)
4a	Macula spared (Figs. 4.12–4.14)
4b	Macula involved
Stage 5	Total retinal detachment (Figs. 4.15 and 4.16)
Open	Open funnel R.D (Fig. 4.15)
Closed	Closed funnel R.D (Fig. 4.16)

Stage 1: Demarcation Line

The demarcation line is a flat white line within the plane of the retina that clearly delineates the vascularized posterior retina from the avascular anterior portion.

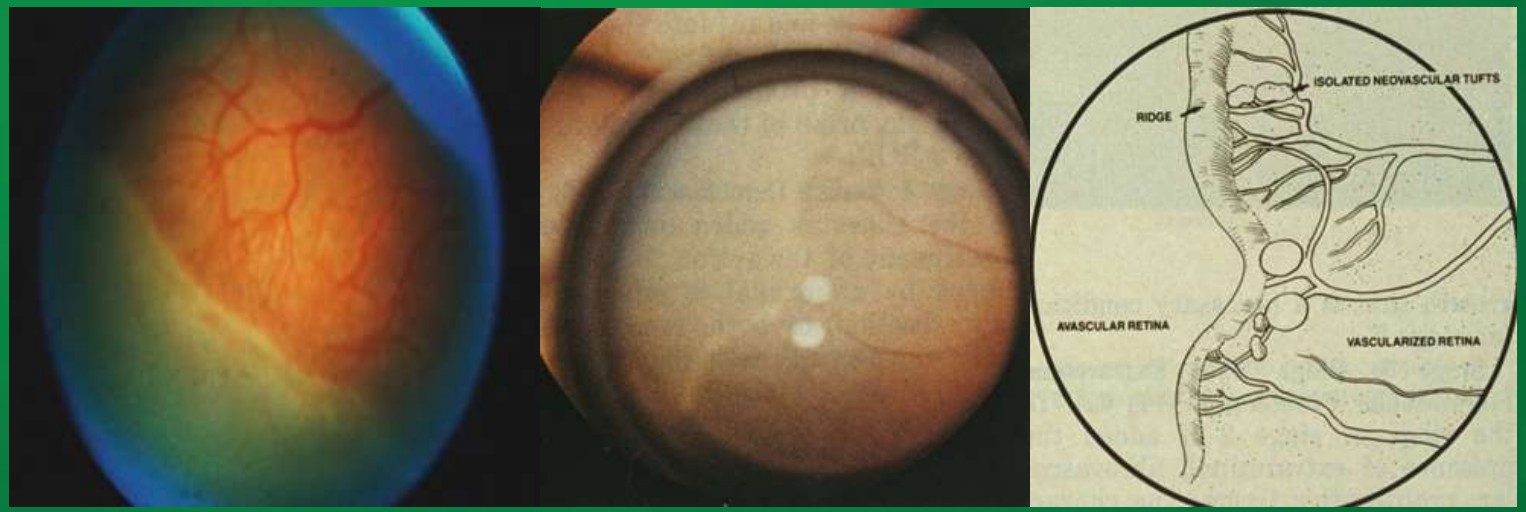
Abnormal branching or arcading of vessels is recognizable immediately posterior to the demarcation line.





Stage 2: Ridge

The ridge is an expanded demarcation line that has three dimensions because it has grown in height and width, rising above the plane of the retina. The color may be white to pink. Small tufts of new vessels may lie on the surface of the retina posterior to the ridge.



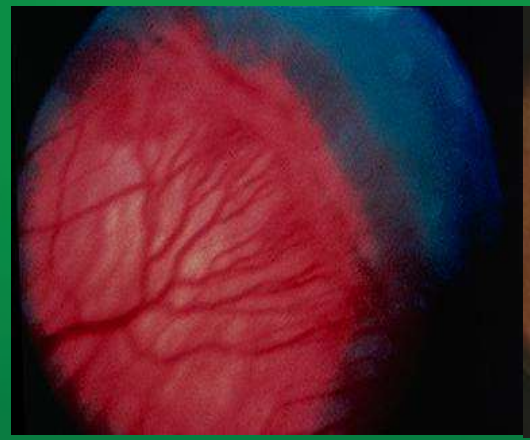
Stage 3: Ridge with Extraretinal Fibrovascular Proliferation

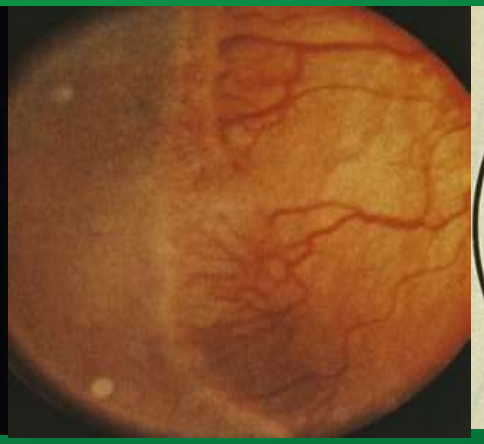
In addition to the structure of stage 2, extraretinal fibrovascular tissue is present. This tissue may

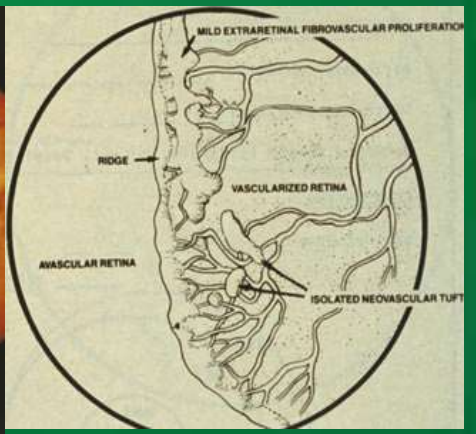
(1) be continuous with the posterior aspect of the ridge, causing a ragged appearance;

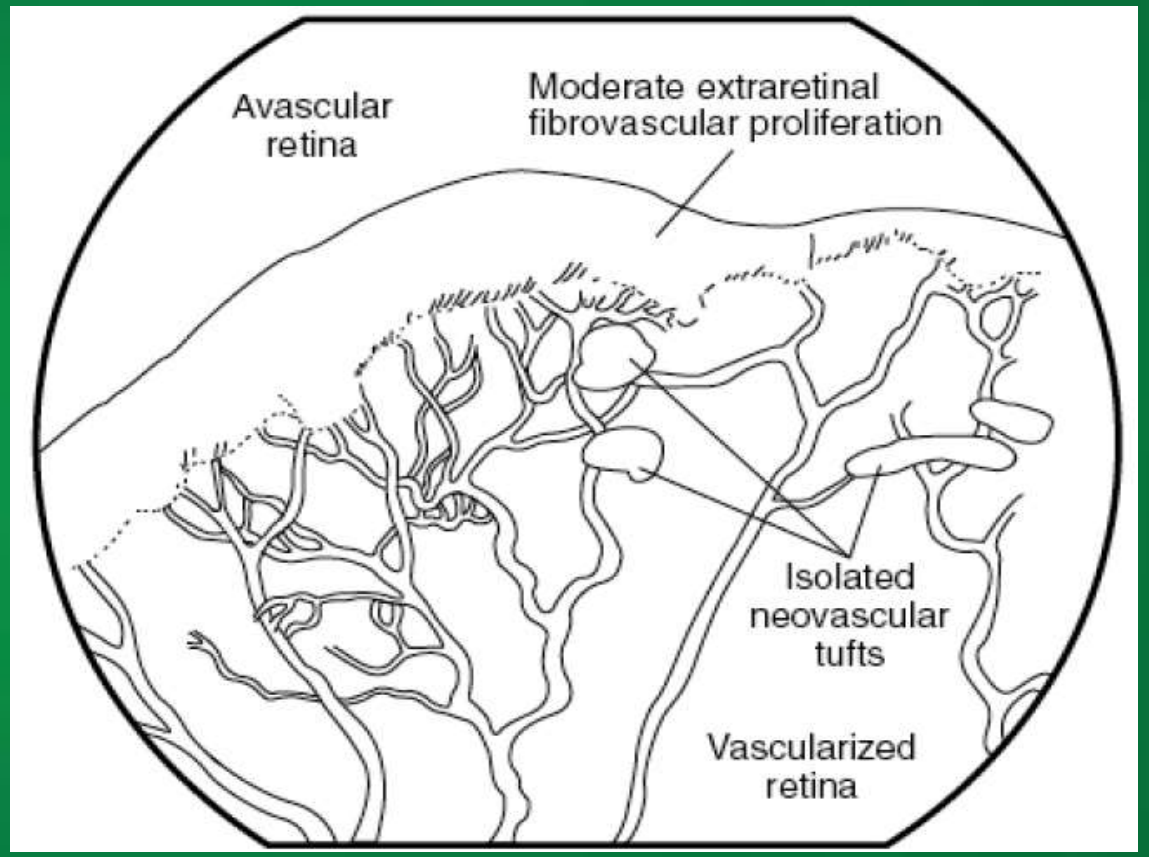
(2) be immediately posterior to the ridge but not connected to it; or

(3) extend into the vitreous perpendicular to the retinal plane

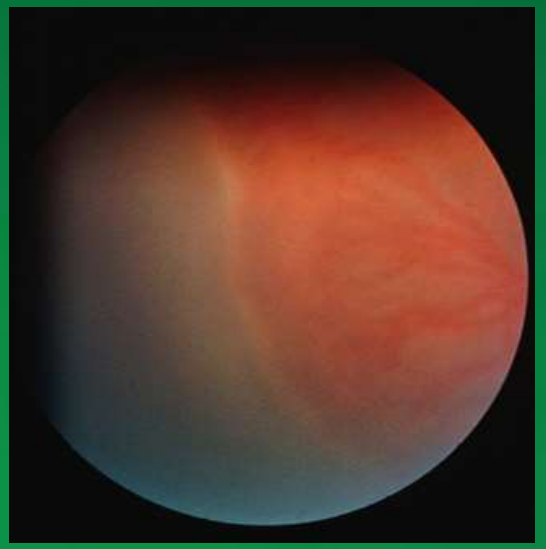




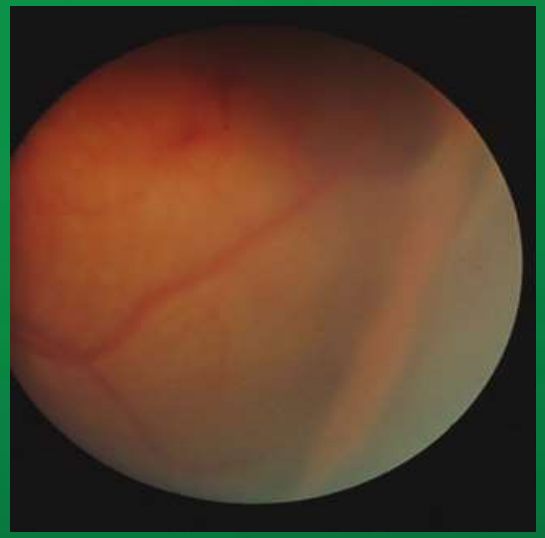




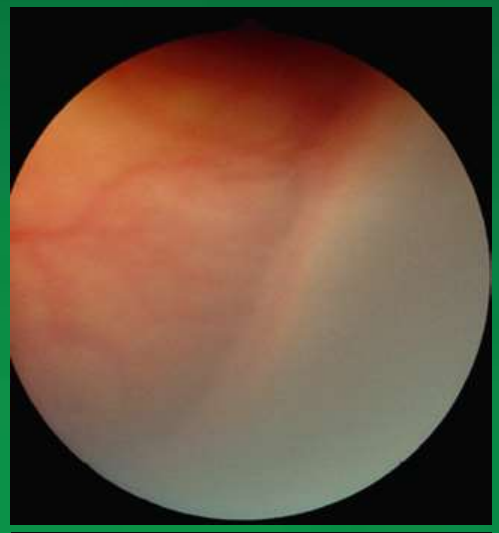
Stage 3 ROP. Mild



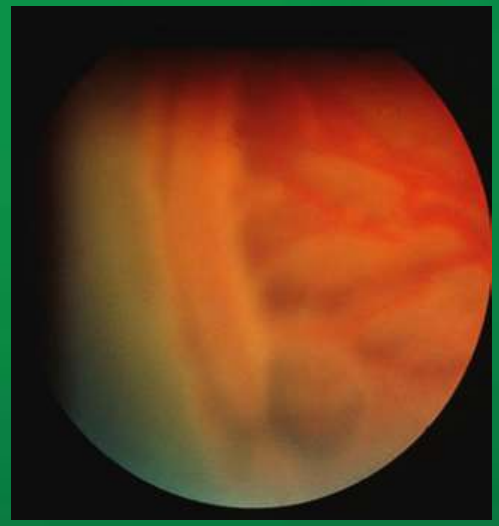
Stage 3 ROP. Moderate



Stage 3 ROP. Moderate to severe



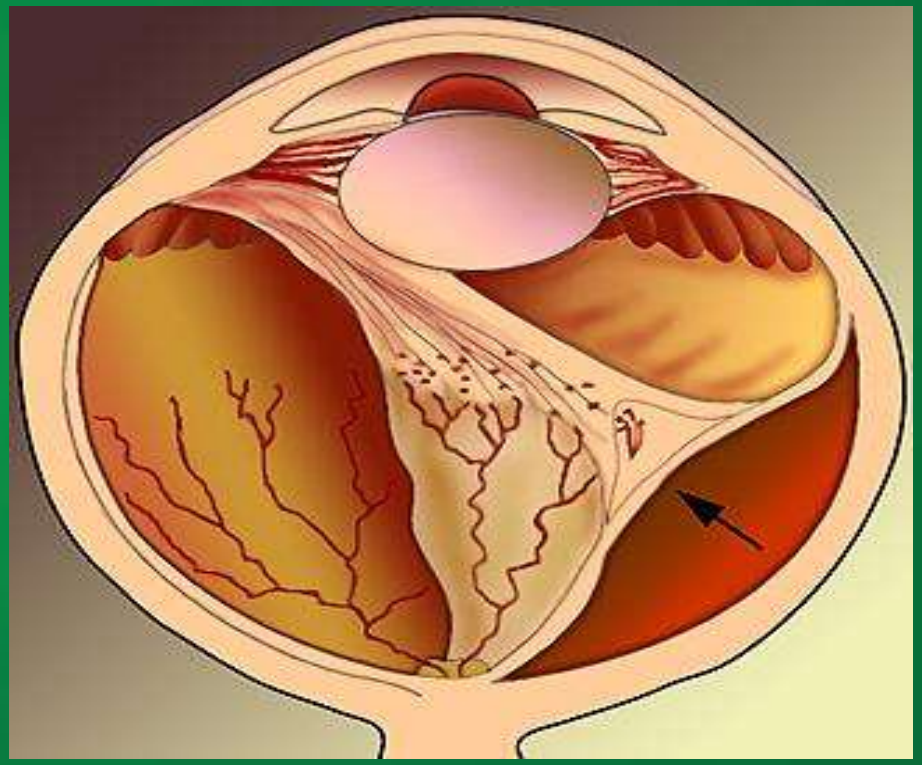
Stage 3 ROP. Severe



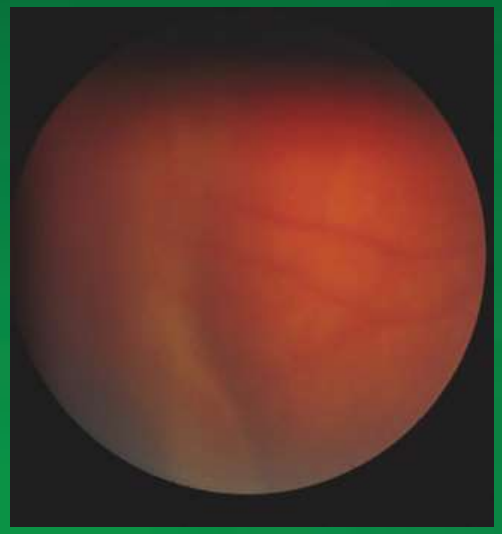
Dr B Barekatain

Stages 4:

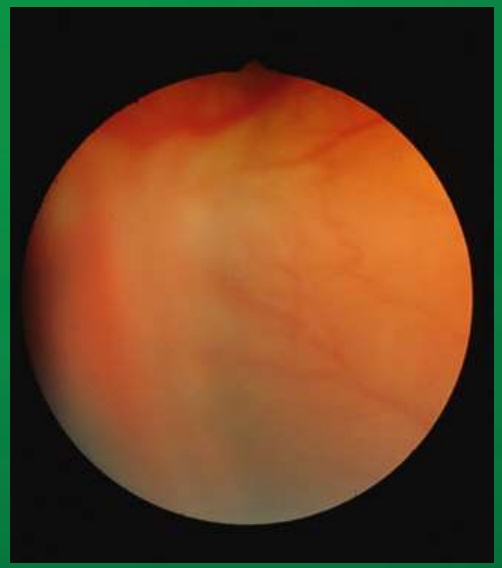
Partial retinal detachment that is caused by the effusion of fluid, traction, or by both.



Stage 4 ROP. Partial RD. Exudative



Stage 4 ROP. Partial RD. Exudative and tractional

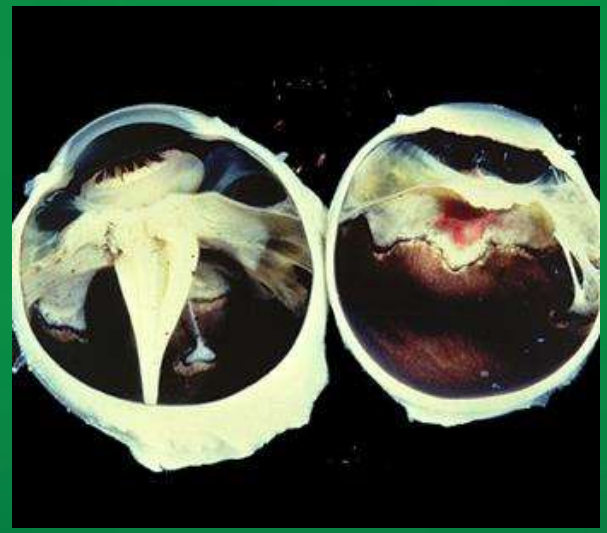


Stage 5:

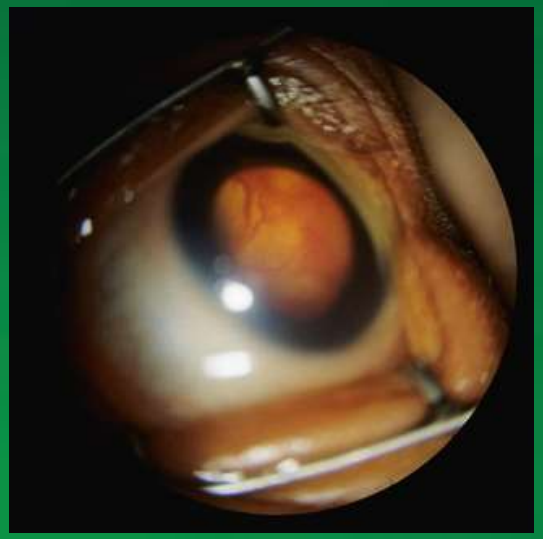
Total retinal detachment

.Open funnel R.D

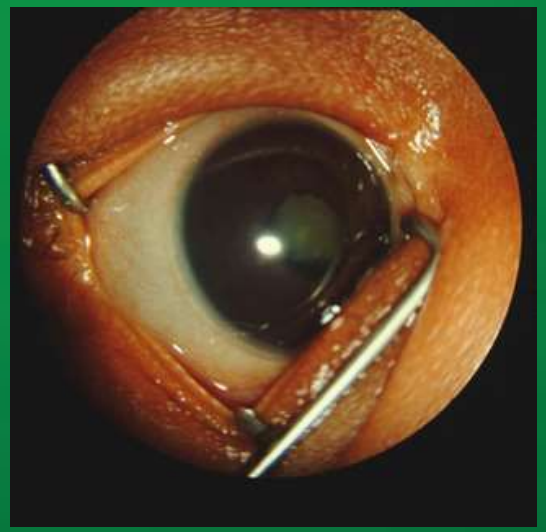
.closed funnel R.D



Stage 5 ROP. Open funnel RD



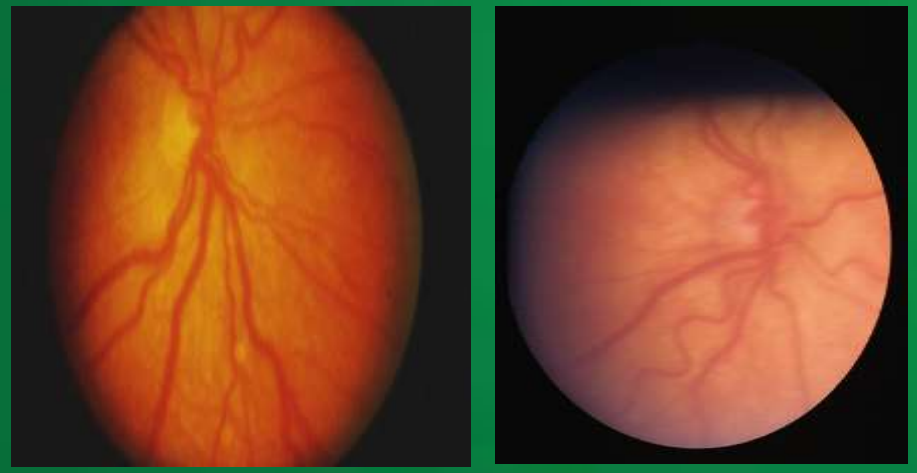
Stage 5 ROP. Closed funnel RD



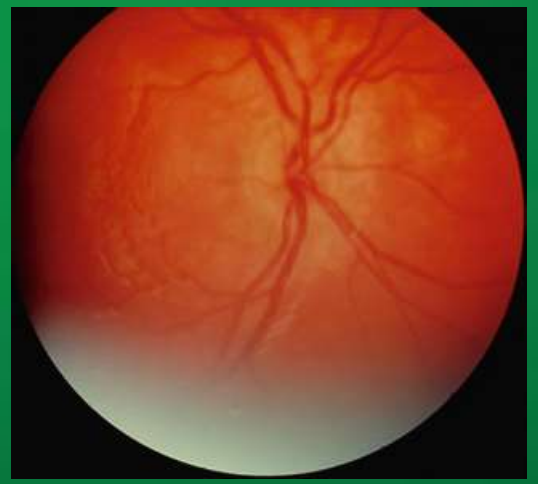
Additional classification definitions are as follows:

Plus disease: posterior venous dilation and arteriolar tortuosity of at least a photographically defined minimum.

Plus disease



normal



Clinical Manifestations and Prognosis:

In >90% of at-risk infants, the course is one of spontaneous arrest and regression, with little or no residual effects or visual disability.

Less than 10% of infants progress to severe disease, with significant extraretinal vasoproliferation, cicatrization, detachment of the retina, and impairment of vision.

The clinical picture is often that of a retrolental membrane, producing leukocoria (a white reflex in the pupil).

Some patients develop cataracts, glaucoma, and signs of inflammation.

The end stage is often a painful blind eye or a degenerated phthisical eye.

The spectrum of ROP also includes myopia, which is often progressive and of significant degree in infancy. The incidence of anisometropia, strabismus, amblyopia, and nystagmus may also be increased.

Rates of progression are variable, and the worst prognosis is associated with onset in one I (most immature) followed by rapid progression in time through stages 1, 2, and 3 to plus disease and retinal detachment. When this progression proceeds over a few weeks, the Japanese named it *rush disease.*

Onset in zone II, or a slower evolution of the disorder, leads more often to complete resolution or to just a partial cicatrix (retinal scar). This slower resolution can take as long as a year to stabilize, but most often results in full recovery.

ROP with an onset in zone III has a good prognosis for full recovery.

Disease with Little or No Risk

- Immature vascularization, zone II or III
- Stage 1, zone II or III, no plus
- Stage 2, zone II or III, no plus

Disease with Moderate Risk

- Immature vascularization zone I
- Stage 3, zone II or III, no plus
- Stage 1 or 2, zone I, no plus

Disease with High Risk

- Stage 3, zone II, plus
- Stage 3, zone I, no plus
- Stage 3, zone I, plus

ATTENTION TO:

.What is the ‘screening window’ ?
.Which babies should be screened ?
.When and how often to screen ?
.Where to examine the baby ?
.How to dilate the pupils ?
.What does the examination entail ?
.How to record findings during screening ?
.What precautions are taken during examination ?
.Use of wide-field digital camera (RetCam) for screening

Screening:

Screening for acute ROP is a critical and absolutely necessary clinical activity.

To paraphrase, ROP is a progressive disease and in early, not serious disease, treatment is not indicated, but in late, advanced acute/cicatricial disease treatment response is not optimal.

So each retinal disease state has a *narrow window screening* along the rogression trajectory and has a critical timing component to it.

Fanaroff and Martin's neonatal-perinatal medicine : diseases of the fetus and infant

BOX 53–7 Schedule for First Indirect Ophthalmoscopy in Premature Infants

WHO

All infants 30 weeks' gestation or less, or weighing less than 1500 g at birth

Infants born at 1500 to 2000 g who have a medically unstable course

WHEN

By the later of 31 weeks' postmenstrual age* or 4 weeks after birth

Recommend first examination before discharge from the hospital

*Postmenstrual age in weeks is equal to the gestational age at birth plus the chronologic age in weeks after birth.

Adapted from American Academy of Pediatrics, American Association for Pediatric Ophthalmology and Strabismus, and American Academy of Ophthalmology: Screening examination of premature infants for retinopathy of prematurity, *Pediatrics* 117:152, 2006 and 118:1324, 2006.

Avery's Neonatology, 6th Edition MacDonald, Mhairi G.; Seshia, Mary M. K.; Martha D.

The decision of which babies to screen is somewhat controversial.

Most nurseries desire an examination of any infant with a birth weight below 1,250 g, whereas others use a weight as high as 1,600 g.

A University of Pittsburgh study found that above a birth weight of 1,500 g, ROP developed only in infants exposed to at least 6 weeks of continuous oxygen.

Because vision-threatening ROP has been shown to arise at 33 to 41 weeks postconception, it would be wise to time the first examination at approximately 32 weeks, if possible.

Larger preterm newborns may need their first examination sooner after birth than smaller ones.

The subsequent examinations should be conducted as indicated by the findings of the first examination.

.If no ROP is found but the retina is still being vascularized, the examination should be repeated **every 1 to 2 weeks.**

.If ROP is found, the examinations should be repeated **weekly.**

.If “plus disease” (tortuosity and dilation of the blood vessels in the posterior pole of the fundus) is noted, the disease may be progressing faster, justifying a repeat evaluation in **3 to 4 days.**

The examinations are continued until the:

.retinal vascularization has reached zone III

.the threshold for treatment is achieved

.the disease has definitely regressed.

There are some rare cases in which regression was followed by reactivation.

Nelson textbook of pediatrics

.Infants with a birth weight of <1,500 g or gestational age of <32 wk

and

.selected infants with a birth weight between 1,500 and 2,000 g or gestational age of >32 wk with an unstable clinical course, including those requiring cardiorespiratory support

and

.who are believed by their attending pediatrician or neonatologist to be at high risk, should have retinal screening examinations.

Manual of neonatal care,by stark & Cloherty,6th edition,2008.

The current recommendation is to screen

.all infants with a birth weight <1,500 g or gestational age <30 weeks.

.Infants who are born after 30 weeks gestational age may be considered for screening if they have been ill:

.those who have had severe respiratory distress syndrome
.hypotension requiring pressor support
.surgery in the first several weeks of life

Because the timing of ROP is related to postnatal age

.infants who are born at <26 weeks gestation are examined at the postnatal age of 6 weeks
.those born at 27 to 28 weeks at the postnatal age of 5 weeks
.those born at 29 to 30 weeks are examined at the postnatal age of 4 weeks
.those >30 weeks at the postnatal age of 3 weeks

Patients are examined every 2 weeks until their vessels have grown out to the oraserrata and the retina is considered mature.

If ROP is diagnosed, the frequency of examination depends on the severity and rapidity of progression of the disease.

University of IOWA,children hospital of iowa

Any one of the following criteria qualifies the patient for ROP screening

- Infants with a birth weight of ≤1500 grams
- Infants with an estimated gestational age at birth of ≤ 32 weeks
- Infants who do not meet the first two criteria but are deemed at risk due to other medical conditions

Method for Determining the Timing of the first ROP examination

- For infants born at ≤ 27 weeks gestation: first eye exam at 32 weeks postnatal age (gestation age at birth + chronologic age).
- For infants born at > 27 weeks gestation: first eye exam at five weeks chronological age.

Cambridge University Press The Edinburgh Building, Cambridge CB2 8RU, UK

■ indirect ophthalmoscopy after pupillary dilation at 32 wk postmenstrual age of

➢ All infants <=1,500 g OR <=28 wks gestation

➢ Infants 1,500–2,000 g at risk because of severity of illness

■ Follow-up examination q 2–3 wk [q wk if progression to threshold disease] until:

➢ Retinal vascularization complete

and

➢ Disease regresses (~95%) or threshold disease develops (~5%)

note: ELBW infants may require an examination at an earlier age (30 wks) &more frequent intervals (at least twice/ wk) because of the possibility of AP ROP

Neonatology Clinical Guidelines,King Edward Memorial/Princess Margaret Hospitals,Perth Western Australia

GESTATIONAL AGE at BIRTH	FOR INITIAL ASSESSMENT AT
1. 23 – 29 +6 weeks (high risk)	32 weeks
2. 30 – 31+6 weeks (low risk)	34 weeks
Further screening is carried out at 37 – 38 weeks CGA. More frequent review, or for follow up of lesions, will be at the request of the visiting ophthalmologist.	

joint statement of the AAP, AAPOS, and AAO

A 2001 joint statement by the American Academy of Pediatrics, American Association for Pediatric Ophthalmology and Strabismus, and American Academy of phthalmology provided recommendations for ROP screening examinations in premature infants.

It is noted that these recommendations are evolving and may change as longer-term ROP outcomes are recognized.

A. Infants weighing <1500 g or <28 weeks' gestation

And

B. those weighing >1500 g with an unstable clinical course

should have dilated eye examinations starting at 4-6 weeks of age or 31-33 weeks' postconceptional age.

Exams should continue every 2-3 weeks until retinal maturity is reached, or no disease is present.

Infants with ROP or very immature vessels should be examined every 1-2 weeks until vessels are mature or the risk of threshold disease has passed. Those at greatest risk should be examined every week.

Data from: American Academy of Pediatrics. Screening examination of premature infants for retinopathy of prematurity.

Gestational age at birth week	Age at initial examination, week	
	Postmenstrual	Chronologic
22	31	9
23	31	8
24	31	7
25	31	6
26	31	5
27	31	4
28	32	4
29	33	4
30	34	4
31[a]	35	4
32[a]	36	4

Recommended follow-up exam intervals based on ET-ROP findings

One week or less Stage 1 or 2 ROP: zone I Stage 3 ROP: zone II
One to two week Immature vascularization: zone I – no ROP Stage 2 ROP: zone II Regressing ROP: zone I
Two week Stage 1 ROP: zone II Regressing ROP: zone II
Two to three week Immature vascularization: zone II – no ROP Stage 1 or 2 ROP: zone III Regressing ROP: zone III

Table 2. The number of probable missed patients, according to the application of our NICU's results to the some guidelines and local studies from around the world (4,6-8,12-16).

Recommendations based on country or study	Criteria for screening	No. of probable missed patients
Joint Statement of the AAP, AAPOS, and AAO, 2002	GA ≤28 weeks or BW ≤1500	7 (13.7%)
United Kingdom	GA <32 weeks or BW <1500	4 (7.8%)
Sweden	GA ≤32 weeks	3 (5.9%)
Denmark	GA ≤32 weeks or BW ≤1750	0 (0%)
Canada	GA ≤30 weeks or BW ≤1500	5 (9.8%)
Singapore	GA <32 weeks or BW <1250	13 (25.4%)
Japan	GA <31 weeks or BW <1500	5 (5.9%)
Chile	GA <32 weeks or BW <1750	1 (2%)
Brazil and Latin America	BW <1750	1 (2%)
India	GA <35 weeks or BW <2000	0 (0%)
Argentina	GA ≤32 weeks or BW ≤1500	0 (0%)
Lithuania	GA ≤32 weeks or BW ≤1500	0 (0%)
Restricted screening criteria applied to our patients	GA ≤30 weeks or BW ≤1250	27 (52.9%)

First author Year	Screening criteria	n	Incidence	Risk factors
Gopal L 1995[12]	Premature neonates with birth weight <2000 g	50	ROP: 38% (19/50) Threshold ROP: 16% (8/50)	No formal analysis. All with threshold ROP had received oxygen and 6 of 8 had received blood transfusion.
Charan R 1995[6]	Birth weight ≤ 1700 gm& admitted to the neonatal unit	165	ROP: 47% (78/165)	Not studied
Maheshwasri R 1996[8]	Gestation <35 wk or birth weight <1500 g or premature neonate needing oxygen for more than 24 h	66	ROP: 20% (13/66) Threshold ROP: 6/66 (9.1%)	Not studied
Rekha S 1996[11]	Gestation <35 wk or birth weight <1500 g	100	ROP: 46% (46/100) Threshold ROP: 9/100 (9%)	Anemia, duration of oxygen therapy
Varughese S 2001[13]	Gestation <34 wk or birth weight <1500g	79	ROP: 52% (41/79) Threshold ROP: 6.3% (5/79)	Not studied
Aggarwal R 2002[9]	Gestation <35 wk or birth weight <1500 g or premature neonate needing oxygen for more than 24 h	76	ROP: 32% (24/76) Threshold ROP: 2/76 (2.6%)	Apnea, clinical sepsis, male gender
Gupta VP 2004[7]	Gestation <35 wk or birth weight <1500 g	60	ROP: 21.7%	Apnea, sepsis, oxygen therapy
Dutta S 2004[10]	Gestation ≤32 wk or birth weight ≤1700 g or premature babies of any gestation who have received prolonged oxygen therapy (≥ 30 days)	108	Not reported	Administration of packed cells and double-volume exchange transfusion
Chaudhari S 2009[5]	Gestation ≤ 32 wk or birth weight < 1500 g or additional risk factors	552	ROP: 22.3% (123/552) Threshold ROP: 7.4% (41/552)	Apnea, septicemia and oxygen therapy
Sharma P 2009[17]	Preterm infants with birth weight ≤1500 g or gestation ≤32wk. Infants with birth weight 1501-1800 g or gestation 33-34 wk screened if additional risk factors present	704	ROP: 11.9% (84/704) 33 (4.7%) infants had severe ROP requiring laser therapy	Respiratory distress syndrome

اندیکاسیون های انجام معاینه چشم

بر اساس آخرین شواهد ملی ، نوزادان با سن جنینی کمتر از 34 هفته و یا وزن تولد کمتر از 2000 گرم، می بایست از نظر رتینوپاتی نارسی غربالگری شوند.

همچنین همه نوزادانی که صرف نظر از سن حاملگی و وزن تولد، مسیر درمانی پیچیده ای را در بخش مراقبت ویژه نوزادان، مانند تعویض خون طی می کنند، یا وضعیت ناپایدار بالینی داشته باشند و یا توسط پزشک معالج در معرض خطر تشخیص داده شوند، می بایست از نظر رتینوپاتی معاینه شوند

* تشخیص آسیفکسی هنگام تولد، با داشتن PH< 7/1 در خون بند ناف یا در یک ساعت اول تولد در نمونه خون نوزاد، و یا نمره آپگار 3 یا کمتر، در دقیقه 5 پس از تولد

* شیرخواری که وضعیت بی ثبات شدید یا مستمر و تظاهراتی مانند هیپوکسی طولانی مدت، اسیدوز شدید، هیپوگلیسمی یا هیپوتانسیون جدی نیازمند به دریافت داروهای وازوپرسور داشته باشد

* نیاز به حمایت قلبی- تنفسی

* سندرم دیسترس تنفسی، نیاز به تهویه مکانیکی

* نیاز به تجویز داروهایی مانند دوپامین جهت افزایش فشار خون
* خونریزی داخل بطنی
* نیاز به تجویز خون کامل یا گلبولهای قرمز متراکم یا تعویض خون
* دریافت اکسیژن به مدت بیشتر از 48 ساعت
* بیماری مزمن ریویBPD
* حملات مکرر آپنه
* سایر مشکلاتی که از نظر متخصص کودکان یا فوق تخصص نوزادان، نوزاد بیمار را در معرض خطر ROP قرار می دهد

اولین زمان انجام معاینه شبکیه بر مبنای جدول زیر می با شد . با توجه به این که برخی مطالعات نشان داده اند که در نوزادان بسیار نارس و کم وزن یک نوع شدید رتینوپاتی نارسی خلفی پیشروند ه (Aggressive posterior) مشاهده می شود، ممکن است براساس تشخیص پزشک نیاز به انجام اولین معاینه در سن کمتری باشد

جدول سن نوزاد در اولین معاینه	
سن حاملگی در زمان تولد (هفته)	زمان اولین معاینه پس از تولد (هفته / روز)
22	9 هفته پس از تولد یا 63 روزگی
23	8 هفته پس از تولد یا 56 روزگی
24	7 هفته پس از تولد یا 49 روزگی
25	6 هفته پس از تولد یا 42 روزگی
26	5 هفته پس از تولد یا 35 روزگی
27 و بیشتر	4 هفته پس از تولد یا 28 روزگی

جدول زمان معاینات پیگیری بر اساس یافته های معاینه نوبت قبلی چشم

منطقه شبکیه	*Stage of retinal findings*	فواصل پیگیری
Zone I	Immature vascularization, no ROP	1-2 هفته
	Stage 1 or 2	1 هفته یا کمتر
	Regressing ROP	1-2 هفته
Zone II	Immature vascularization, no ROP	2-3 هفته
	Stage 1	2 هفته
	Stage 2	1-2هفته
	Stage 3	1 هفته یا کمتر
	Regressing ROP	1-2 هفته
Zone III	Stage 1 or 2	2-3 هفته
	Regressing ROP	2-3 هفته

معاینه چشم (چگونه و توسط چه کسی و در کجا):

پزشک معالج و پرستار مسئول مراقبت نوزاد باید در صورت نیاز به انجام معاینه چشم ، نام نوزاد را در لیست مربوطه ثبت و هماهنگی لازم را برای معاینه انجام دهند.

معاینه چشم را می توان با یا بدون بیهوشی انجام داد. اگر چه در اغلب موارد معاینه چشم نیاز به بیهوشی ندارد ولی در صورتی که نیاز به بیهوشی وجود داشته باشد ، حضو ر یک متخصص بیهوشی ماهر در زمینه بیهوشی شیرخواران کم وزن و پرخطر در اتاق عمل ضروری است. این معاینات باید در بیمارستان دارای بخش مراقبت ویژه نوزادان انجام گیرد و همواره یک تخت مراقبت ویژه رزرو شده و در صورت نیاز شیرخوار جهت مراقبت پس از بیهوشی به بخش منتقل گردد.

معاینه بدون بیهوشی می تواند بر بالین نوزاد یا در درمانگاه مجهز به امکانات مانیتورینگ و احیای نوزاد انجام شود. البته در صورت بستری بودن نوزاد ، معاینه باید حتما در بالین نوزاد صورت گیرد. همچنین لازم است در طی انجام معاینات، نوزاد از نظر آپنه و افت درصد اشباع اکسیژن خون شریانی یا برادیکاردی از طریق مانیتورینو یا پالس اکسی متری تحت نظر باشد و تا 4 ساعت پس از معاینه نیز مراقبت از نوزاد ادامه یابد.

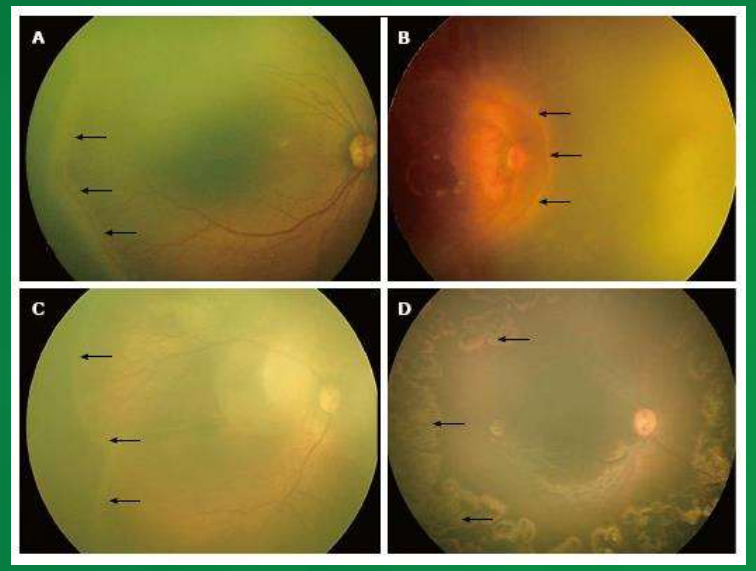
قبل از انجام معاینه باید با والدین شیرخوار درباره لزوم انجام معاینه صحبت و مشکلات معاینه چشم و احتمال وجود درگیری های چشمی توضیح داده شده و رضایت نامه کتبی از والدین گرفته شود.

وسایل مورد نیاز:

* افتالموسکوپ غیر مستقیم
* بلفارواستات سیمی نوزاد
* لنز معاینه افتالموسکوپی غیرمستقیم (لنز 20+ و 30+)
* دپرسور
* قطره آنتی بیوتیک

وسایل احیای نوزاد (شامل آمبوبو، ماسک و کپسول اکسیژن، وارمر، لوله تراشه شماره 2.5 تا 4، لارنگوسکوپ با تیغه صفر و 1، دستگاه ساکشن و لوله های مربوطه، لوله معده شماره 5 تا 8)

* پالس اکسی متر



Dr B Barekatain

روش انجام معاینه چشم

مردمک چشم نوزاد باید با قطره میدریاتیک رقیق در حدود یک ساعت قبل از انجام معاینه، دیلاته شود تا معاینه امکان پذیر گردد. روش پیشنهادی استفاده از ترکیب قطرات تتراکائین 5/. %، تروپیکامید1 %، فنیل افرین 2/5% (با ترکیب یک سوم از هر کدام) 2 تا 3 بار با فواصل 10 تا 15 دقیقه است.

آتروپین توصیه نمی شود.

قطرات اضافی باید از روی صورت شیرخوار با دستمال پاک شود تا جذب پوستی به حداقل برسد.

دادن مقادیر زیاد قطر چشمی، خطر تاکیکاردی و هیپرترمی را به دنبال دارد.

معاینه رتین یک پروسه دردناک است. قنداق کردن شیرخوار و دادن محلول سرم قندی ساکارز خوراکی 24 به میزان 5/. تا 1 سی سی با کمک سرنگ از راه دهان می تواند درد شیرخوار را کاهش داده و به انجام معاینه بدون بی قراری زیاد شیرخوار کمک کند.

روشنایی محیط معاینه نوزاد باید تا حد 10 لوکس کاهش یابد. در صورتی که در محیط مراقبت این امکان وجود ندارد نوزاد را می توان به اتاق دیگری در داخل یا جنب بخش مراقبت ویژه نوزادان انتقال داد.

معاینه با افتالموستکوپ غیرمستقیم با یا بدون قرار دادن بلفارواستتات انجام می گیرد و در صورت لزوم و با فراهم بودن امکانات احیای نوزاد، دپرسیون نواحی محیطی شبکیه می تواند با دپرسور سیمی ظریف انجام شود.

نتایج معاینه در باید فرم مخصوص ثبت گردیده، تاریخ معاینه بعدی مشخص و به والدین و پز شک و پرستار مسوول پیگیری نوزاد اطلاع داده شود.

Prevention:

1. Judicious oxygen therapy

.Oxygen is a drug and it should be administered in a quantity that is absolutely necessary.

.Each neonatal care unit should have a written policy outlining appropriate use of oxygen therapy.

.If a preterm neonate born at < 32 weeks gestation needs resuscitation at birth, inhaled oxygen concentration (FiO_2) should be titrated to prevent hyperoxia and achieve gradual increase in oxygen saturation (70% at 3 minute and 80% at 5 minute and 85-95% at >10 min after birth).

.Oxygen level in blood should be continuously monitored using pulse oximeter. It has been observed that if oxygen saturation in a baby on oxygen therapy is kept between 85% and 93%, in about 90% samples partial pressure of oxygen is in desirable range (40 to 80 mm Hg).

2.Judicious use of blood transfusions

Transfusion of packed RBCs is another risk factor of ROP.

Adult RBCs are rich in 2,3 DPG and adult Hb binds less firmly to oxygen, thus releasing excess oxygen to the retinal tissue.

Packed cell transfusions should be given when hematocrit falls below following ranges:

.ventilated babies 40%,
.babies with cardio-pulmonary disease but not on ventilators 35%
.sick neonates but not having cardiopulmonary manifestations 30%
.symptomatic anemia 25%
.asymptomatic anemia 20%

3.Vitamin E Supplementation

Very low birth weight neonates should receive 15-25 IU of vitamin E daily as supplement.

However, higher doses given by intravenous route have been associated with increased risk of neonatal sepsis.

4.Prenatal steroids

Use of prenatal steroids is a well-known approach to prevent respiratory distress and intraventricular hemorrhage, two important risk factors of ROP.

Although there are some concerns that prenatal steroids may induce ROP, this is not borne out by other studies.

.We believe prenatal steroids prevent acute illnesses in premature babies and should be administered to all mothers with preterm labor between 24-34 weeks of gestation.

.The preferred preparation of steroids for prenatal used is betamethasone in two doses of 12 mg each given intramuscularly, 24 hours apart.

5.Bevacizumab

.Intravitreal injection of bevacizumab, a neutralizing anti-VEGF moleculehas been demonstrated to diminish the neovascular response significantly in animal models.

.However, due to uncertainties with respect to the dosing, frequency, timing, and adjunct therapies to be used and potential to cause serious systemic adverse effects, use of bevacizumab is not recommended outside the scope of clinical trial.

Management:

A. Circumferential cryopexy

.has been proven to be an effective treatment for progressive (stage III+) disease in an attempt to prevent further progression by destroying cells that may be releasing angiogenic factors.

.Results of the large, collaborative NIH-sponsored trial indicate that cryopexy carried out at stage III+ can reduce the incidence of severe visual impairment by ~50% if performed within 72 h of detecting threshold disease.

.If both eyes are involved, cryopexy is usually performed in one eye only because there are some risks with the procedure, such as vitreal hemorrhage. If there are enough risk factors for retinal detachment, however, cryopexy may be performed in both eyes.

.Although myopia is a common feature of ROP, 10-year follow-up shows significant improvement in visual acuity of treated versus control eyes.

.It is imperative that an ophthalmologist skilled in cryopexy perform the procedure.

B. Laser photocoagulation

.Data suggest that this technique is equally effective yet safer than cryopexy.

.In 1994, the Laser ROP Study Group was formed to carry out a meta analysis of four laser- ROP trials.

Treatment was based on the same criteria used in the CRYO-ROP trial.

Recognizing the limitations of a meta-analysis, the study group concluded that laser therapy is at least as effective as cryotherapy for ROP, despite a small risk of cataract formation.

Ten-year follow-up of a small group of patients suggests better outcomes with laser photocoagulation.

C. Oxygen for treatment of ROP

.In an attempt to reduce angiogenic factors from the hypoxic retina and the progression of ROP from prethreshold to threshold (III+) levels, oxygen therapy was attempted in a large collaborative trial, the STOP-ROP Study.

.Oxygen saturations were targeted at 96- 99% in the treatment group and 89-94% in the conventional group once prethreshold ROP was diagnosed.

No significant difference was seen in the rate of progression to threshold disease between the two groups.

D. Vitamin E

.The administration of pharmacologic doses of vitamin E for ROP is controversial; currently, there is no proof of clear benefit.

Reported side effects include sepsis, necrotizing enterocolitis, and intraventricular hemorrhage.

.Even so, maintenance of normal serum vitamin E levels is a prudent management objective.

E. Decreased lighting intensity

. A prospective, randomized, multicenter trial of 409 premature infants weighing <1251 g and 31 weeks' gestation concluded that a reduction in ambient light exposure does not alter the incidence of ROP (Reynolds et al, 1998).

F.inositol and D-penicillamine

.Data are limited. Further work is needed.

G. Retinal reattachment

.Stage IV disease has been treated by attempts at retinal reattachment without significant success to date.

.Reattachment of late retinal detachments in childhood has met with more success.

H. Vitrectomy

.has not substantially improved the outcome in cicatricial disease.

I. Follow-up eye examinations

.are advocated every 1-2 years for infants with fully regressed ROP and every 6-12 months for those with cicatricial ROP.

Premature infants are at risk for myopia even in the absence of ROP and should have an eye exam by 6 months of age.

درمان رتینوپاتی نارسی:

برخی از نوزادانی که بیماری آنها خفیف یا متوسط است ، بدون نیاز به درمان بهبود می یابند. اما در صورتی که بیماری نوزاد شد ید باشد ، درمان لازم است .

برای جلوگیری از افزایش غیرطبیعی عروق شبکیه بیشتر از لیزر درمانی استفاده می شود . گاهی نیز ممکن است نیاز به تزریق دارو در داخل چشم باشد . این درمان ها معمولا در اتاق عمل انجام شده و ممکن است نیاز به بیهوشی داشته باشند.

بر حسب مرحله بیماری از درمان های مختلفی استفاده می شود:

*امروزه لیزر درمانی نواحی فاقد رگ شبکیه تا حد زیادی جایگزین کرایوتراپی شده ا ست زیرا مقرون به صرفه تر است و عوارض سیستمیک کمتری دارد .

* برای پسرفت عروق غیر طبیعی خصوصا در موارد شدید با درگیری قطب خلفی از تزریق داخل زجاجیه ای داروهای ضد فاکتور رشد اندوتلیوم عروق مانند Avastin استفاده می شود.

•در مراحل 4 و 5 بسته به مورد از اسکلرال باکلینو یا ویترکتومی ± لنزکتومی استفاده می شود .

در موارد زیر درمان انجام می شود:
zone I ROP در هر stage همراه با بیماری plus
zone I ROP در stage 3 بدون بیماری plus
zone II ROP در stage 2 یا stage 3 همراه با بیماری plus

- در نوزادان دچار بیماری threshold نوع 1 درمان باید طی 72 ساعت پس از تشخیص و قبل از شروع جداشدگی شبکیه شروع گردد.
- از عوارض ROP پیشرفته درمان شده یا خودبخود پسرفت کرده ، تغییرات شبکیه است لذا معاینات دوره ای چشم ضروری ا ست.

احتمال جدا شدگی شبکیه در دهه اول و دوم زندگی وجود دارد. نزدیک بینی، کشیدگی ماکولا و استرابیسم می توانند منجر به تنبلی چشم شوند. احتمال کاتاراکت و گلوکوم نیز وجود دارد.

بنابراین توجه به این مسایل و درمان آنها نقش بسیار مهمی در بازتوانی دید و بینایی نوزادان دارد و تاکید بر انجام معاینات دوره ای خصوصا برای والدین ضروری است.

معاینات چشمی بر اساس سن پس از قاعدگی نوزاد و یافته های معاینات قبلی زمانی خاتمه می یابد که نوزاد، دیگر در معرض خطر ابتلا به رتینوپاتی تهدید کننده بینائی نباشد.

در موارد زیر می توان معاینه را خاتمه داد:

* تکمیل رگدار شدن طبیعی شبکیه تا انتهای zone III که معمولا در 40 هفتگی سن پس از قاعدگی مشاهده و اغلب در 45 هفتگی تکمیل شده است.

* مشاهده توقف و پسرفت واضح علائم رتینوپاتی که شامل موارد زیر است:

- تغییر رنگ لبه ها از صورتی به سفید
- عدم افزایش شدت بیماری
- عبورعروق از مرز demarcation line
-شروع پروسه جایگزینی ضایعات فعال با بافت اسکار

معمولا معاینه چشم نوزاد هر 1 تا 2 هفته تا زمانی که نوزاد حداقل به سن 38 تا 40 هفتگی پس از قاعدگی برسد ادامه میابد.

Blackboard-styled Thank You Slide Design

Thank You