



## وبینار رتینوپاتی تارسی (ROP)

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با امتیاز آموزش مداوم

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برگزار کننده: بیمارستان بعثت سنج

# RETINOPATHY OF PREMATURITY

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# DEFINITION

- **Retinopathy of prematurity (ROP)** is a multifactorial **vasoproliferative retinal disorder** that increases in incidence with decreasing gestational age
- It's a disease of **developing retinal vasculature**

# INTRODUCTION

- ◎ 1942- Terry first identified ROP as ‘retrolental fibroplasia’ in 6 month premature infant.
- ◎ 1951 - Heath suggested term “Retinopathy of Prematurity”
- ◎ Campbell: relationship of intensive oxygen therapy & subsequent development of ROP.
- ◎ Kinsey: ROP was inversely proportional to birth weight.

# DEFINITION

- **Retinopathy** → Affects retinal vasculature
- **Prematurity** → typically in **<30 weeks** or **<1500gm**

Prevalence:

- **65%** of newborns with B.wt **<1,250g** and
- **80%** of newborns with a B.wt **<1,000 g** will develop some degree of ROP

- ◎ It is a developmental vascular proliferative disorder that occurs in the incompletely vascularized retina of primarily premature infants.
- ◎ ROP is one of the most common causes of blindness in children



# Epidemiology



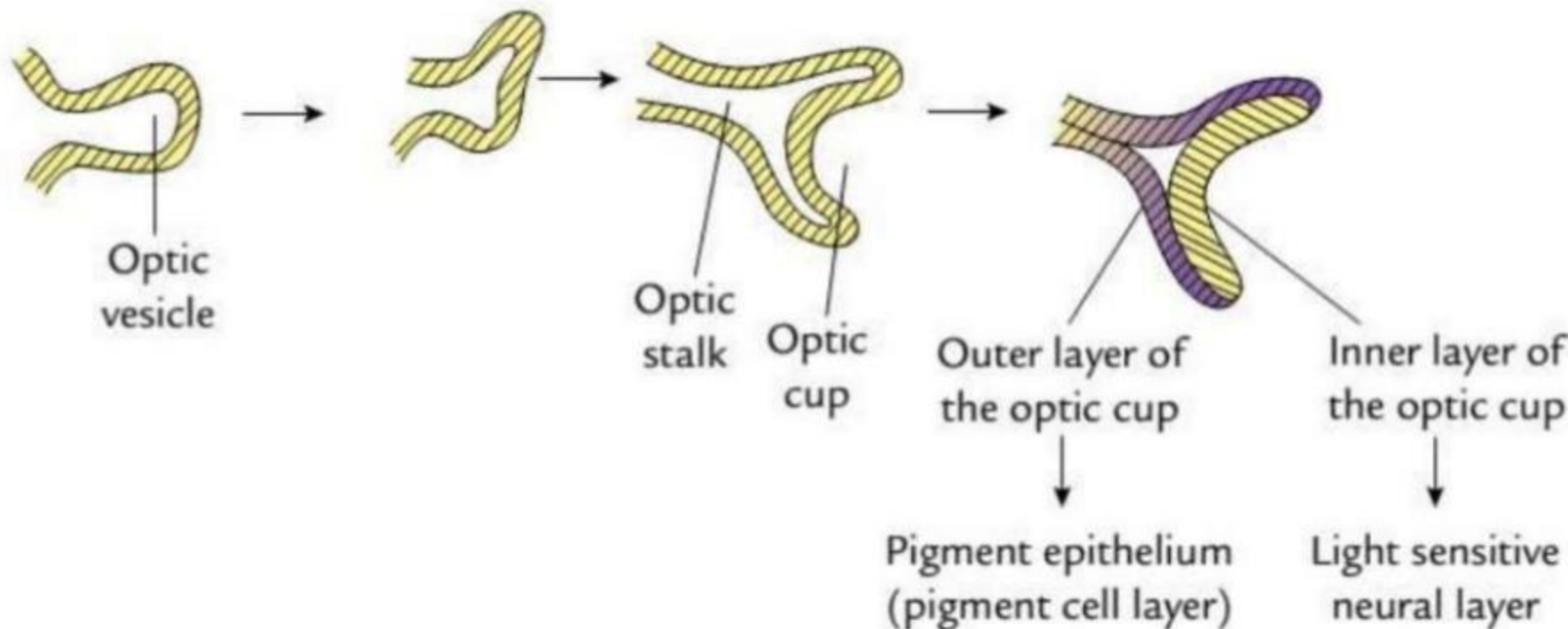
- ▶ Every year, an estimated 15 million babies are born preterm (normal gestation is 37–42 weeks)
- ▶ Approximately 20,000 of these babies will become blind from retinopathy of prematurity (ROP) every year
- ▶ An additional 12,300 will be left with visual impairment.

# PATHOPHYSIOLOGY



# NORMAL RETINAL DEVELOPMENT

## Stages in the development of retina.



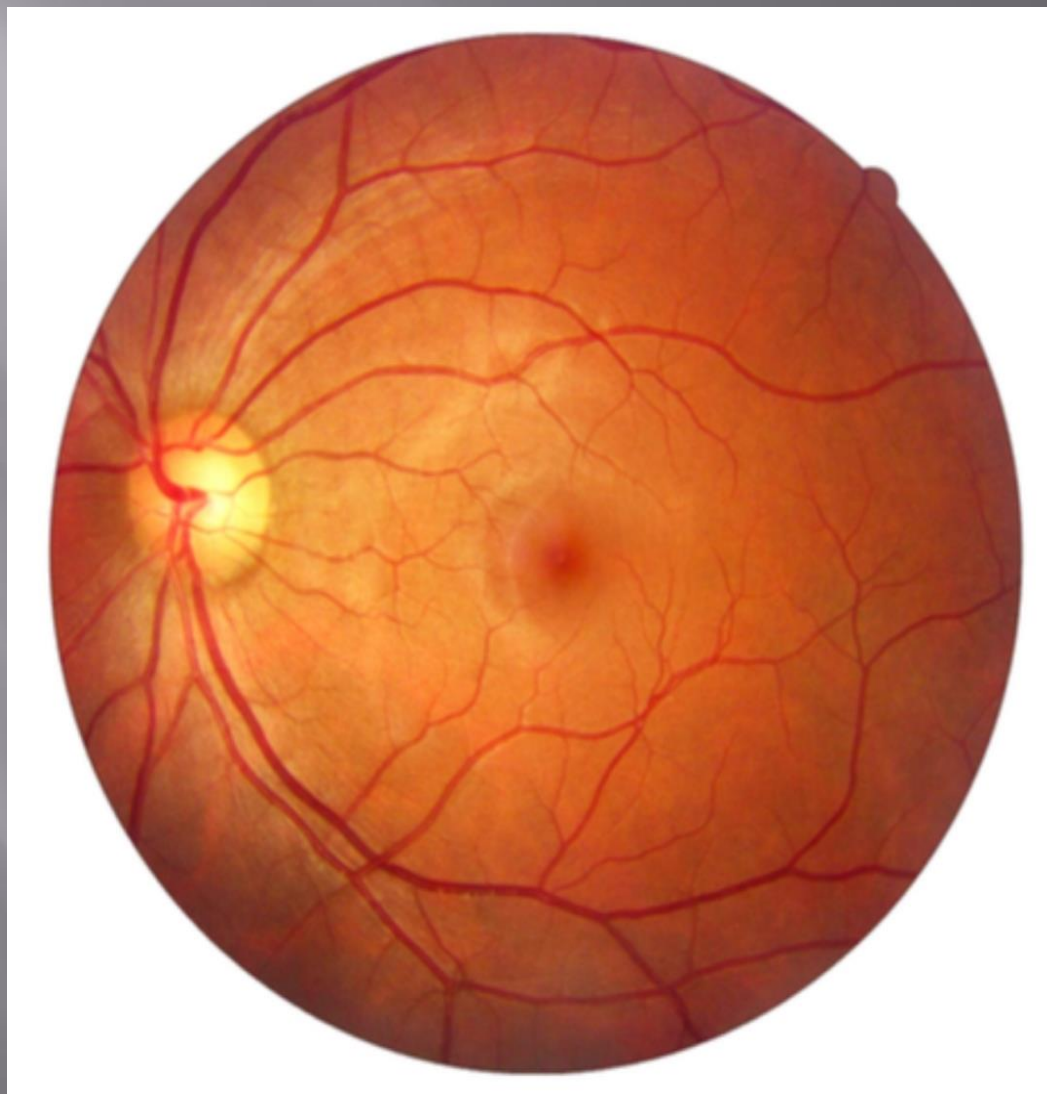
# NORMAL RETINAL DEVELOPMENT

- Sclera → Choroid → Retina
- Retinal layers: Nerve fibers, ganglion cells, photoreceptors migrate from **center of optic disc to the periphery**
- **By 28 weeks:** The photoreceptors migrate 80% of the distance towards ora-serrata
- Before the retinal vessels develop the **avascular retina** receives oxygen by diffusion from the choroid vessels

# NORMAL RETINAL DEVELOPMENT

- **16 weeks** → Retinal vessels arise from hyaloid vessels at optic disc and begin to migrate outwards
- **36 weeks** → Migration is complete on **nasal side**
- **40 weeks** → Migration is complete on **temporal side**





# Pathogenesis of ROP

Various theories proposed are:

1. The Classical Theory
2. Gap Junction Theory
3. **Current VEGF Theory**



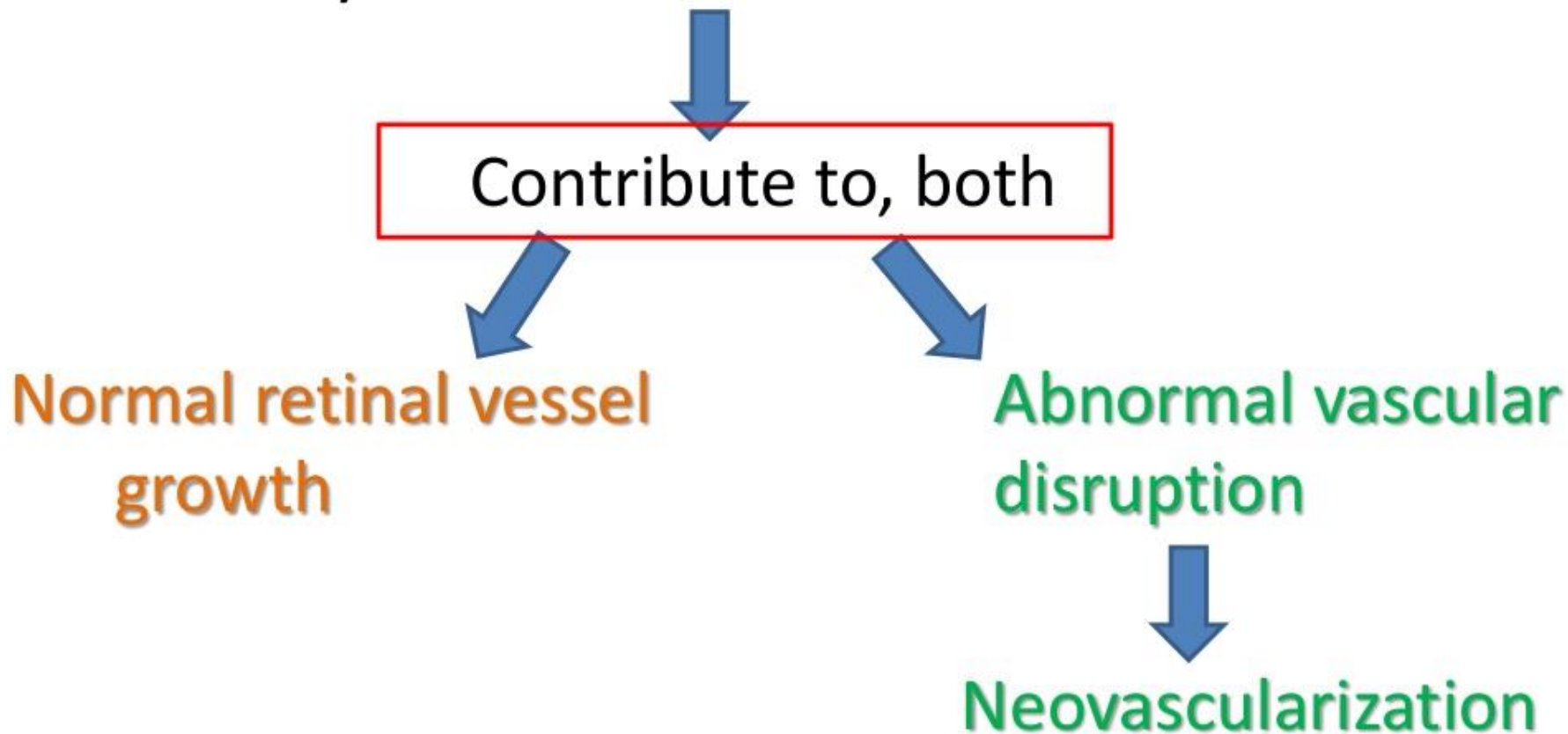


# VEGF theory:

- ▶ The nasal retina is normally fully vascularized after 8 months of gestation, the temporal periphery at or by 1 month after delivery.
- ▶ Vascular endothelial growth factor (VEGF) is believed to play an important role in the vascularization process.

- **PATHOGENESIS:**

Vascular Endothelial Growth Factor (VEGF) and other cytokines





- **PATHOGENESIS:**
- IGF-1 interacts with VEGF.
- Insulin-like growth factor-1 (IGF-1) supports normal retinal vascular growth.
- Decreased IGF-1 → Development of ROP.

# STATUS OF EYE

## ⦿ Mature

- Vessels reached with in 1DD of both nasal and temporal ora

## ⦿ Immature

- Vessels not reached with in 1DD of nasal or temporal ora
- Immature I,II,III(depending on zones)

## ⦿ ROP

- **PATHOGENESIS**
- **Vascularization in ROP: Pathogenesis of ROP involves two stages.**

Initial injury (factors such as hypotension, hypoxia, or hyperoxia, with free radical formation)



Injures newly developing blood vessels



Disrupts normal angiogenesis

*Stage 1*



Vessels



Either resume normal growth  
(or)

*Stage 2*



New vessels grow abnormally out from retina into vitreous



Increased permeability of these abnormal new vessels  
(neovascularization)



Retinal edema and hemorrhage

- **PATHOGENESIS**
- **Vascularization in ROP: Pathogenesis of ROP involves two stages.**

Increased permeability of these abnormal new vessels  
(neovascularization)

Retinal edema and hemorrhage

Abnormal fibrovascular tissue develop along with  
neovascularization

*Contract*

Produces traction on the retina

*If severe*

Retinal detachment

*(However, in most instances, the abnormal vascular tissue regresses with little residual effect.)*



# PATHOGENESIS

Stage I

- **Hyperoxia, Hypoxia**
- **Hypotension**

Stage I

- **Vasoconstriction** and decreased blood flow to developing retina
- **Arrest of vascular development**

Stage I

- **Hyperoxia** causes **down regulation of VEGF** that is essential for normal development of retinal vessels

# PATHOGENESIS

## Stage II

- Stage of **Neovascularization**
- **Hypoxic** avascular retina → **upregulates VEGF**

## Stage II

- **Aberrant retinal vessels** growth in to retina and vitreous
- **More permeable** → Hemorrhage and edema

## Stage II

- Extensive extraretinal **fribovascular proliferation** → **Retinal detachment** and abnormal retinal function
- Most infants its mild and **regresses spontaneously**

# CLASSIFICATION & NOMENCLATURE

- ◎ ICROP (1984 & 1987 )

- Zone, Stage, Extent, Plus

- ◎ ICROP revisited

- APROP
- Pre plus
- Practical clinical tool for extent of Zone I



# INTERNATIONAL CLASSIFICATION FOR RETINOPATHY OF PREMATURITY (ICROP)

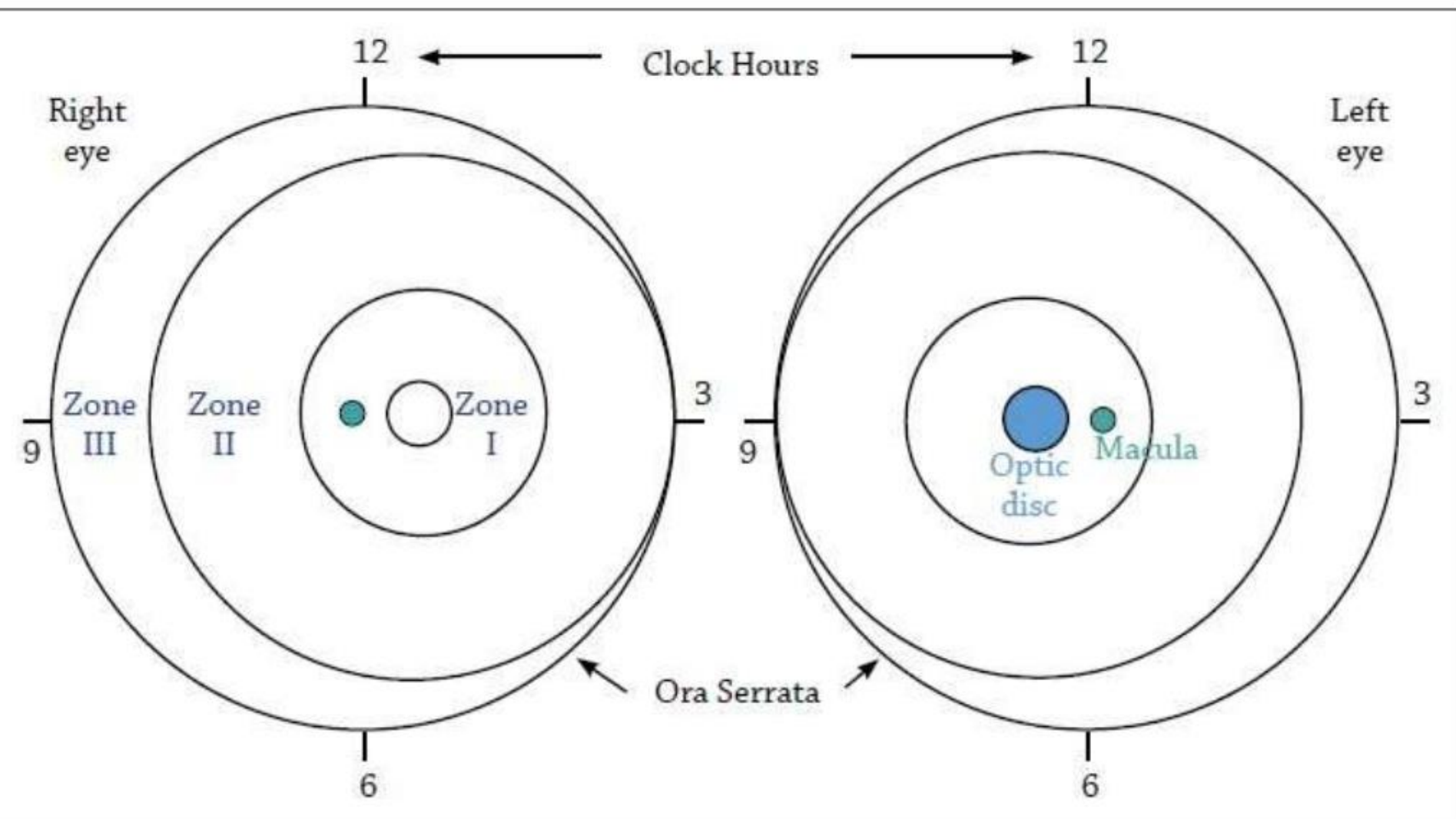
- ◎ Four features are evaluated:
  - Zone (1-3)
  - Extent
  - Stage (1-5)
  - Presence or absence of plus disease

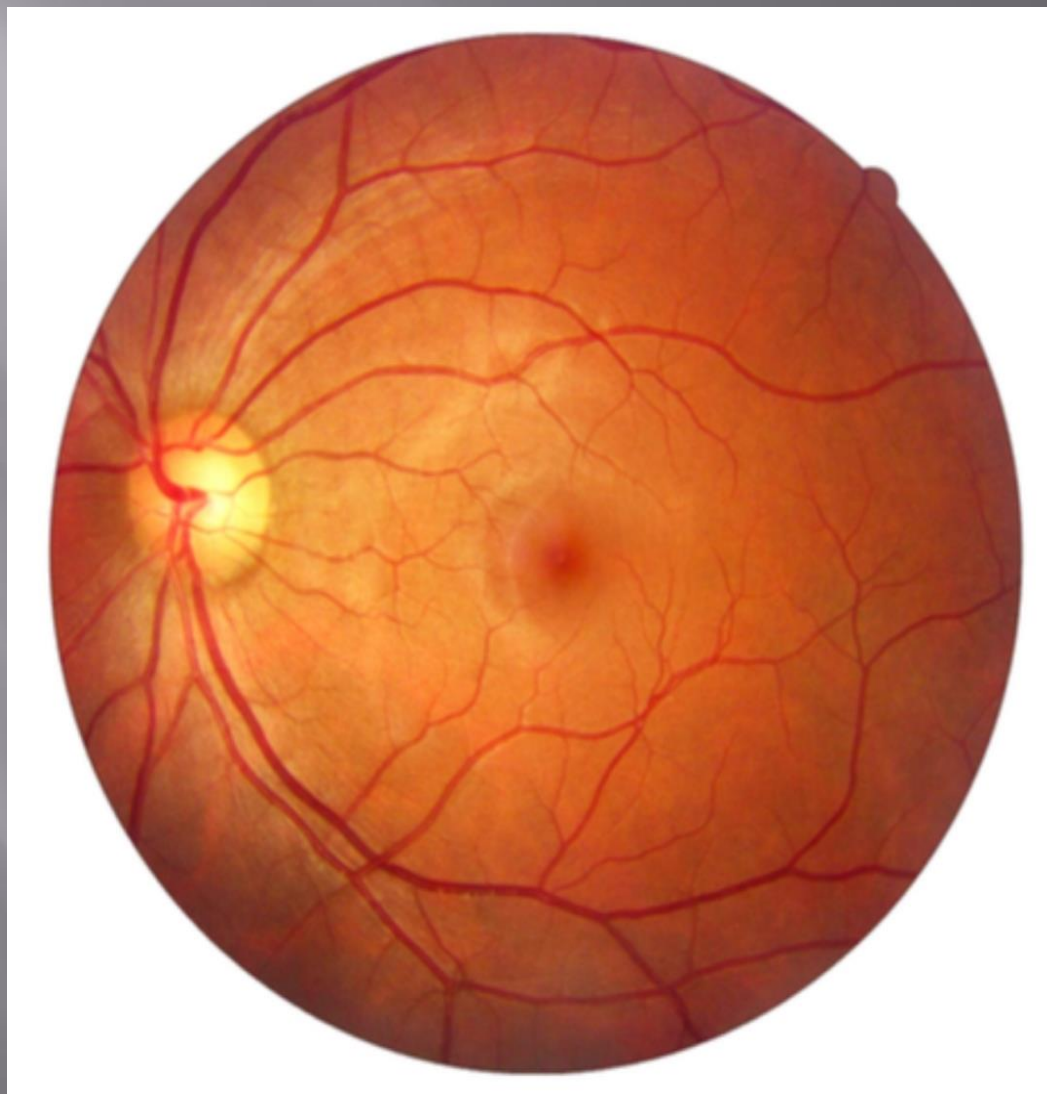
# CLASSIFICATION - ICROP 2005

## I-ANTERIOR-POSTERIOR LOCATION

- ZONE I:
  - Centre: Optic disc
  - Radius: 2 x Disc-foveal distance
  - Boundaries: Completely surrounded by Zone II
- ZONE II:
  - Centre: Optic disc
  - Radius: Distance from optic disc to nasal ora-serrata
  - Boundaries: Inner-Zone I, Outer-Zone-III temporally
- ZONE III:
  - a crescent-shaped retinal area extending beyond zone-II to the temporal ora-serrata

- Disease location

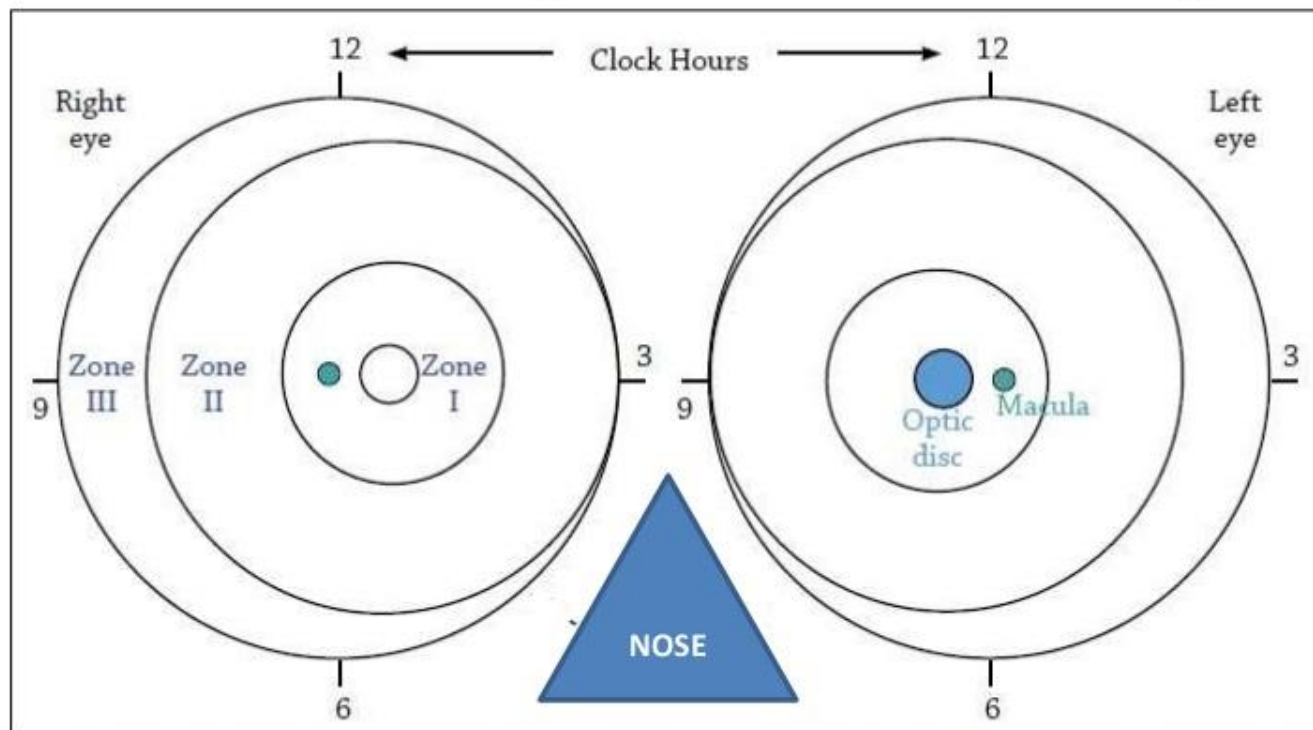






- Disease location

- Retina is divided into 3 concentric circles, each centered on optic disc.
- Retinal vessels grow out from the optic disc to the periphery.
- Designation of zones corresponds to vascular developmental pattern.



**Zone1:** Defined by a circle whose radius is twice the distance from the centre of the optic disc to the centre of macula (Fovea).

**Zone 2:** Defined by a circle whose radius is the distance from the centre of the optic disc to the nasal margin of the retina (ora serrata)

**Zone3:** The remainder of the retina. This is crescent-shaped zone that largely involves temporal retina.

# CLASSIFICATION - ICROP 2005

## II SEVERITY – STAGING OF ROP

- STAGE-1:
  - a thin, sharp **line of demarcation** between vascularized central retina and more peripheral avascular retina
- STAGE-2:
  - an **intraretinal** elevation (**ridge of fibrovascular tissue**) at the junction between vascularized and avascular retina
- STAGE-3:
  - a **ridge with extra-retinal fibrovascular extension** into the vitreous

# CLASSIFICATION - ICROP 2005

- STAGE-4: Partial retinal detachment (fibrovascular tissue pulls the retina)
  - 4A: does not involve the fovea (better vision)
  - 4B: involves the fovea (poor vision)
- STAGE-5: Total retinal detachment (funnel shaped retina)

## III-EXTENT

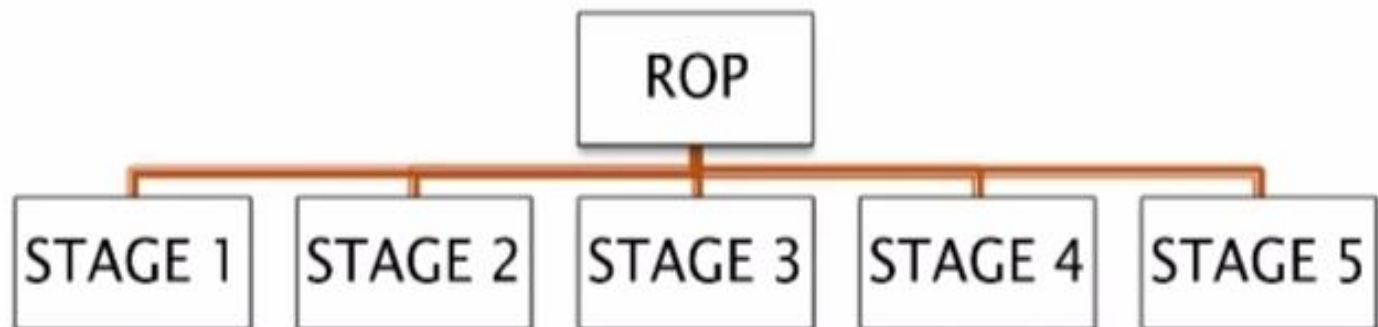
- Number of clock hours of ROP along the circumference of the vascularized retina
- No longer used for treatment decisions



# Staging of ROP



- ▶ The condition has been divided into active ROP and cicatricial ROP.
- ▶ Clinically the evolution of the active ROP has been divided into five stages



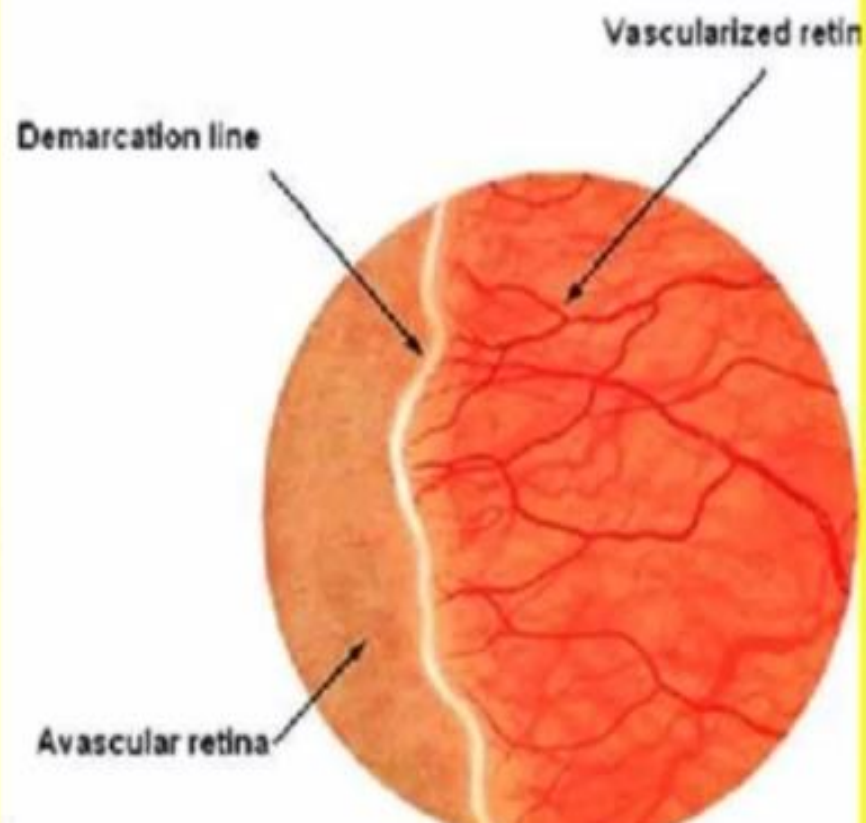


# Stage 1 (Demarcation Line)

- ▶ It is characterised by formation of a **demarcation line** dividing the vascular from the avascular retina.
- ▶ It is a thin, flat, tortuous, grey–white line running roughly parallel with the ora serrata.
- ▶ It is more prominent in the temporal periphery.



# Stage 1 ROP



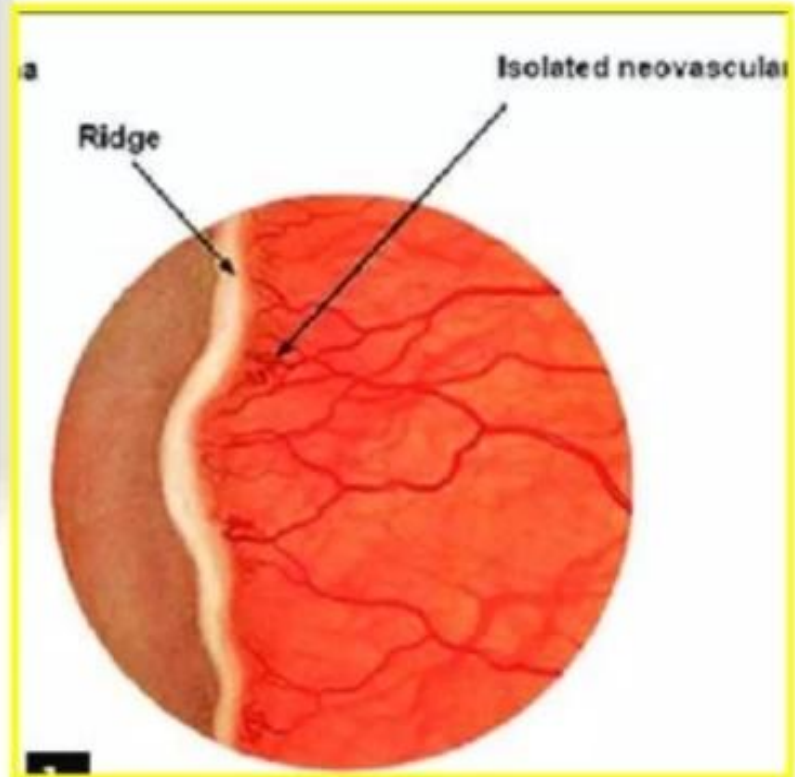
## Stage 2 (Ridge Formation)



- ▶ Ridge arises in the region of the demarcation line
- ▶ Ridge is a scar tissue
- ▶ It has height and width, and extends above the plane of the retina.
- ▶ Blood vessels enter the ridge and small isolated neovascular tufts may be seen posterior to it




# Stage 2 ROP

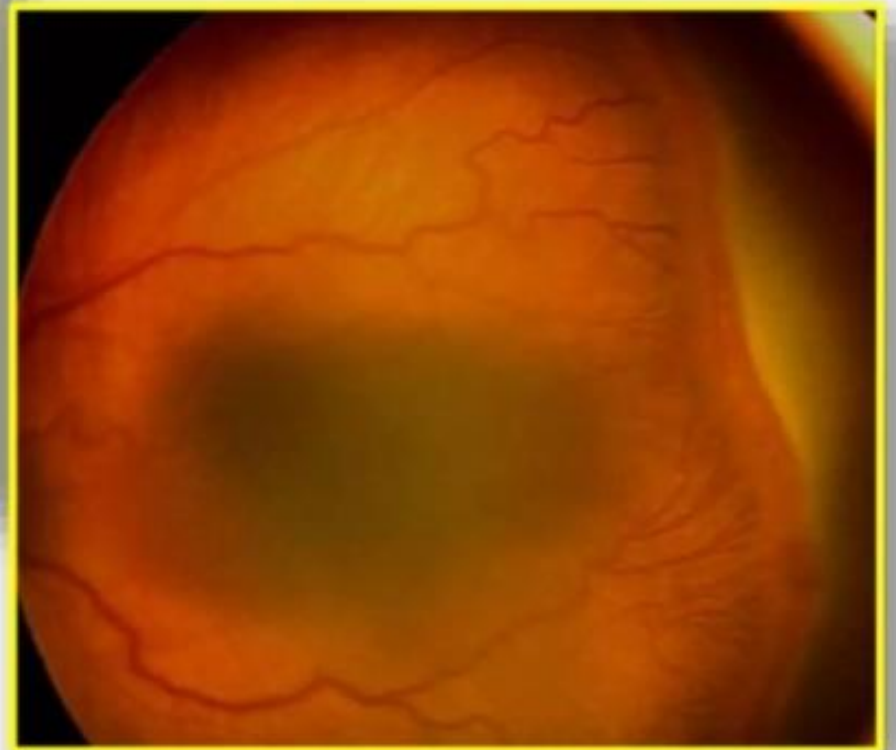




## Stage 3 (Extraretinal Fibrovascular Proliferation)

- ▶ It is characterised by a ridge with extraretinal fibrovascular proliferation into the vitreous.
  - ▶ This stage is further subdivided into mild, moderate and severe, depending on the amount of fibrovascular proliferation.
  - ▶ The highest incidence of this stage is around the post-conceptual age of 35 weeks
- 

# Stage 3 ROP





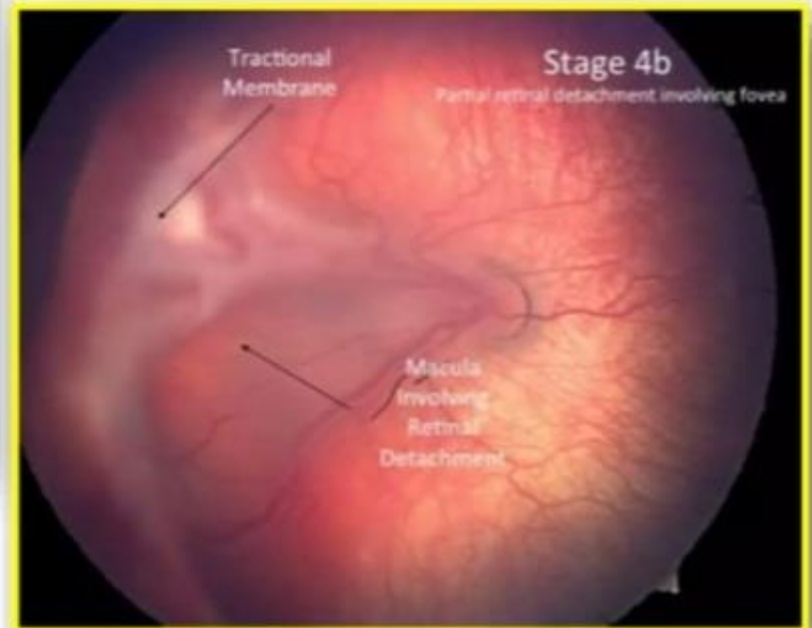
## Stage 4 (Sub total RD)



- ▶ It is a stage of subtotal retinal detachment
- ▶ Sub divided into stage 4a and stage 4b
- ▶ Stage 4a: It includes subtotal retinal detachment not involving the macula.
- ▶ Stage 4b: It includes subtotal retinal detachment involving the macula



# Stage 4 A and B ROP



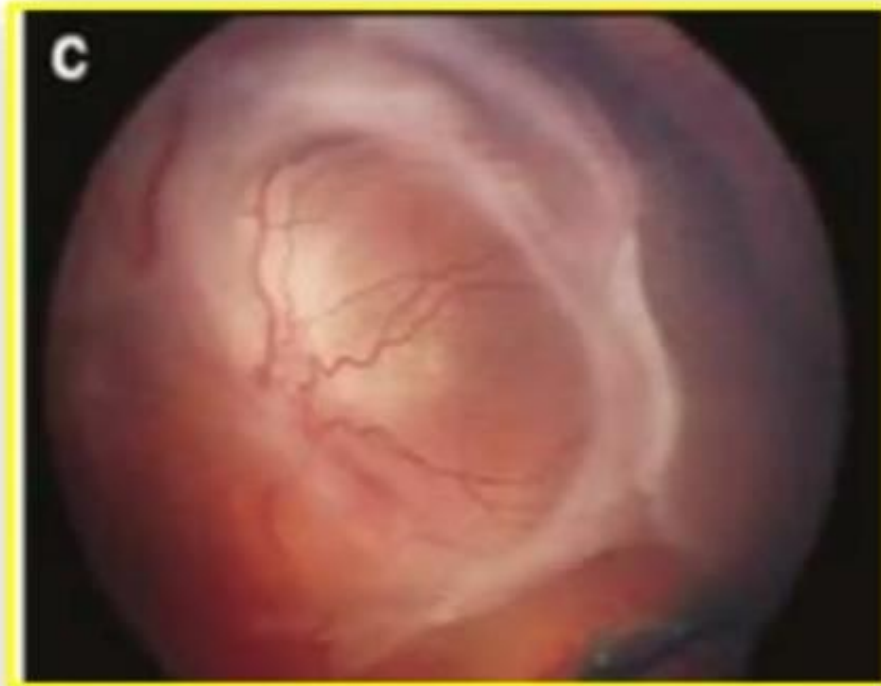
# Stage 5 (Total RD)



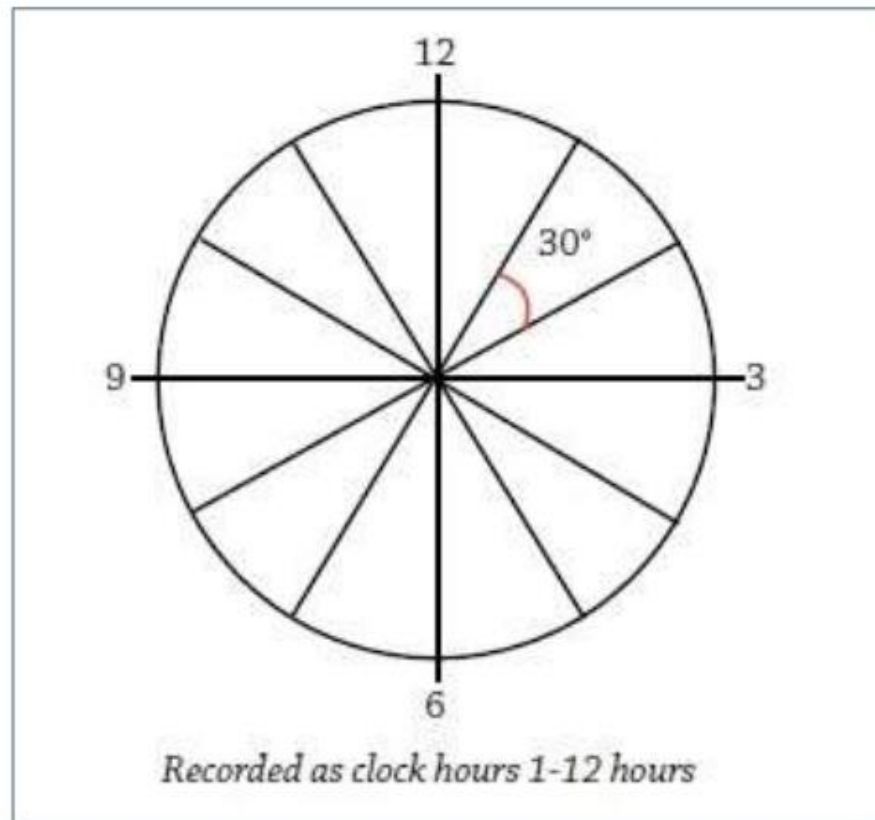
- ▶ It is marked by total retinal detachment which is always funnel-shaped.
- ▶ RD is due to exudation from poorly developed new vessels
- ▶ RD can also be due to fibro vascular traction



# Stage 5 ROP



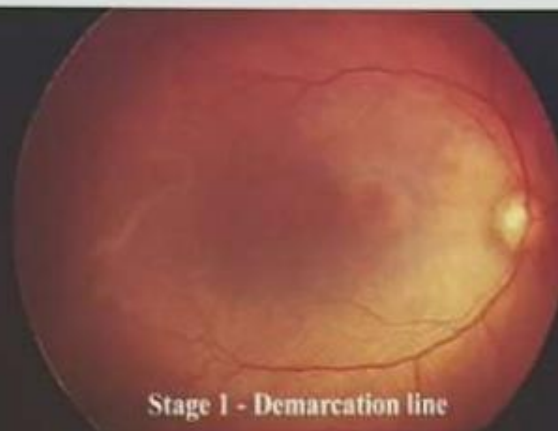
- **Disease extent**
- Disease extent is recorded as clock hours 1-12 hours or as twelve  $30^\circ$  sectors or  $360^\circ$
- The clock hours recorded is the total clock hours involved, not just the contiguous sectors.







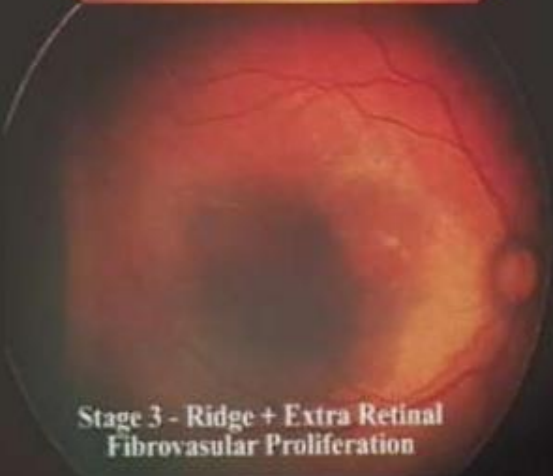
Normal Retina



Stage 1 - Demarcation line



Stage 2 - Ridge



Stage 3 - Ridge + Extra Retinal  
Fibrovascular Proliferation



Stage 4a - Partial Retinal Detachment  
with Foveal Sparing



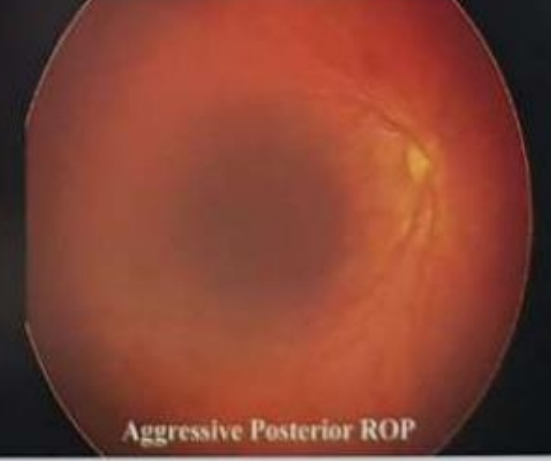
Stage 4b - Partial Retinal  
Detachment involving the Fovea



Stage 5 - Total Retinal Detachment

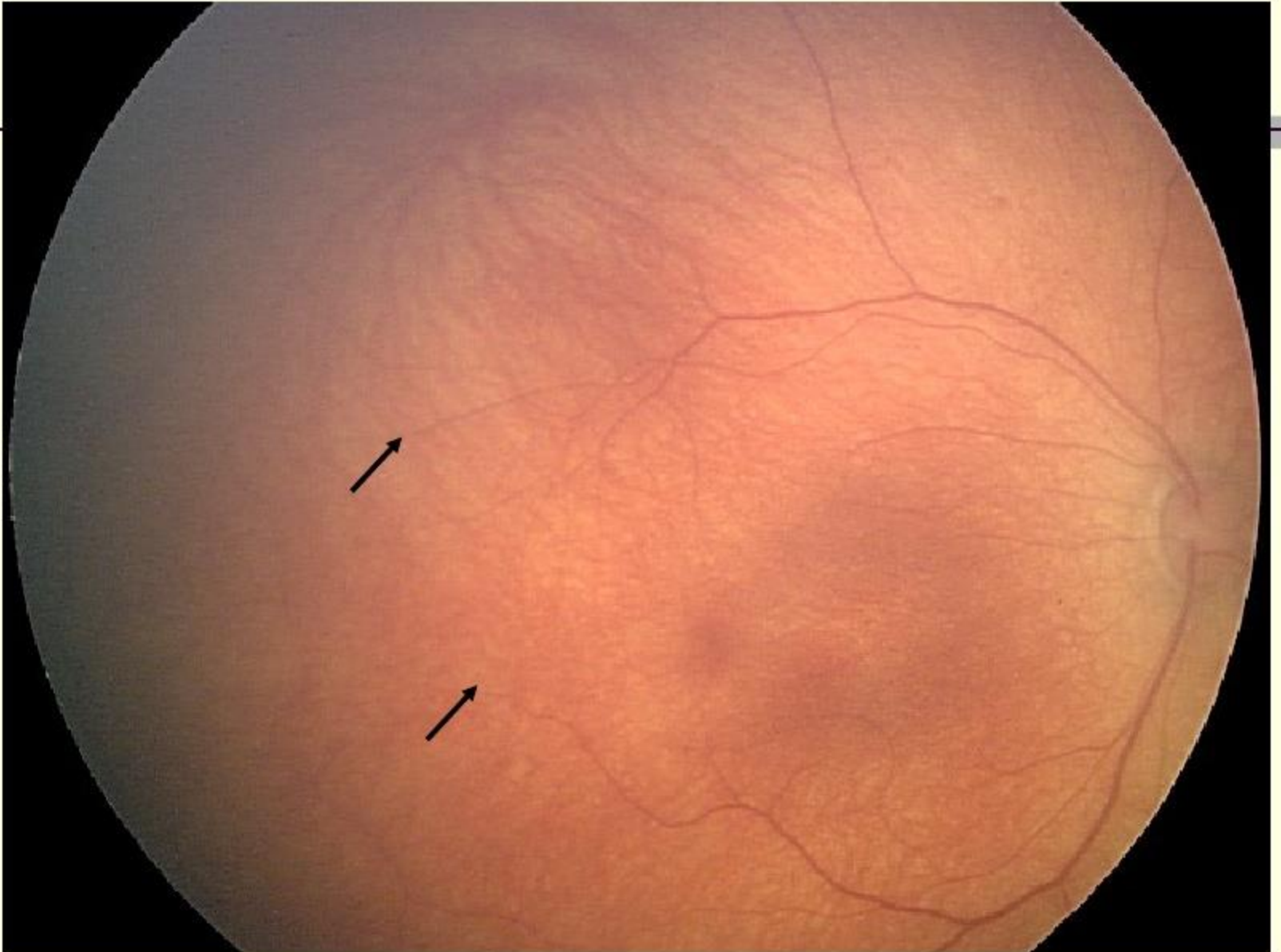


Plus Disease



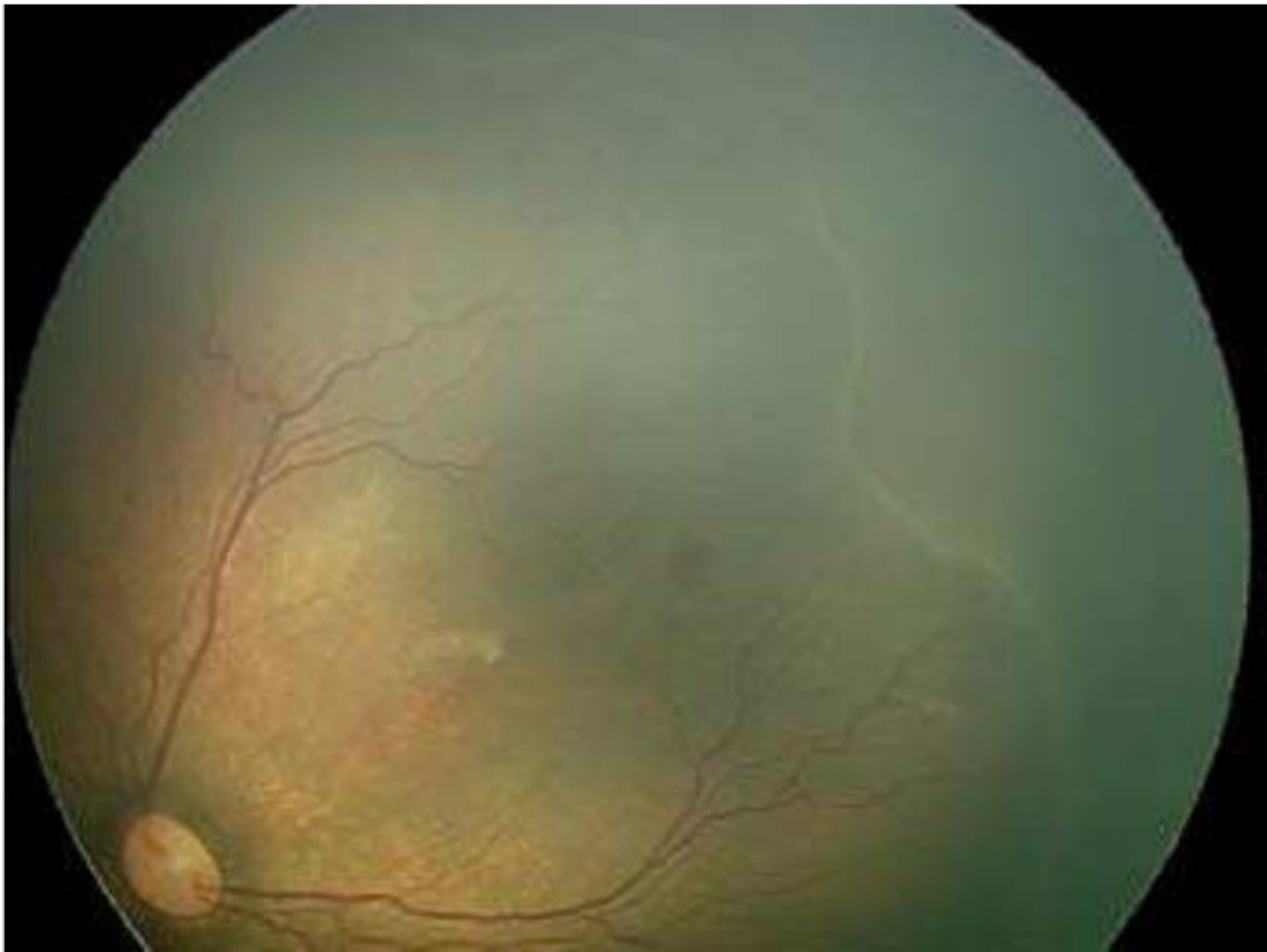
Aggressive Posterior ROP

# Immature retina

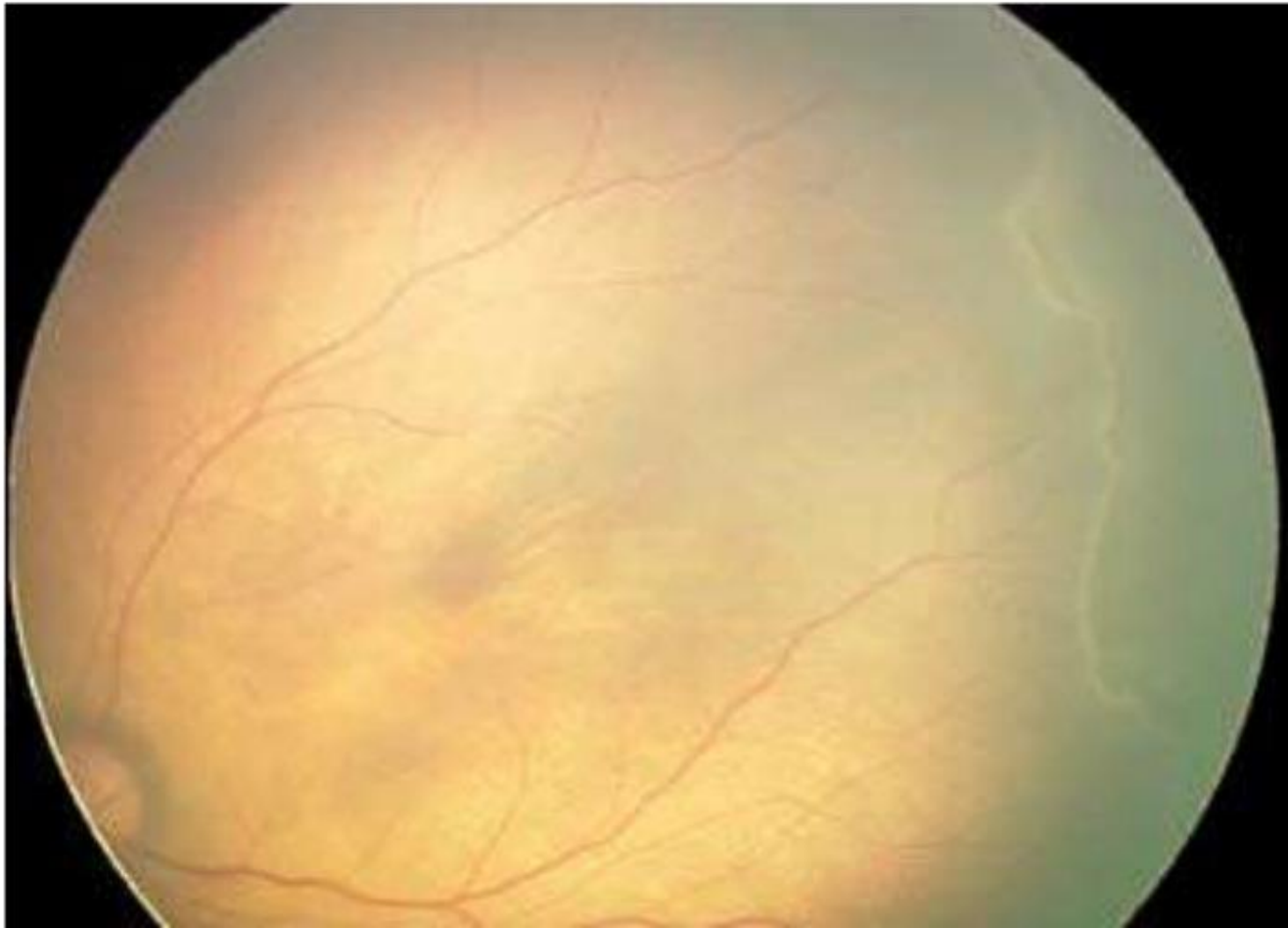


Retinal vessels taper

- **Stage 1. Demarcation line**
- A thin but definite structure separating the avascular retina anteriorly from the posteriorly vascularized retina.

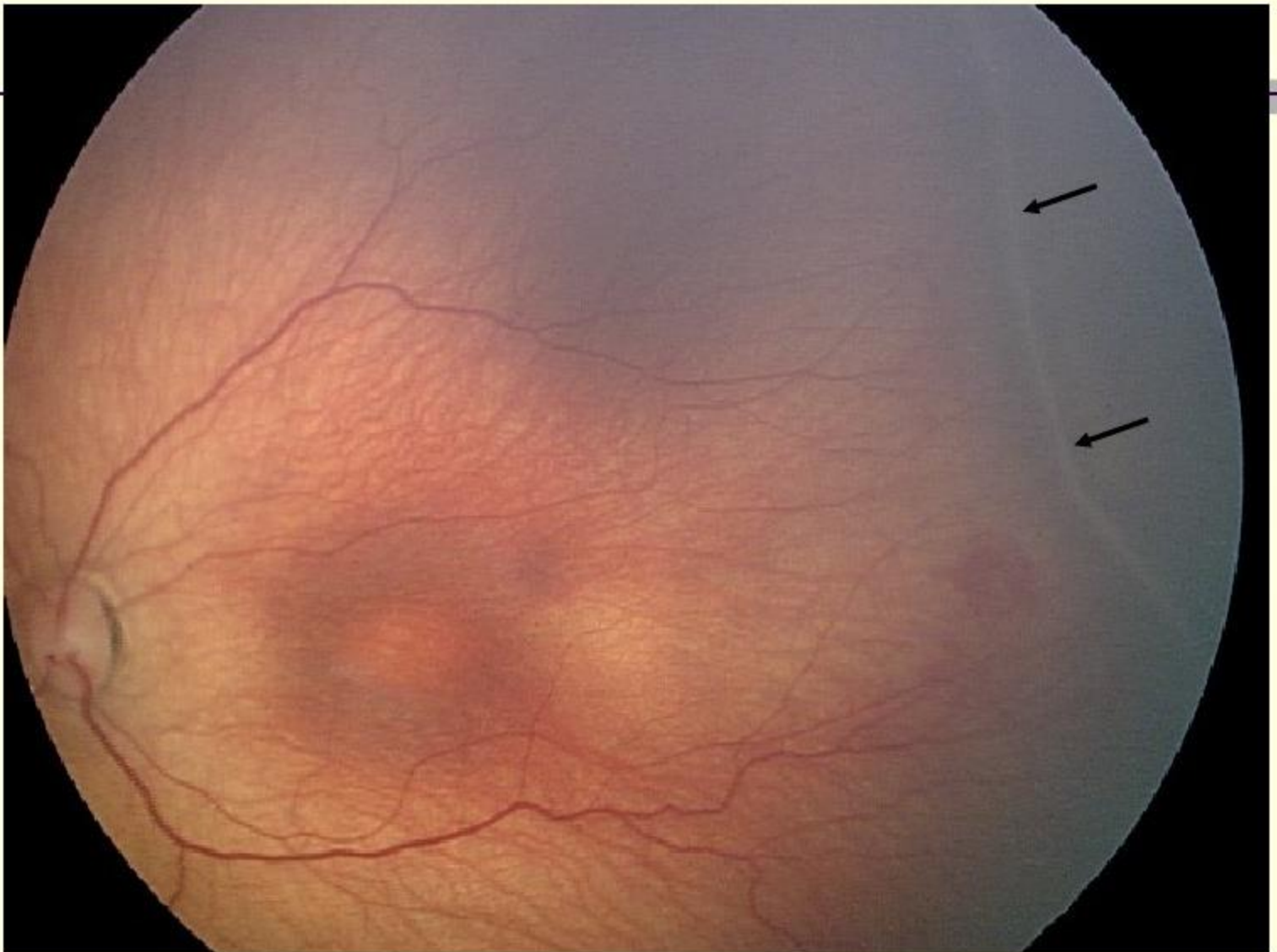


- **Stage 2. Ridge**
- A ridge arising from the demarcation line which has 3 dimensions (height and width) and extends above the retina.





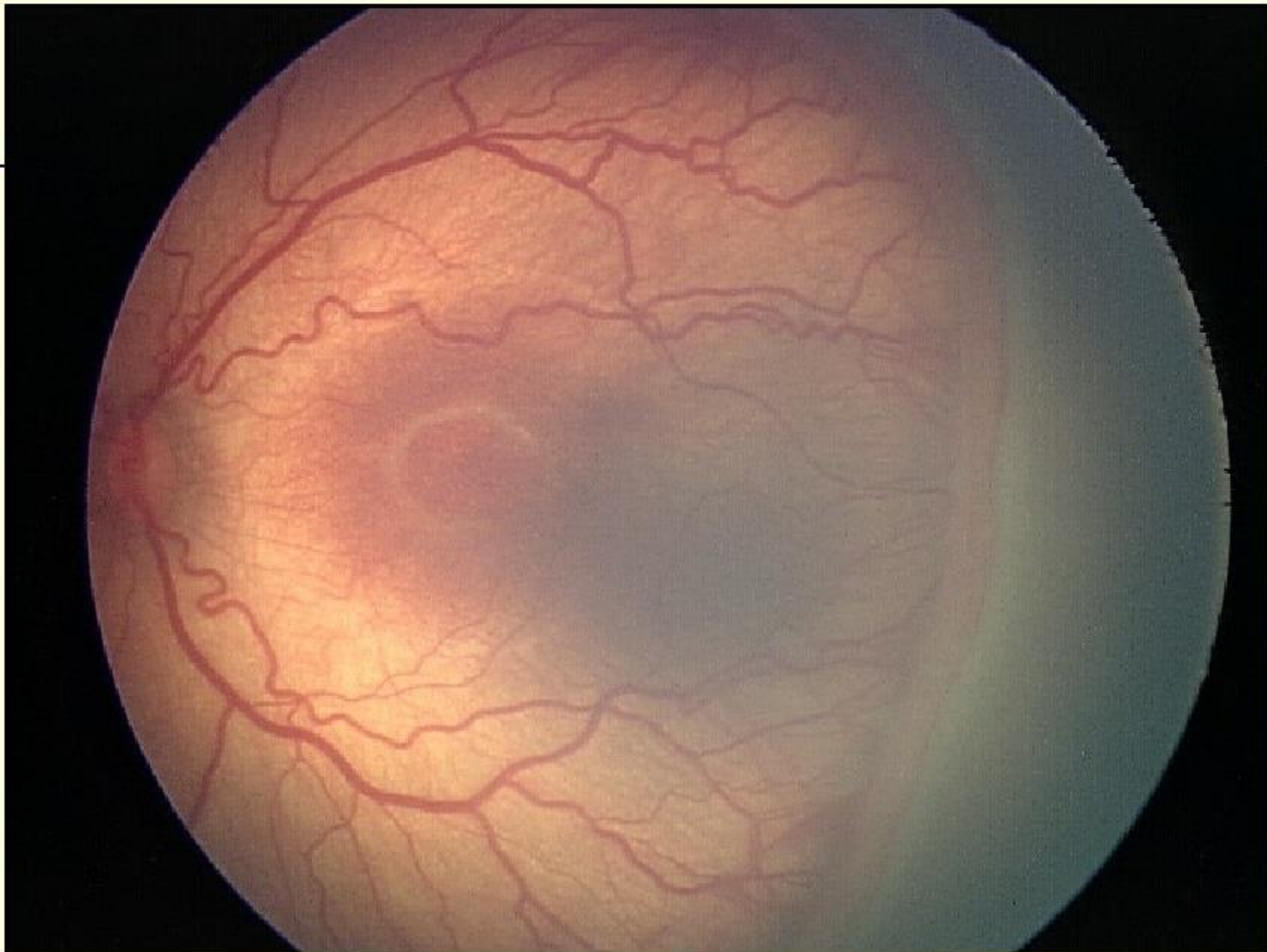
## Stage 2: Ridge



Ridge occupies volume



### Stage 3: Ridge + Epiretinal Fibrovascular Proliferation



Arborization of vessels into EFP lesion

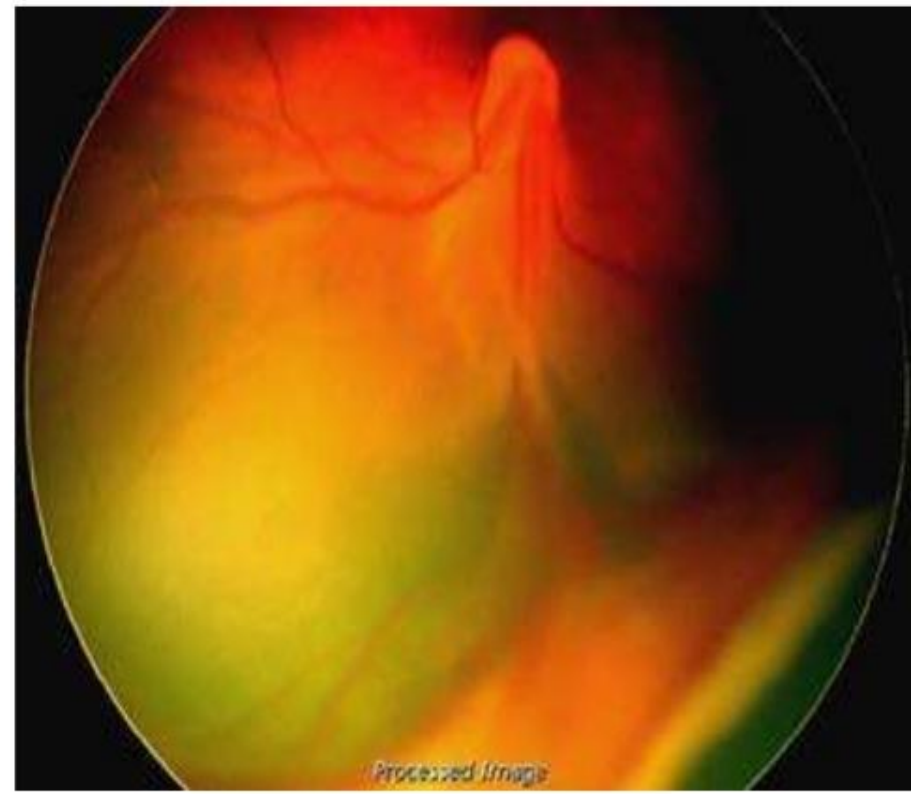
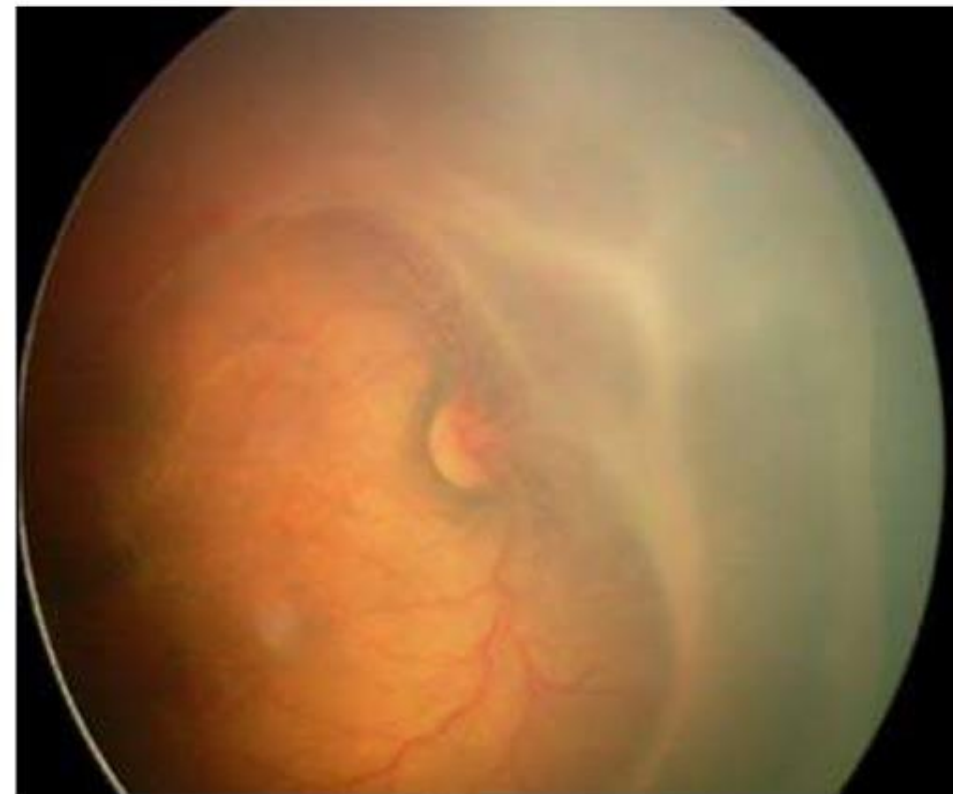
- **Stage 3. Extra retinal fibro vascular proliferation**
- Extra retinal fibro vascular proliferation or neovascularization extends *into the vitreous* from the ridge.



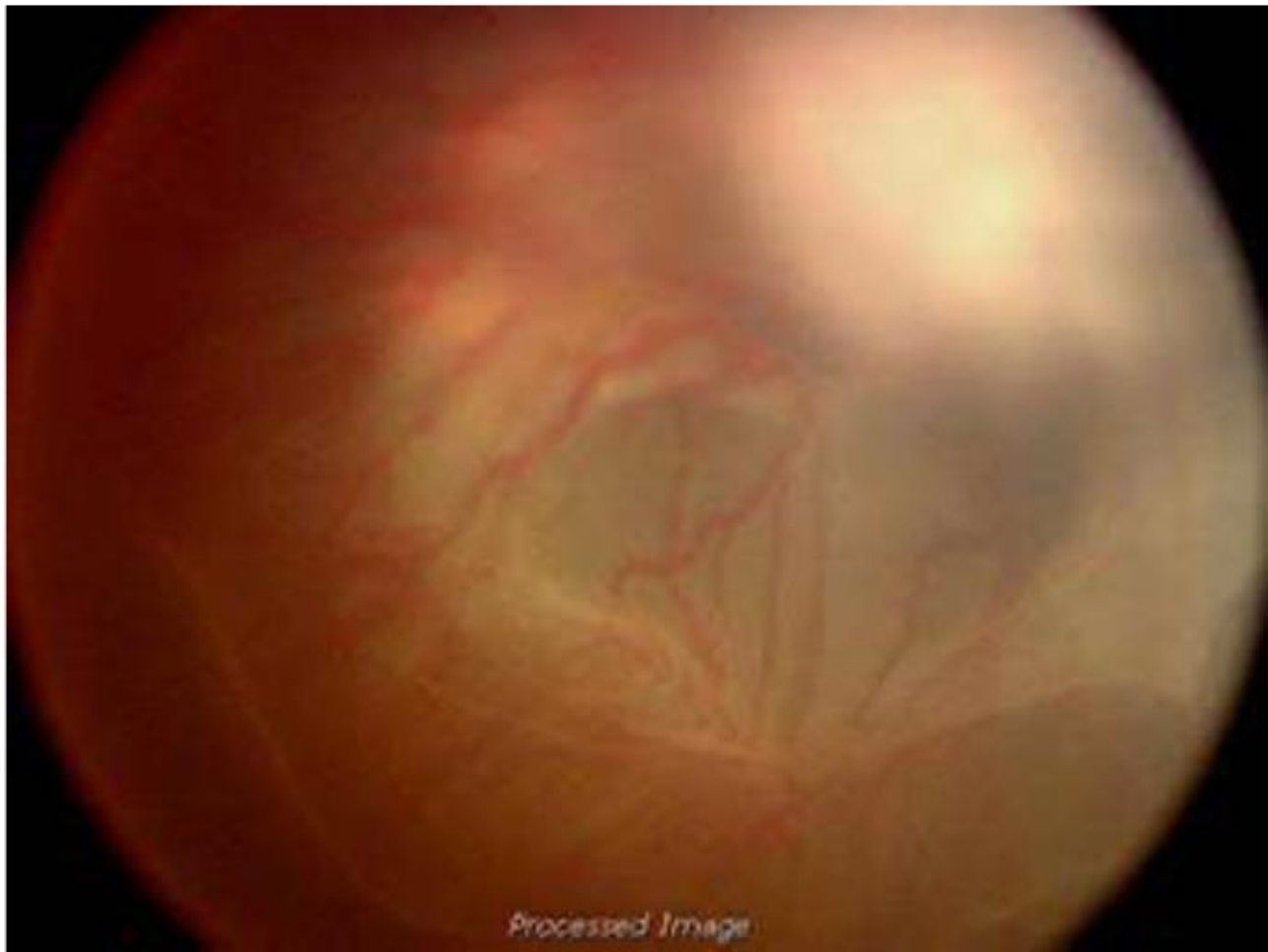
- **Stage 4. Partial retinal detachment**

- 4A: Extra foveal

4B: Foveal



- **Stage 5. Total retinal detachment**
- Retinal detachments are generally tractional but may occasionally be exudative.
- They are usually funnel-shaped.





## Rop: Stages

## Description

Stage 1

Demarcation Line

Stage 2

Ridge

Stage 3

Ridge with Extra Retinal

Mild / Moderate / Severe

Fibrovascular Proliferation

Stage 4

Subtotal Retinal Detachment

A

A. Not Involving Macula

B

B. Involving Macula

Stage 5

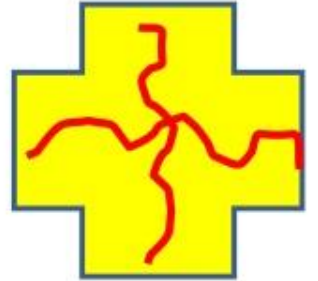
Total Retinal Detachment



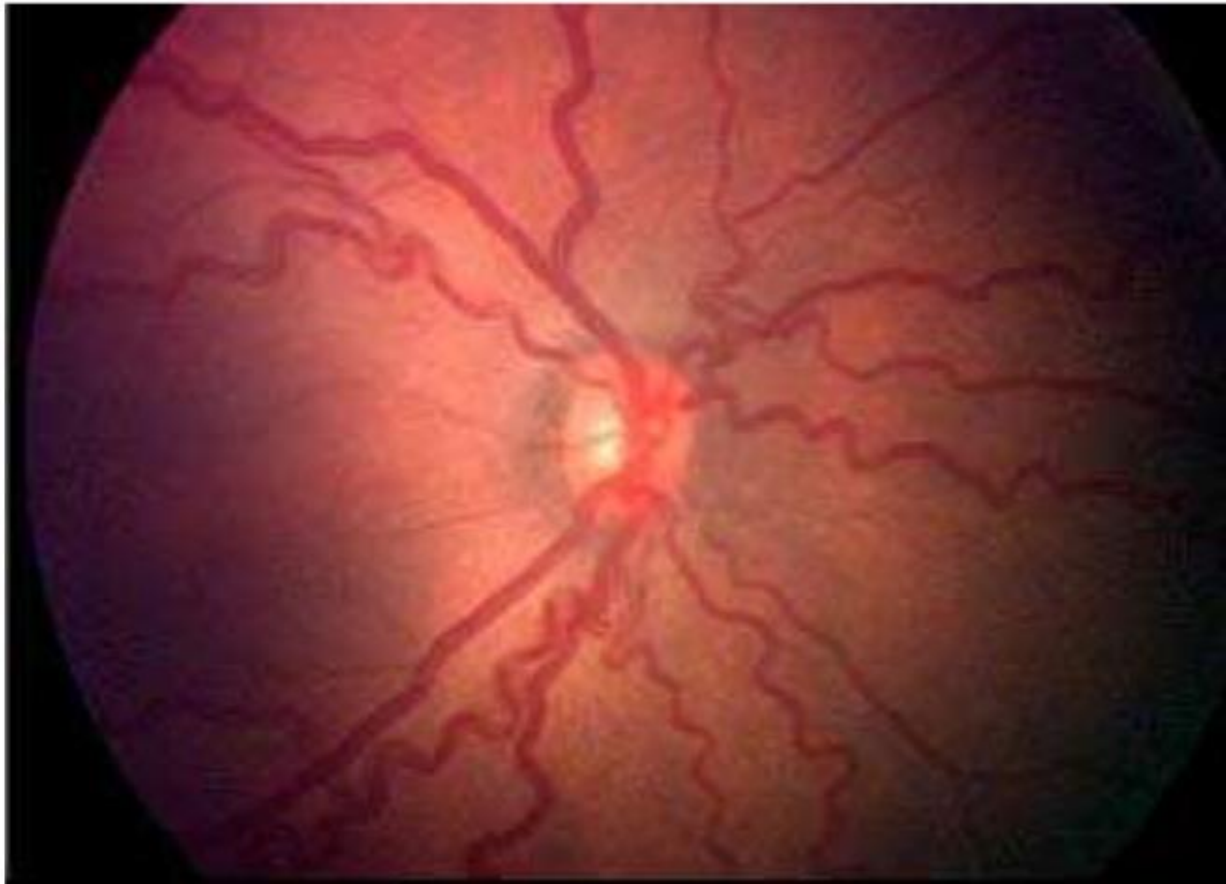
# INTERNATIONAL CLASSIFICATION FOR RETINOPATHY OF PREMATURITY (ICROP)

- ◎ Four features are evaluated:
  - Zone (1-3)
  - Stage (1-5)
  - Extent
  - Presence or absence of plus disease

- **Plus disease**
- Plus disease can be present as a *major complicating factor at any stage.*
- It is characterized by:
  - 1. Significant level of **venous** dilation and
  - 2. **Arteriolar** tortuosity of the **Posterior** retinal vessels.  
(This reflects the increase of blood flow through the retina)
- **Two quadrants** of the eye retina must be involved for the changes to be characterized as plus disease.
- Associated changes may include:
  - Iris vascular engorgement
  - Poor pupillary dilatation (rigid pupil)
  - Vitreous haze and anterior chamber haze



- **Plus disease**
- It is characterized by:
  - 1. Significant level of **venous** dilation and
  - 2. **Arteriolar** tortuosity of the posterior retinal vessels.(This reflects the increase of blood flow through the retina)



- **Pre-plus disease**

- Pre-plus disease indicates posterior pole tortuosity and dilatation that are not sufficiently abnormal to reach the criteria of plus disease, but is nevertheless greater than that regarded as normal.

(More than normal, less than Plus)

- 2. Pre-plus disease may or may not progress to plus disease.



- Preplus disease:

Abnormal vascular dilation and tortuosity that is insufficient for diagnosis of plus disease present in two or more quadrants





- **Aggressive, Posterior ROP (AP-ROP)**
- This is an uncommon, rapidly progressive, and severe form of ROP that has previously been referred to as “Rush disease”.
- It usually occurs in the **smallest, most immature infants**.
- Untreated, it usually progresses to Stage 5 ROP.
- **Characteristic features are:**
  - 1. **P**osterior location,
  - 2. **P**rominence of **P**lus disease, and
  - 3. **Ill-defined, mild-appearing, easily over-looked retinopathy at the junction** between the avascular and vascular retina.

**PP junction- mild**

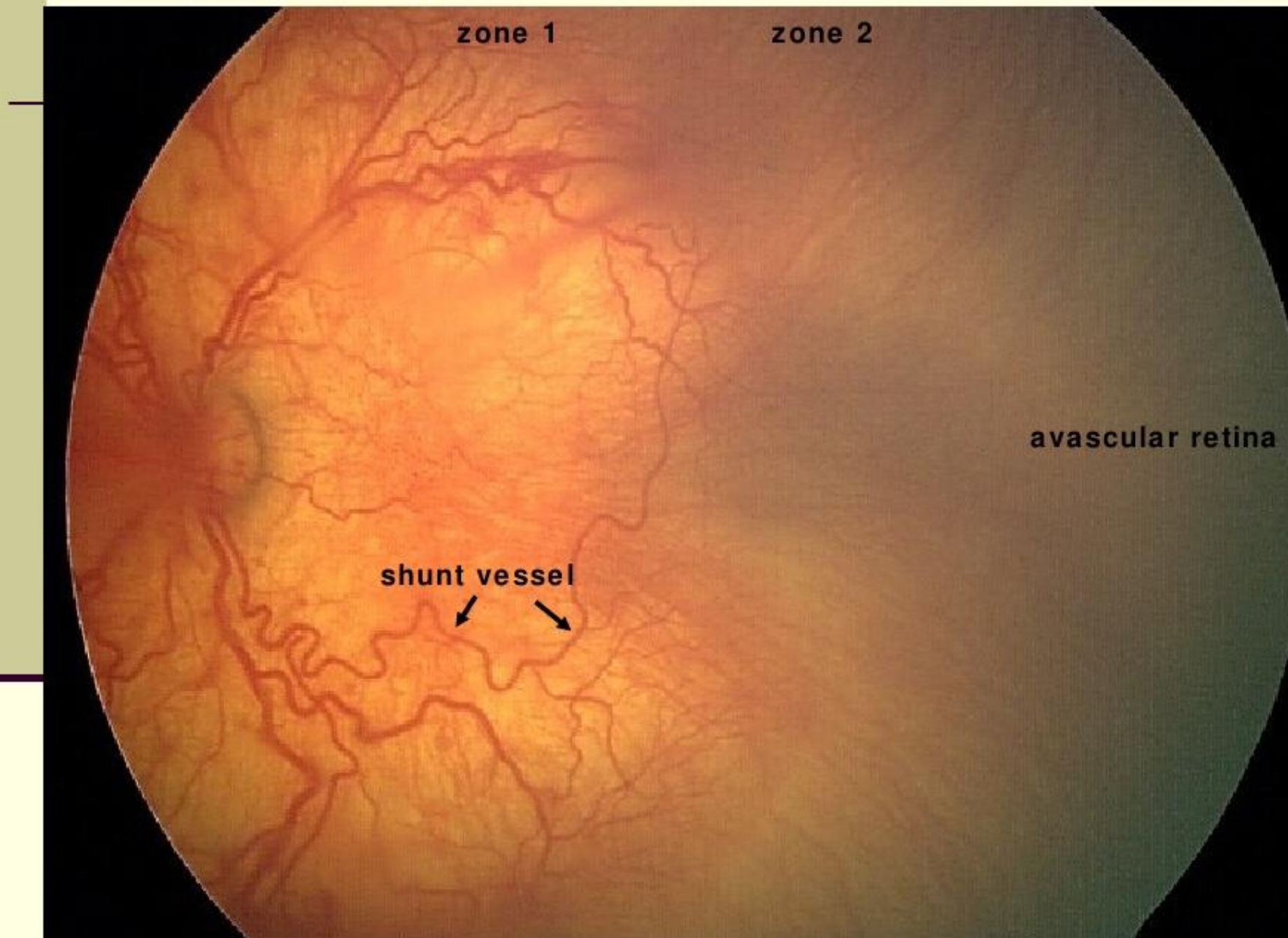
- **Aggressive, Posterior ROP (AP-RO P)**
- This type of ROP is likely to get missed by inexperienced examiners.
- Observed **most commonly in Zone I**, it may also occur in **posterior Zone II**.
- It may not progress through the classic stages 1-3 before retinal detachment occurs.
- *Indirect ophthalmoscopy using a 20-D condensing lens instead of a 25-D or 28-D lens may assist with determining the presence of the featureless neovascularisation characteristic of AP-ROP.*

- **Aggressive, Posterior ROP (AP-ROP)**





# Aggressive Posterior ROP (AP-ROP)







# CLASSIFICATION - ICROP 2005

Status of ROP is determined by

- Highest stage
  - Mild to moderate – Stage I & II
  - More serious - Stage III
  - Emergency – Stage IV & V
- Lowest zone
  - Mild – Zone III
  - Most severe – Zone I & Posterior Zone II
  - Most common – Zone II
- Plus disease - more serious
- Additional serious signs – Vitreous haze, iris vascular engorgement, pupillary rigidity

# CLASSIFICATION - ICROP 2005

- Threshold ROP:
  - $\geq 5$  contiguous or 8 cumulative clock hours (30-degree sectors) of stage 3
  - with plus disease in either zone 1 or 2.
  - This is the level of ROP at which the risk of blindness is predicted to be at least 50% and at which the CRYO-ROP study showed that the risk of blindness could be reduced to approximately 25% with appropriate treatment.

# CLASSIFICATION - ICROP 2005

- Pre-Threshold ROP:
  - **Type 1**
    - In zone 1, any ROP and **plus disease** or stage 3 with or without plus disease
    - In zone 2, stage 2 or 3 ROP **with plus disease**
  - **Type 2**
    - In zone 1, stage 1 or 2 ROP, **without plus disease**
    - In zone 2, stage 3 ROP **without plus disease**

# RISK FACTORS

- ⦿ The most important risk factor for developing ROP is prematurity.
- ⦿ More than 50 separate risk factors have been identified.
- ⦿ On multivariate analysis, low birth weight, low gestational age, assisted ventilation for longer than one week, surfactant therapy, high blood transfusion volume, and cumulative illness severity were independently associated with higher rates of ROP



### PREVENTIVE FACTORS

- Antenatal steroids
- Restrict use of Oxygen
- If baby on Oxygen target SpO<sub>2</sub> between 90-95%
- Use CPAP when required
- Early enteral nutrition (breast milk preferred)
- Aggressive nutrition therapy
- Following aseptic precautions
- Restrictive blood transfusion policy

### AGGRAVATING FACTORS

- Small for gestational age
- Uncontrolled Use of Oxygen
- Patent ductus arteriosus
- Sepsis
- Inadequate weight gain
- Prolonged ventilation
- Transfusion of blood products

The most important risk factor for developing ROP is prematurity.

However, more than 50 separate risk factors have been identified: low BW, low GA, assisted ventilation for >1 week, **surfactant therapy**, high blood transfusion volume, cumulative illness severity, low caloric intake, **hyperglycemia**, insulin therapy have been independently associated with higher rates of ROP.

Breastmilk feeding appears to play a protective role in preventing ROP.



# PREVENTION OF ROP

## DO'S AND DON'TS TO PREVENT ROP

- Avoid iatrogenic premature births
- Stringent regulated use of oxygen
  - Use a pulse-oximeter
    - Soon after the birth
    - During resuscitation
    - Transport to NICU
    - Transport to another facility
    - During NICU stay

# PREVENTION OF ROP

- Aggressive Nutrition
  - Poor postnatal weight gain is a risk factor for ROP
  - Use TPN for all babies <31 weeks / <1250gm
  - Start enteral feeds early or as soon as baby is hemodynamically stable
- Avoid Hypotension
  - Target Mean BP as per norms for GA

# PREVENTION OF ROP

- Target SPO<sub>2</sub> of 88-92%  
always(resuscitation/NICU/transport)
- Avoid large changes in FiO<sub>2</sub> during desaturation episodes n NICU. Increase or decrease by 5% at a time and evaluate each time
- Have a display of Oxygen saturation recommendation on a wall in NICU
- Remember: Sicker the baby, higher is the risk of developing ROP

# PREVENTION OF ROP - STUDIES

- **Lower or more tightly controlled oxygen saturation limits** early in the neonatal course reduce severity of ROP without any adverse effects on mortality, BPD & neurological sequelae.
- **Antenatal Steroids & Surfactant:** Decrease RDS and hence may decrease serious ROP
- **Prophylactic Vitamin E:** Till now no benefit was shown in the trials but further research is warranted
- **Reduction in light exposure:** No clear benefit
- **Administration of penicillamine:** No clear benefit



- Whom to screen

- Screen infants with **either of the following:**
- 1. Birth weight <2000 gm
- 2. Gestational age <34 weeks
- 3. Gestational age between 34-36 weeks with risk factors such as:
  - a) Cardio-respiratory support,
  - b) Prolonged oxygen therapy,
  - c) Respiratory distress syndrome,
  - d) Chronic lung disease,
  - e) Fetal hemorrhage,
  - f) Blood transfusion,
  - g) Neonatal sepsis,
  - h) Exchange transfusion,
  - i) Intraventricular haemorrhage,
  - j) Apneas,
  - k) Poor postnatal weight gain.
- 4. Infants with an unstable clinical course who are at high risk (as determined by the neonatologist or paediatrician).



## • When to screen

- First screening at **4 weeks** of birth.
- Infants with **Gestational age < 28 weeks or < 1.2 Kg birth wt** should be first screened **at 2-3 weeks** after delivery.
- **However, ROP usually does not manifest before 2-3 weeks of PNA.**
- **Treatable ROP rarely occurs before 31 weeks PMA.**
- In Indian context, ROP may be detected even before 32 weeks of PMA .
- **The median age at detection of stage 1 ROP is 34 weeks.**
- Threshold ROP appears at 34 to 38 weeks.
- Vascularization is normally completed by 40 weeks of gestation.

براساس شواهد مطالعات ملی و آیین‌نامه اجرایی وزارت بهداشت اصلاحیه ۱۳۹۴، با سن حاملگی کمتر از ۳۴ هفته (۳۳ هفته و ۶ روز یا کمتر) و یا وزن تولد ۲۰۰۰ گرم یا کمتر، می‌بایست از نظر رتینوپاتی ناری غریب‌الگری شوند. نوزادان متولد شده با سن حاملگی ۲۷ هفته یا بیشتر، می‌بایست ۴ هفته پس از تولد (سن حاملگی اصلاح شده) غریب‌الگری شوند.

جدول سن نوزاد در اولین معاینه

سن حاملگی در زمان تولد (هفته)	زمان اولین معاینه پس از تولد (هفته / روز)
۲۲	۹ هفته پس از تولد یا ۶۳ روزگی
۲۳	۸ هفته پس از تولد یا ۵۶ روزگی
۲۴	۷ هفته پس از تولد یا ۴۹ روزگی
۲۵	۶ هفته پس از تولد یا ۴۲ روزگی
۲۶	۵ هفته پس از تولد یا ۳۵ روزگی
۲۷ و بیشتر	۴ هفته پس از تولد یا ۲۸ روزگی

• همچنین همه نوزادانی که صرف‌نظر از سن حاملگی و وزن تولد، مسیر درمانی پیچیده‌ای را در بخش مراقبت ویژه نوزادان، مانند اکسیژن درمانی و تعویض خون طی می‌کنند، یا وضعیت ناپایدار بالینی داشته باشند و یا توسط پزشک معالج در معرض خطر تشخیص داده شوند، می‌بایست از نظر رتینوپاتی معاینه شوند.

• اولین زمان انجام معاینه شبکیه بر مبنای جدول فوق می‌باشد. با توجه به اینکه برخی مطالعات نشان داده‌اند که در نوزادان بسیار نارس و کم‌وزن یک نوع شدید رتینوپاتی ناری خلفی پیش‌رونده (Aggressive posterior) مشاهده می‌شود، ممکن است براساس تشخیص پزشک نیاز به انجام اولین معاینه در سن کمتری باشد. (۶)

## جدول زمان معاینات پیگیری بر اساس یافته‌های معاینه نوبت قبلی چشم

منطقه شبکیه	Stage of retinal findings	فواصل پیگیری
Zone I	Immature vascularization, no ROP	۱-۲ هفته
	Stage 1 or 2	۱ هفته یا کمتر
	Regressing ROP	۱-۲ هفته
Zone II	Immature vascularization, no ROP	۲-۳ هفته
	Stage 1	۲ هفته
	Stage 2	۱-۲ هفته
	Stage 3	۱ هفته یا کمتر
	Regressing ROP	۱-۲ هفته
Zone III	Stage 1 or 2	۲-۳ هفته



- **NATURAL HISTORY OF ROP:**

- The course of ROP is more correlated with postmenstrual age (PMA) than postnatal age.
- ROP typically begins **approximately 34 weeks PMA**, although it may be seen as early as 30 to 32 weeks.
- **ROP advances irregularly until 40 to 45 weeks (44!) PMA** but resolves spontaneously in the majority of infants.
- Regression of ROP also depends on PMA & location of disease.
- In one report, **involution began at a mean PMA of 38.6 weeks, and before 44 weeks in 90 percent** of patients.



# OPHTHALMIC EXAMINATION



فصل دوم: ارزیابی			
فضای فیزیکی	بلی	خیر	
۱۵ متر مربع فضا به ازای هر یک تخت معاینه			
تهویه مناسب			
سیستم سرمایش و گرمایش مناسب			
درجه حرارت .... درجه			
نور کافی			
درب ورودی به گونه‌ای باشد که انکوباتور یا تخت نوزاد به راحتی وارد و خارج می‌شود.			
سطوح قابل شستشو است			
تجهیزات مورد نیاز	بلی	خیر	تعداد
بلقارو استات			
لنز لوپ			
ست احیای نوزاد			
لنز ۳۰ و ۲۰			
رت کم			
افتالموسکوپ غیرمستقیم به انضمام دوربین و تجهیزات وابسته			
تخت مناسب به ابعاد ۱۲۰*۷۰ سانتی متر			
وارمر			
فور یا اتو کلاو			
پرینتر			
رایانه			
اینترنت پرسرعت			
سامانه ثبت اطلاعات			
مدارک ثبتی			
نیروی انسانی			
چشم پزشک دوره دیده			
پرستار دوره دیده			
منشی			
اپراتور			

- ◎ To dilate pupil: 2.5%Phenylephrine +1% Tropicamide, twice, 10 minutes apart.
  - Watch the pulse and respiration.
- ◎ Screening & Tt. can be done in minor OR/OPD/NICU.
- ◎ Under topical anesthesia without any sedation
- ◎ Indirect ophthalmoscope and a 20 D or 28 D lens.
- ◎ Record the findings

# Examination Techniques



- ▶ Pupillary dilatation with one drop each of cyclopentolate 0.5%, phenylephrine 2%
- ▶ Indirect Ophthalmoscopy with + 20 D







# RETCAM FOR ROP DOCUMENTATION





# MANAGEMENT OF ROP

- ⊙ Screening of at risk babies
- ⊙ Diagnosis
- ⊙ Decision to treat or not
- ⊙ Treatment
  - Tt. of ROP itself ...
    - Cryotherapy ( mostly outdated)
    - Laser treatment (gold standard)
    - Anti-VEGF (adjuvant) before laser and surgery
    - Surgery
  - Correction of systemic factors
  - Rx of ROP related complications
- ⊙ Post treatment follow up
- ⊙ Rehabilitation

# Follow up??



- ▶ Follow-up examinations should be done every 1–2 weeks thereafter until retinal vessels have grown normally into zone III
- ▶ Or until the risk of developing ROP has passed i.e.(about 44 – 46 weeks ).

# TREATMENT

- ⦿ Cryotherapy ( mostly outdated)
- ⦿ Laser treatment (gold standard)
- ⦿ Anti-VEGF (adjuvant) before laser and surgery
- ⦿ Surgery

**Treatment guidelines for ROP adapted from the current ETROP guidelines.**

ZONE 1	NO PLUS	Stage 1	Follow
		Stage 2	Follow
		Stage 3	Treat
	PLUS	Stage 1	Treat
		Stage 2	Treat
		Stage 3	Treat
ZONE 2	NO PLUS	Stage 1	Follow
		Stage 2	Follow
		Stage 3	Follow
	PLUS	Stage 1	Follow
		Stage 2	Treat
		Stage 3	Treat

# CRYO-ROP (1980'S)

- ⊙ RCT (172 infants)
- ⊙ Peripheral Cryotherapy vs. Observation
- ⊙ “Threshold Disease”
  - Stage 3 (neovascularization)
    - 5 contiguous, 8 noncontiguous clock hours
  - Zone I or II
  - Plus Disease
- ⊙ Cryotherapy superior to Observation:
  - Reduced unfavorable outcomes
  - Related improved visual acuity results



# CRYO-THERAPY

- ⦿ Cryotherapy significantly improves the outcome of severe ROP
- ⦿ *Superceded by laser photocoagulation*
- ⦿ Cryotherapy applications are applied contiguously.
- ⦿ Probe placed trans-sclerally anterior to ridge in avascular zone.
- ⦿ End point of cryotherapy is the appearance of mild whitening.
- ⦿ 360 degrees circumference, under direct visualization avoid the ridge.
- ⦿ *Complications of cryotherapy*
  - Eyelid edema, laceration of the conjunctiva, and pre-retinal and vitreous haemorrhage as well as systemic complications like bradycardia, cyanosis and respiratory depression

# ET-ROP (2003)

- ⊙ RCT (n=317 bilateral; n=84 asymmetric unilateral infants)
- ⊙ Early peripheral laser vs conventional treatment
- ⊙ “High Risk Prethreshold” ROP disease - Type 1 or Type 2
- ⊙ Type 1 ROP
  - Zone I: Any Stage, plus / Stage 3, no plus
  - Zone II: Stage 2 or 3, plus
  - Finding: Early Peripheral laser superior to conventional treatment
- ⊙ Type 2 ROP
  - Zone I: Stage 1 or 2, no plus
  - Zone II: Stage 3, no plus
  - Finding: Observation advised until Type 1 or Regression
- ⊙ Peripheral laser better than conventional treatment for Type 1:
  - Reduced unfavorable anatomic outcome from 15.6% to 9.1%
  - Reduced unfavorable visual acuity grating from 19.5% to 14.5%

# *LASER THERAPY*

- ⊙ Procedure of choice, being less invasive, less traumatic and causes less discomfort to the infant.
- ⊙ *Easy to treat posterior located lesion.*
- ⊙ *Argon green and Diode red*
- ⊙ *1500 to 1800 spots, 100 mm size 1½ burn width apart.*
- ⊙ *Entire avascular retina till ora, avoid the ridge.*
- ⊙ *Complications of laser therapy*
  - Burns in cornea and iris. Other complications include cataract, and retinal and vitreous haemorrhage.

# ANTI-VEGF TREATMENT

## ◉ Monotherapy

- Single injections
- Multiple injections for recurrence
- Less desirable if periphery not perfused

## ◉ Adjunctive therapy

- Injections to allow regression beyond Zone 1
  - Laser for recurrent ROP
  - Anti-VEGF as a Bridge to laser peripherally
- Treatment after laser / cryotherapy failure

## ◉ Perioperative therapy before surgery

- Reduce bleeding
- Promote regression of neovascularization
- Vitrectomy and scleral buckles



# BEAT-ROP (2011)

- ⦿ “Bevacizumab Eliminates the Angiogenic Threat in ROP”
- ⦿ RCT (150 infants, 300 eyes)
- ⦿ Stage 3, plus
- ⦿ Zone 1 and posterior Zone 2
- ⦿ Comparison : Intravitreal Bevacizumab v/s Peripheral Laser (ETROP)
- ⦿ Summary
  - Bevacizumab reduced recurrence of ROP
  - Bevacizumab benefit over laser in Zone 1
  - Bevacizumab allowed continued peripheral vascularization into avascular retina

# COMPLICATIONS OF ROP

- ◎ Myopia occurs in about 80% of infants with ROP
- ◎ Strabismus and amblyopia are also common residual findings.
  - 23% to 47% in infants with ROP
- ◎ RD seen in 22% patients.
  - Can occur as early as 6 months up to 31 years from the time of diagnosis
- ◎ Acute angle closure glaucoma can be seen in cicatricial ROP

# CICATRITIAL ROP





