Retinopathy Of Prematurity

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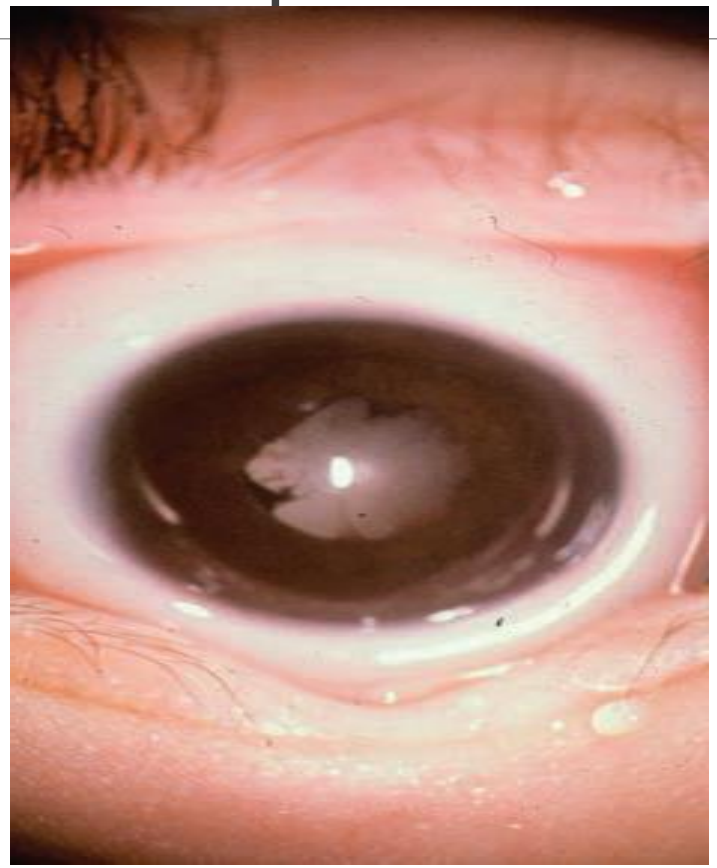
Historty

Was first described in 1942 and quickly became the primary cause of childhood blindness throughout the developed world.

From retrolental fibroplasia to ROP

The discovery of the relationship between supplementary oxygen and ROP in 1950 led to rigid curtailment of oxygen supplementation in the nursery, and a dramatic decrease

Retrolental fibroplasia



Pathophysiology of ROP

- Normally retinal vascularization proceeds from the optic disc to the periphery , begins at week 16 of gestation , and is completed nasally by 36 weeks of gestation , and temporally by 40 weeks gestation .
- The pathophysiology of ROP has 2 phase process :

1 – Cessation of normal retinal vasculature : decrease the level of VEGF and IGF-1

2- the second phase begins at 31-34 weeks postconseptional age : abundance of VEGF and IGF-1 secreted by ischemic retina as well as by the oxidative damage to endothelial cells , which leads to disorganized vascular growth .

Risk factors

Oxygen supplementation

Short gestational period

low birth weight

Genetic predisposition

Intercurrent illness

Blood transfusion

Pco2

Weight gain

Systemic IGF-1 level

Prevalence

Based on 1993 World Health Organization estimates,over 50,000 children are blind from ROP worldwide, with many more with unilateral loss of vision or visual impairment .

In the United States, the incidence of ROP was estimated in the Early Treatment for Retinopathy of Prematurity (ETROP) study to be 68% among infants of <1,251 g, similar to the results seen in the Cryotherapy for Retinopathy of Prematurity (CRYOROP) study, conducted 15 years earlier .

The incidence of ROP increases with decreasing birth weight and has been reported to be 33.2% for infants with birth weight <1,000 g in recent literature, much lower than in the ETROP and CRYO-ROP studies . This may represent a true decrease in the incidence of disease or simply be a reflection of the differences in the methodology of the studies (prospective vs. retrospective).

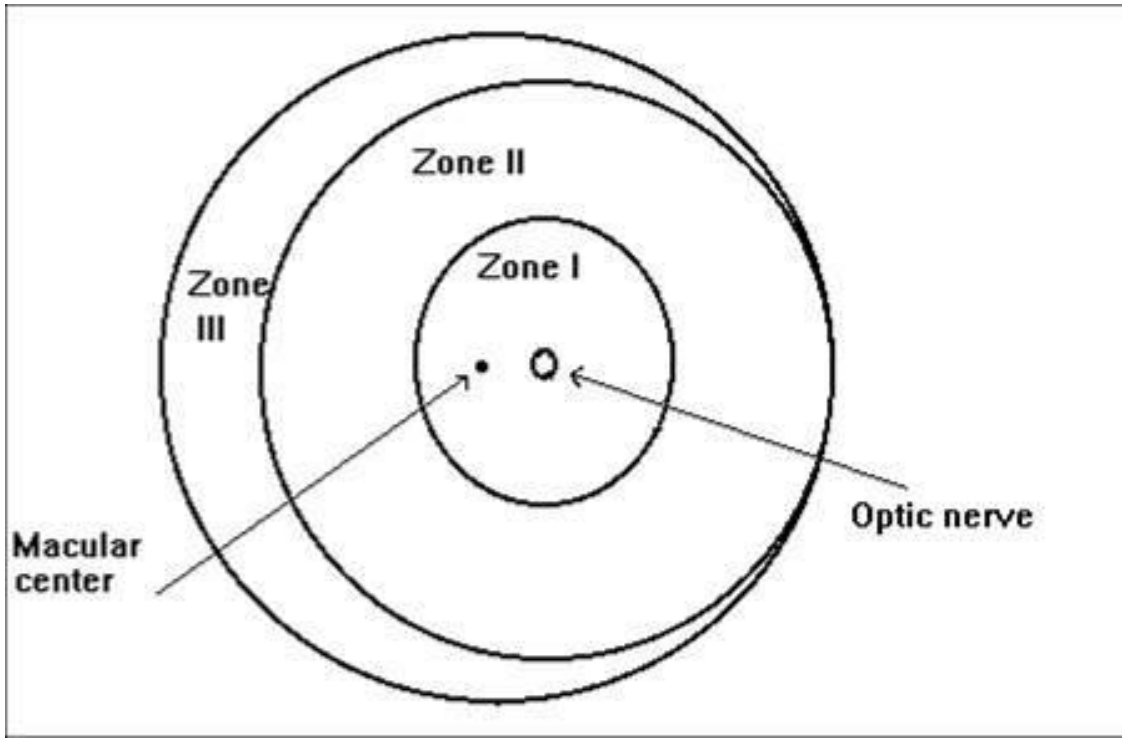
International Classification of ROP

Zone : 1 , 2, 3

Stage : 1 ; 2 ; 3 ; 4A ; 4B ; 5

Extent of stage

Persence of plus disease


Zone II
Zone I
Zone III
Macular center
Optic nerve

Staging of ROP

Stage 1 : A line is apparent between vascular and avascular retina

Stage 2 : there is a ridge having obvious volume

Stage 3 : There is neovascularization growing on to the vitreous at the ridge

Stage 4 : there is partial retinal detachment ; 4A without macular involvement and 4B with macular involvement

Stage 5 : total retinal detachment and is described as close or open

Plus disease

Plus disease refers to dilation and tortuosity of the retinal arterioles and veins in the posterior pole and is based on a standard photograph published in the multicenter trial of CRYO-ROP .

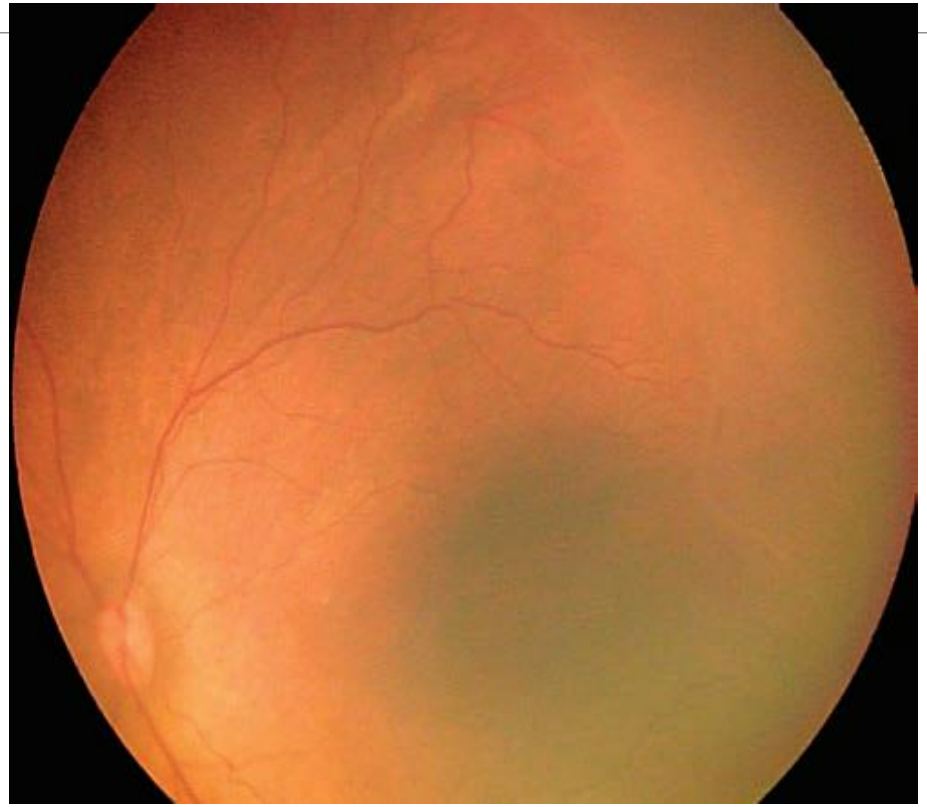
In later clinical trials, the definition of plus disease was modified so that the diagnosis of plus disease could be made if sufficient vascular dilation and tortuosity were present in at least two quadrants .

Pre–plus disease was defined as abnormal dilation and tortuosity of the posterior pole vessels, which is insufficient for the diagnosis of plus disease based on the standard photograph but is more so than normal .

Aggressive posterior ROP

Aggressive posterior ROP (AP-ROP) was defined as aggressive posterior retinopathy observed commonly in zone I or posterior zone II, with dilation and tortuosity of both arteries and veins in all four quadrants that is out of proportion to the peripheral retinopathy. AP-ROP does not usually progress through the classic stages, extends circumferentially, and can be accompanied by a circumferential vessel. Though there may only be a flat neovascularization at the junction of vascularized and nonvascularized retina, this aggressive form of ROP usually progressed to stage 5 if it is not promptly treated .

Stage 1



Stage 2

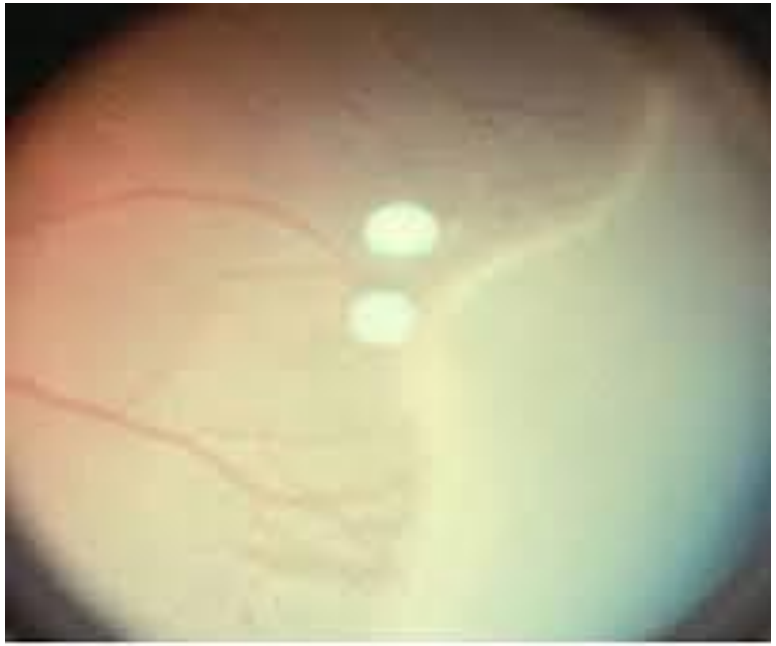
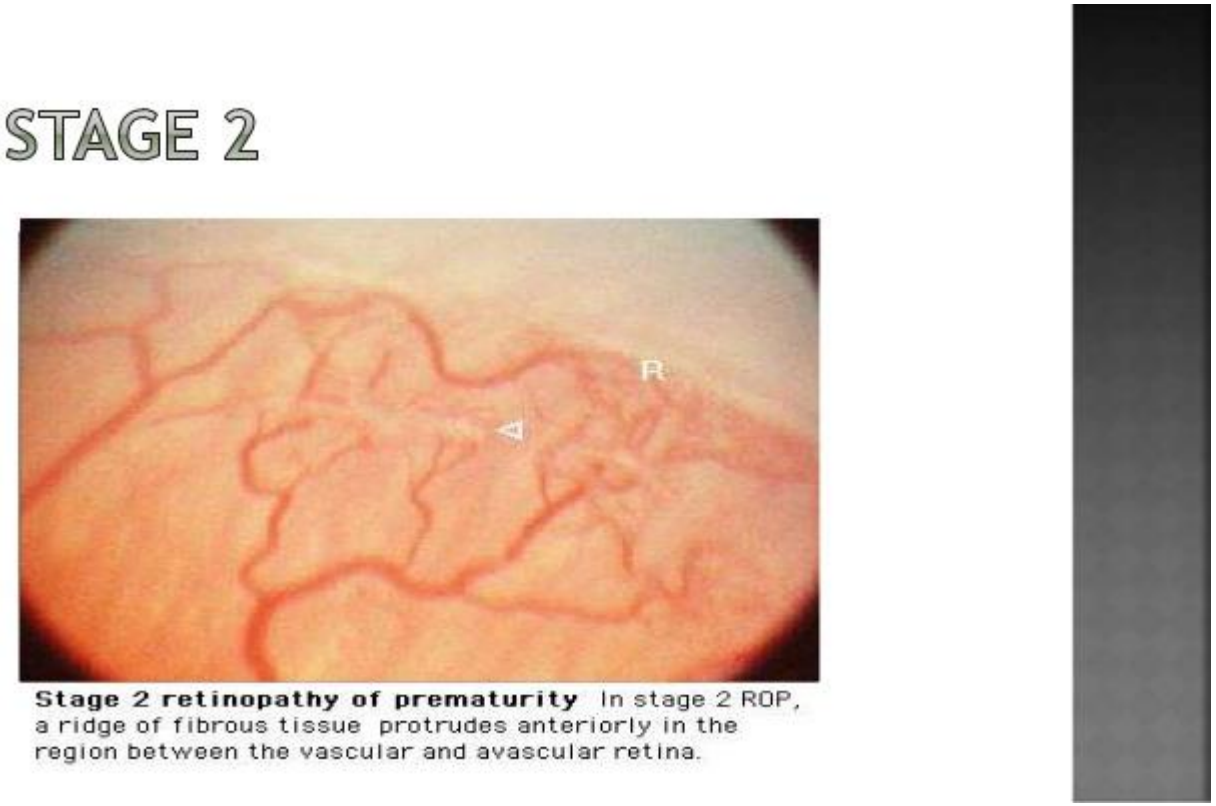
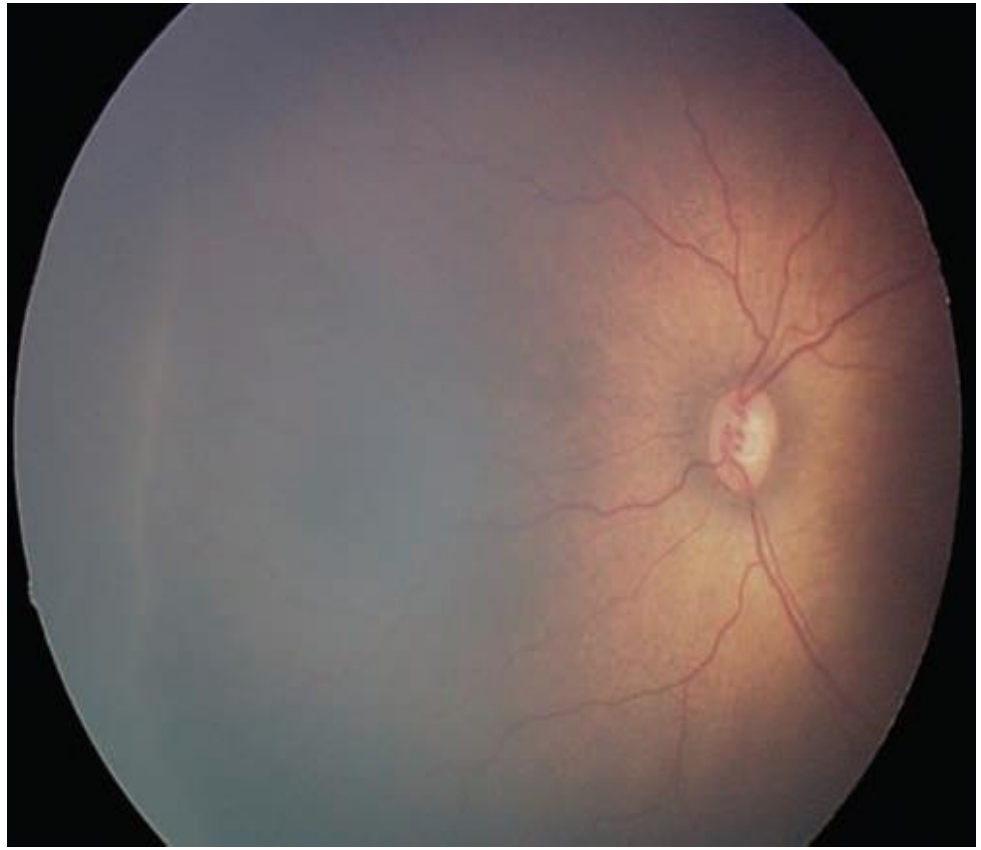


Fig. 2 Stage 2 ROP.

Stage 2

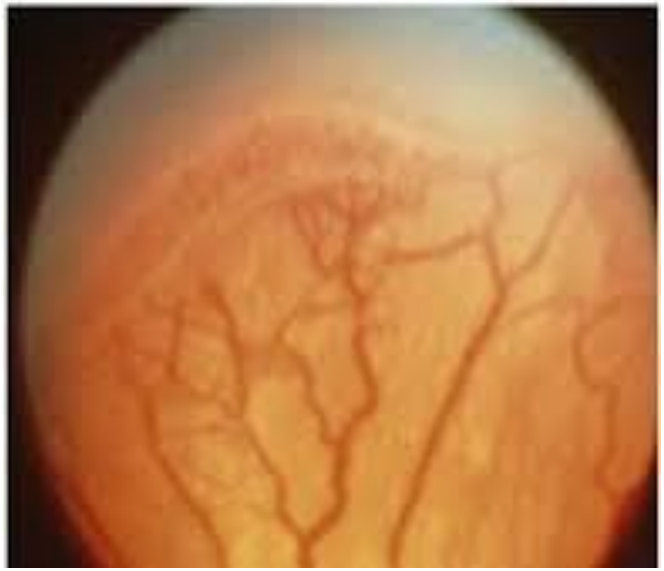

STAGE 2
R
Stage 2 retinopathy of prematurity In stage 2 ROP, a ridge of fibrous tissue protrudes anteriorly in the region between the vascular and avascular retina.

Stage 2

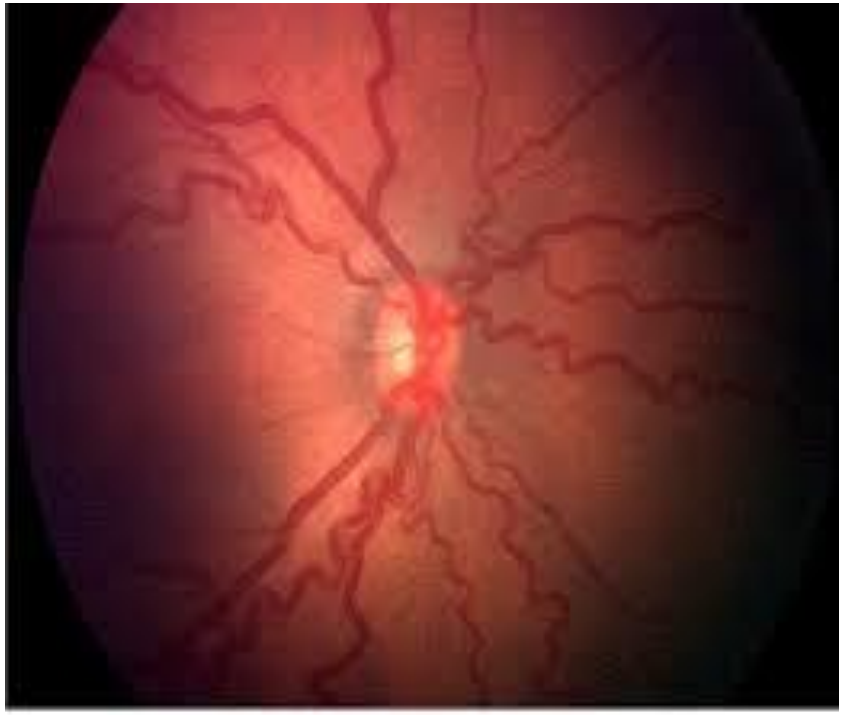


Stage 3

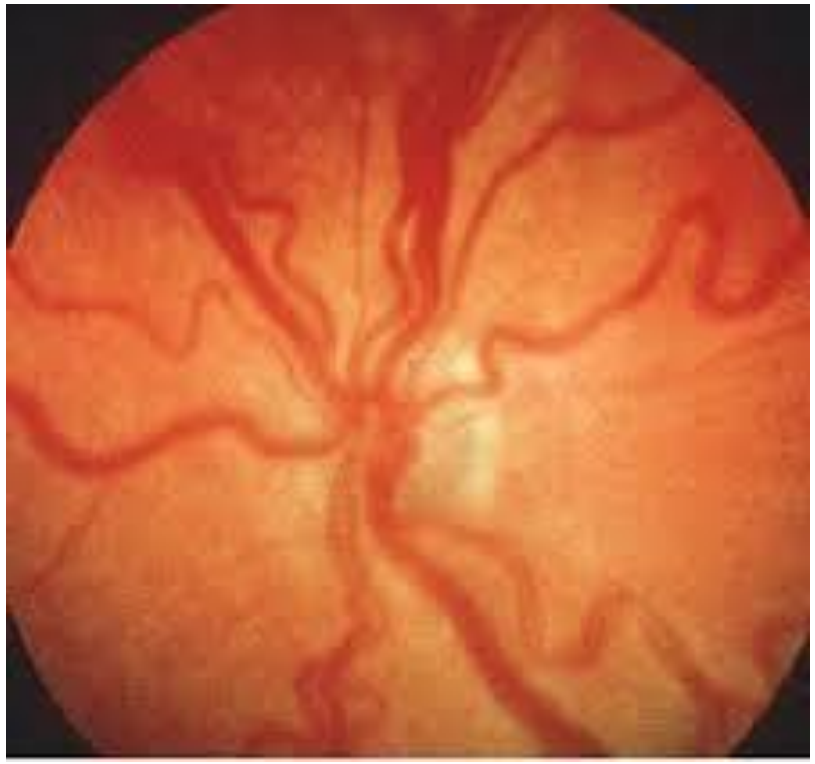
Stage 3

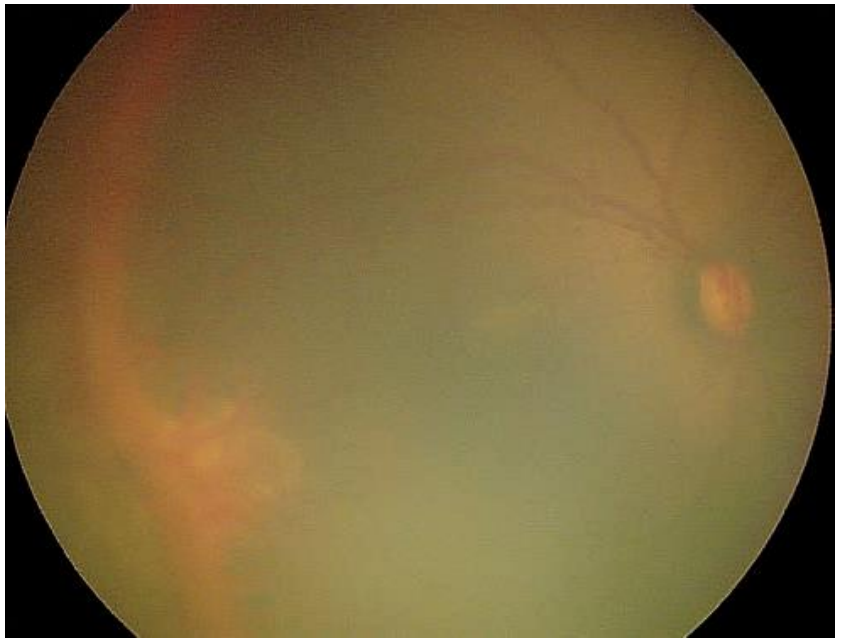


Plus disease



Plus disease





Definitions of prethreshold and threshold ROP

Prethreshold ROP

Zone I, any stage

Zone II, stage 2 with plus disease

Zone II, stage 3 less than threshold

Prethreshold classification used for ETROP trial

Type 1 (high-risk prethreshold where risk of unfavorable outcome is ≥15%)

Zone I, any stage with plus disease

Zone I, stage 3 without plus disease

Zone II, stage 2 or 3 with plus disease

Type 2 (low-risk prethreshold ROP where risk of unfavorable outcome is <15%)

Zone I, stage 1 or 2 without plus disease

Zone II, stage 3 without plus disease

Threshold ROP

Zone I or II, stage 3 (five contiguous or eight total clock hours) with plus disease

Age of onset

Most infants that develop some form of ROP do so at about 32 weeks' postmenstrual age (PMA). PMA equals gestational age plus age after birth in weeks .

Threshold disease, at which the risk of a poor outcome approached 50% , peaks at approximately 37 weeks' PMA and high-risk prethreshold ROP , where risk of a poor outcome is ≥15%, at approximately 35 weeks

Eyes that rapidly progress to prethreshold ROP have a greater risk of developing threshold ROP and will develop threshold disease at an earlier PMA.

When infants achieve 45 weeks' PMA without developing prethreshold ROP, they have a low risk of developing threshold ROP or of having a poor outcome

Time of screening

The first examination should generally be performed :

Between 4-6 weeks of postnatal age or

Between 31 -33 weeks post menstrual age

Whichever is later

Follow up time

1 week or less :

Immature vascularization in zone 1 – no ROP

Immature retina extends into posterior zone 2 ; near the boundary of zone 1

Stage 1 or 2 ROP in zone 1

Stage 3 ROP in zone 2

The presence or suspected presence of aggressive posterior ROP

Follow up time

1-2 weeks

Immature vascularization in posterior of zone 2

Stage 2 ROP in zone 2

Unequivocally regressing ROP in zone 1

2 weeks

Stage 1 ROP in zone 2

Immature vascularization in zone 2 – no ROP

Unequivocally regressing ROP in zone 2

Follow up time

2-3 week

Stage 1 or 2 ROP in zone 3

regressing ROP in zone 3

When can retinal examination be discontinued ?

Criteria for screening

American academy of pediatric : all infants with birth weight of less than 1500 gr or gestational age of 30 weeks or less

In IRAN

All infants with birth weight of less than 2000 gr or gestational age of 34 weeks or less

WINROP algorithm : systemic IGF -1 level and weight gain

Discontinution of retinal screening exam

- Full retinal vascularization in close proximity to the oraserrate for 360
- Zone 3 retinal vascularization attained without pervious zone 1 or 2 ROP
- Postmenstrual age of 50 weeks and no prethreshold disease or worse ROP is present
- Regression of ROP

Course of ROP

Most ROP regresses; however, the disease typically progresses before regressing and this progression can be rapid—in the ETROP study, in infants born weighing <1,251 g, 22% of infants with type 2 prethreshold ROP progressed to type 1 prethreshold and half of these in <7 days .

In about 6% of infants born weighing <1,251 g, threshold ROP develops . Without treatment, this results in an unfavorable outcome in about 52% of eyes at 15-year followup

In the CRYO-ROP trial, approximately 30% of eyes experienced an unfavorable anatomic outcome even after treatment for threshold ROP . Unfavorable visual outcomes were 45% for treated eyes and 64% for untreated eyes, respectively .

However, based on outcome data from the ETROP trial, treatment at a less severe level of ROP, that is, for type 1 prethreshold ROP (type 1 ROP), reduces poor visual and functional outcomes compared to waiting until threshold ROP develops

Differential dignosis

Familial exudative vitreoretinopathy

Norrie disease

Incontinentia pigmenti

Congenital retinal fold

Toxocara canis infection

Causes of leukocoria

Treatment

Crayotherapy of avascular retina

Lasertherapy of avascular retina

Anti-VEGF treatment

Surgery : scleral band

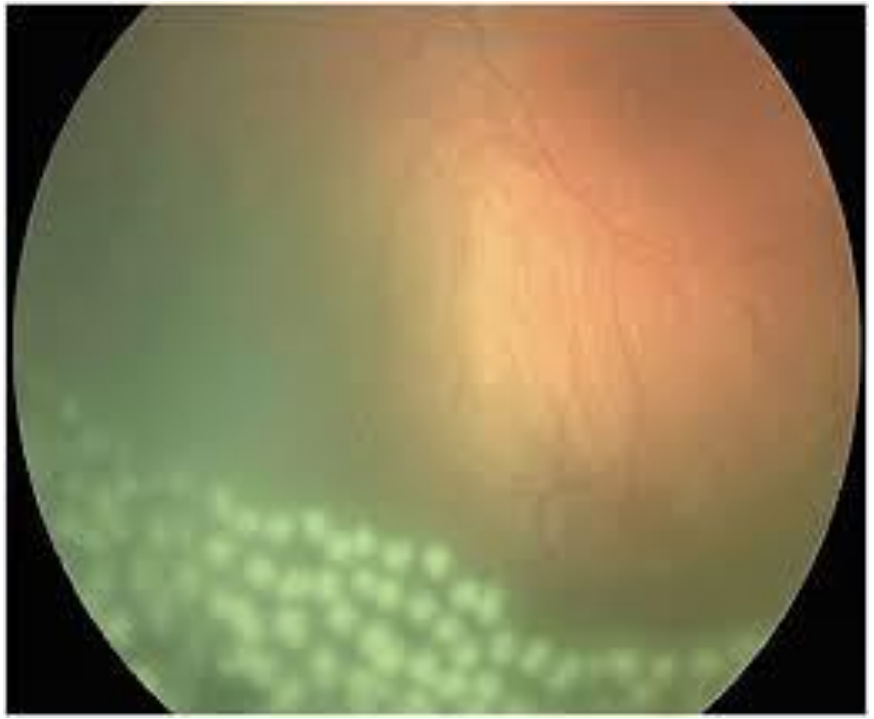
deep vitrectomy

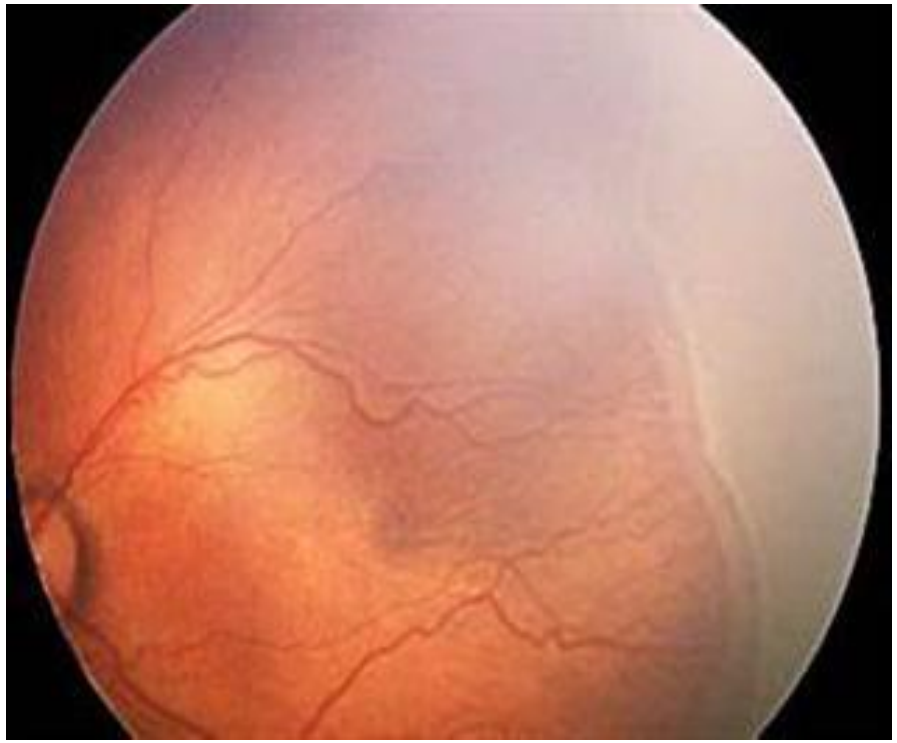
TREATMENT

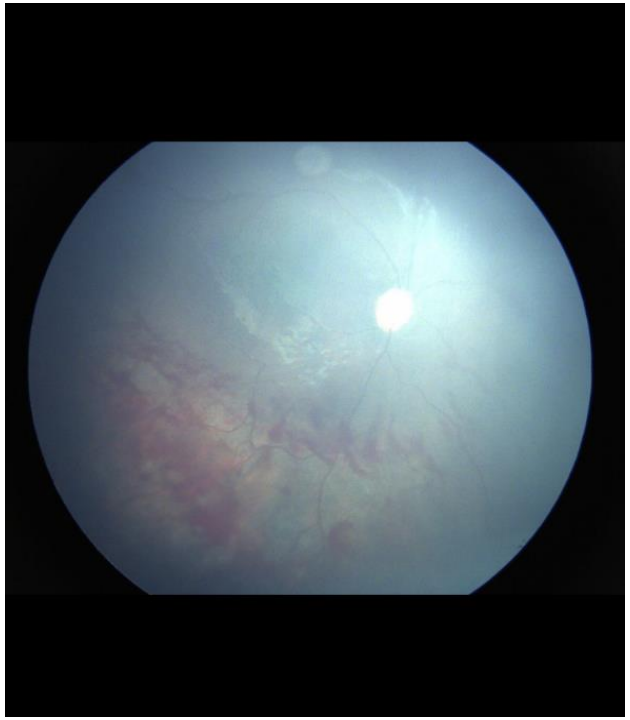
Cryotherapy for ROP : 1988

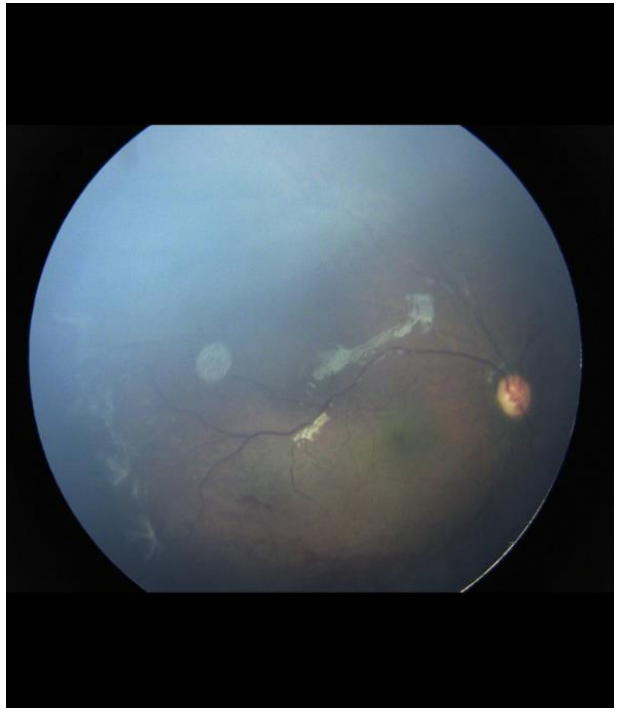
ETROP : laser ablation treatment of avascular retina in type 1 and threshold ROP

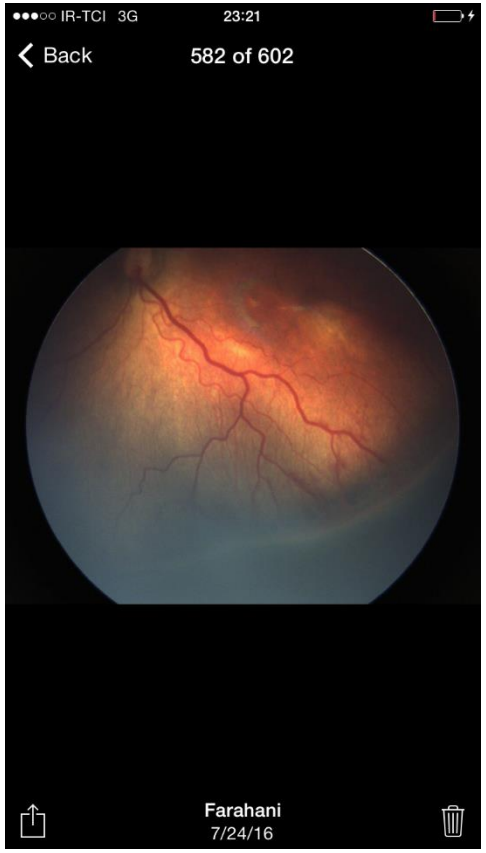
Beat ROP study : compared with conventional laser therapy ; a stastically significant treatment benefit for bevacizumab was demonstrated for zone 1 ROP ; where as zone 2 ROP had similar outcomes with either treatment .







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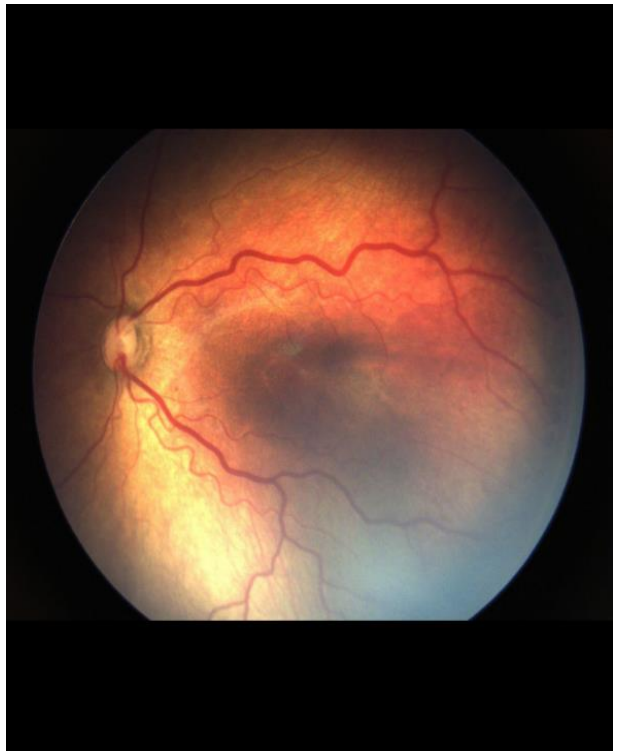

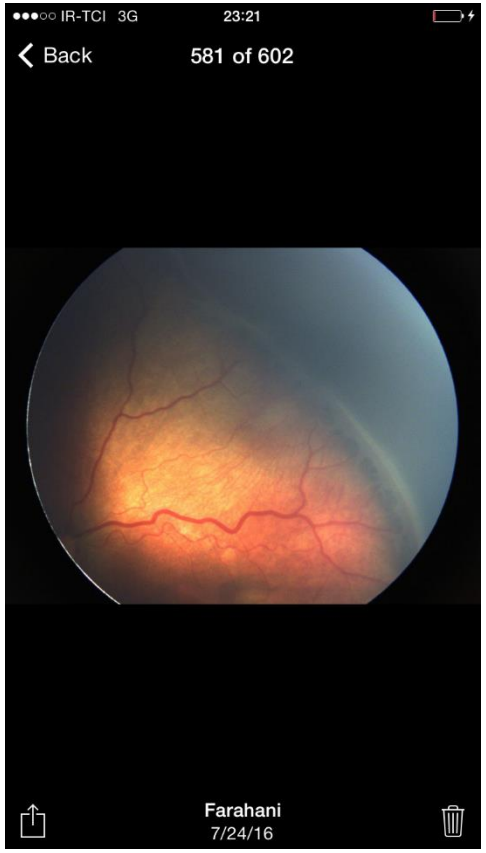
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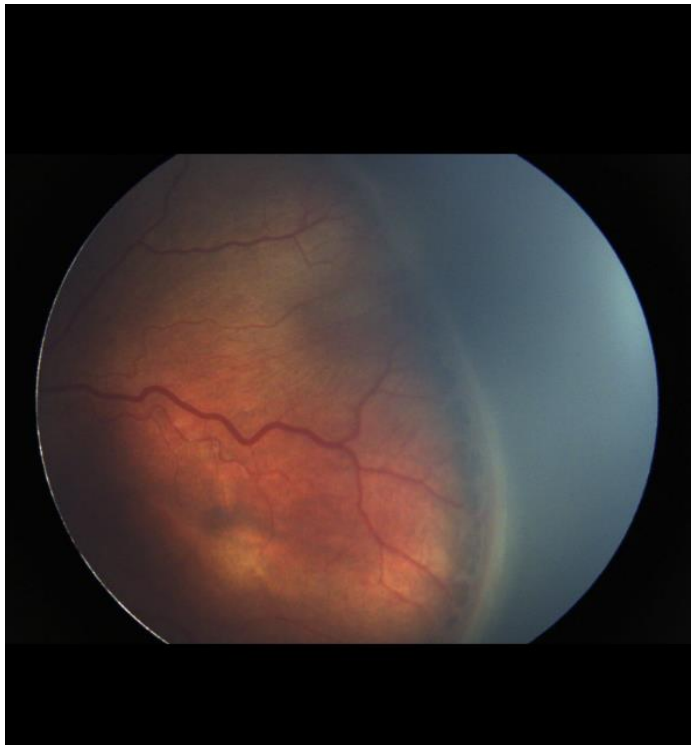

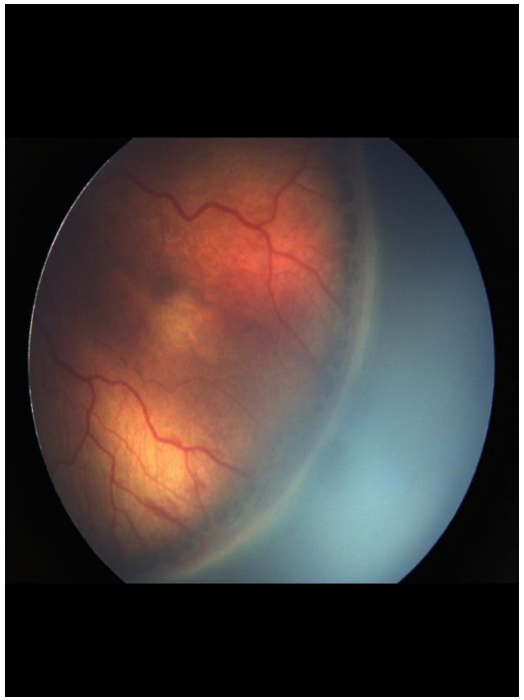

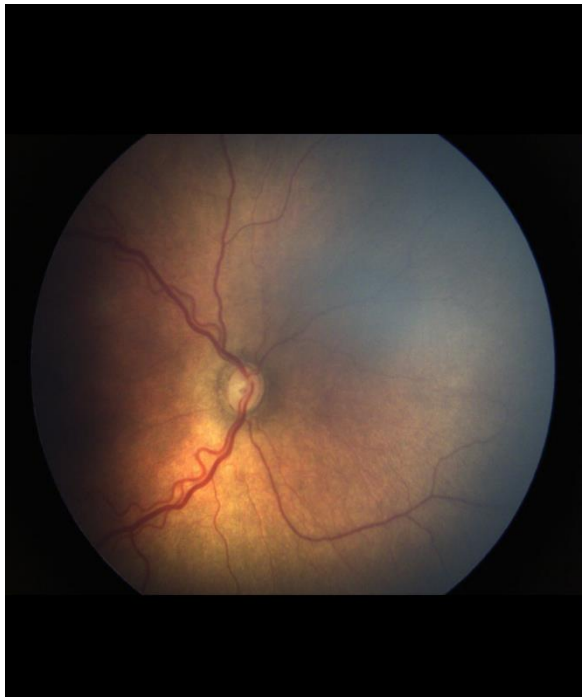

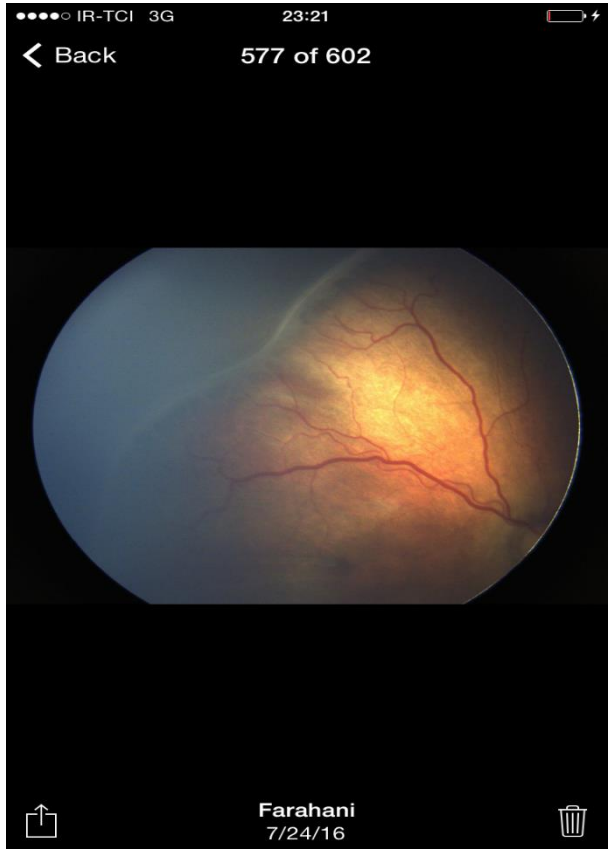
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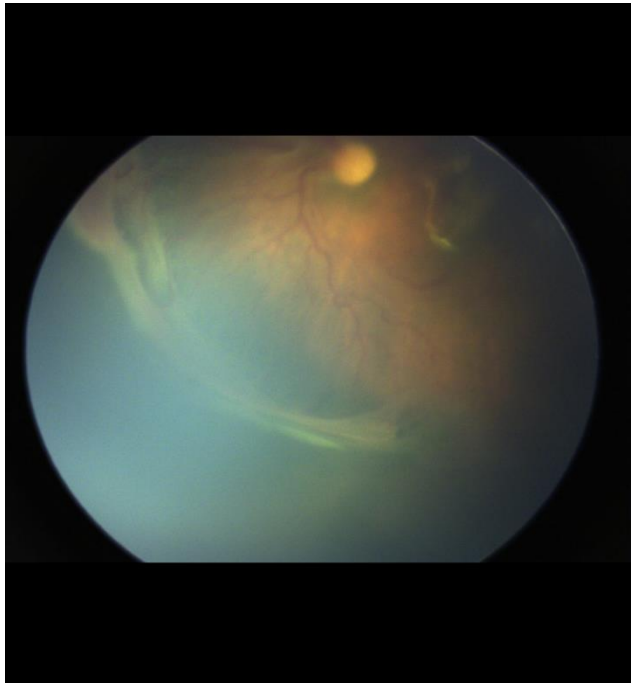

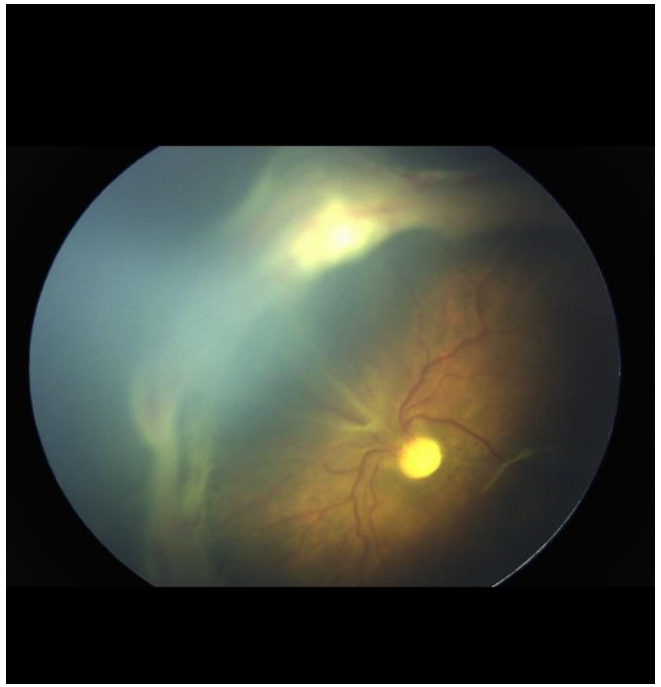

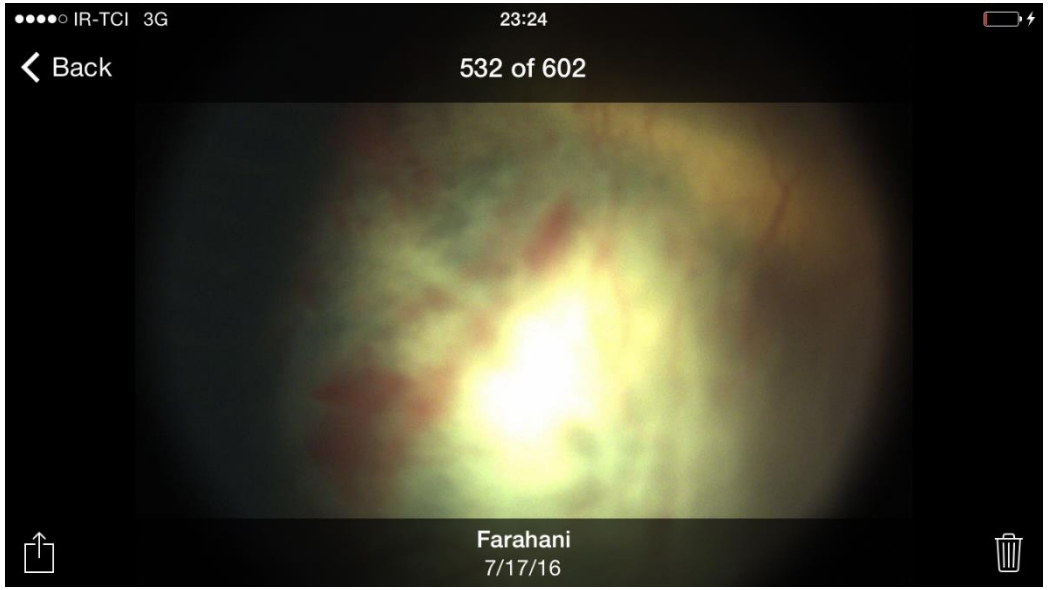
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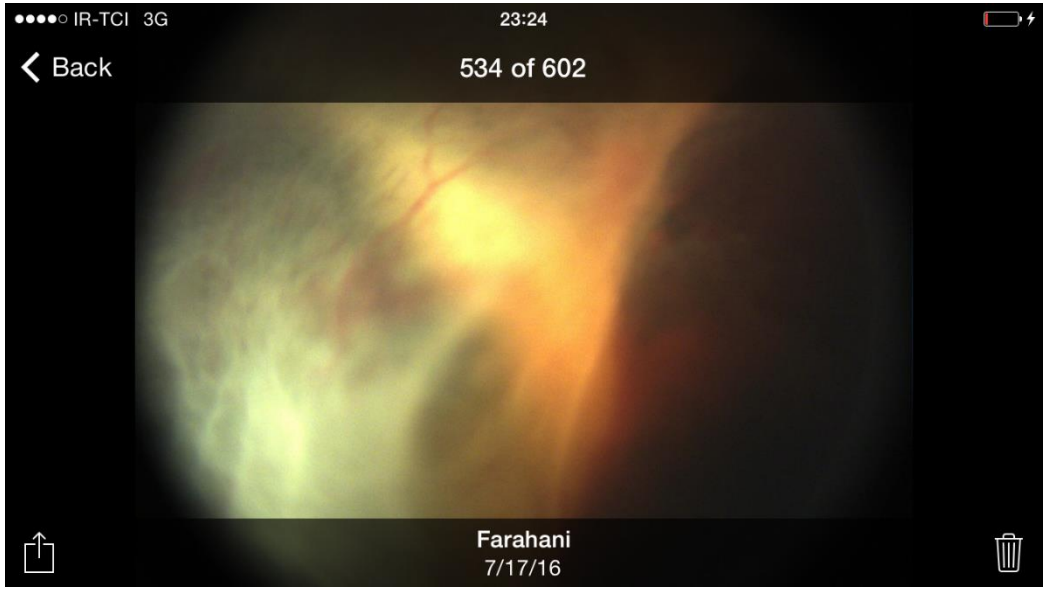
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