

Retinopathy of Prematurity (ROP)



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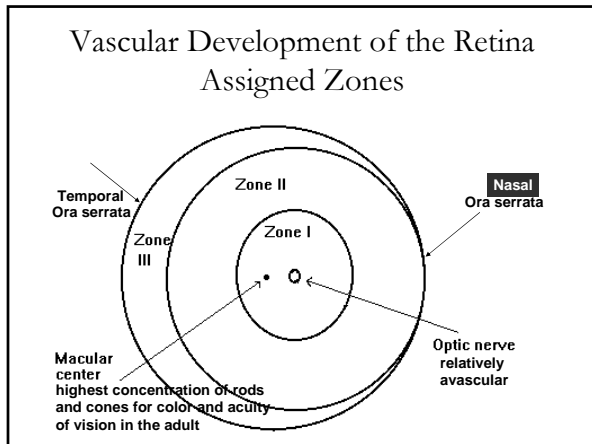
OBJECTIVES

To understand:

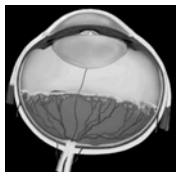
- The natural history of retinal development
- Pathogenesis of ROP
- ROP Stages/ Terminology
- Prevention
- Screening and CNMC Protocol
- Treatment
- Outcome

Retinal Development

- Ganglion cells develop in the retina by the 5th month of gestation
- Photoreceptor layer develops radially outwards from the optic disk thereafter at 26 wks reaching the temporal *ora serrata* by 29 wks
- With increasing maturity, interstitial retinal binding protein proliferates binding vitamins A & E almost everywhere by 28 wks.



- ### Development of the Retina's Vascular Supply, 2 parts
- [1] Choroidal vessels that lie under the retina and pigmented epithelium
 - [2] Retinal vessels that serve the inner retina.
 - Choroidal vasculature is virtually mature by 21 wks gestation.
 - Development of inner retinal vessels during gestation parallels retinal cell maturation and is probably driven by metabolic demand of the developing fetal retina

- ### Normal Development of the Retinal Arteries in the Fetus
- Early retinal vasculature develops from spindle cell precursors beginning at the optic disk and migrating peripherally to the ora serrata
 - The *primordial central retinal artery* extends from the optic disk posteriorly to the posterior surface of the lens anteriorly
 - By 21 weeks vessels are seen 2-3 mm around the optic disk
- Vasularization proceeds twice as fast to 28 wks gestation, then slows to near term at 36 wks maturing into Zone III as late as 49 wks post-conception.
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Development of ROP

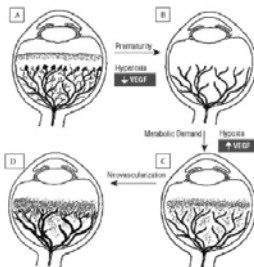
- Premature birth interrupts the developing retinal vasculature.
- Postnatal vascular development follows the fetal time table (28-49wks PCA).
- Injurious event(s) occur at birth & postnatally in the NICU.
- These lead to abnormal proliferation of blood vessels in developing retina (neovascularization).

Development of ROP

- Probably the initiating event is hypoxemia with preterm parturition,
- followed by resuscitation-reperfusion with hyper-oxygenated blood, generating cytotoxic oxygen free radicals in the retina rich with PUFA's and no anti-oxidant Vitamin E protection.
- Hypoxic-hyperoxic swings in oxygenation postnatally probably exacerbate this process.

Pathogenesis

In Utero:
PaO₂ 22-40 mmHg
SaO₂ 65-85%



Disruption in normal Vessel growth:
Hyperoxic
Vasoconstriction,
Vaso-obliteration

Hypoxic avascular retina

Terminology

Zones (I-III): describes *location* of disease

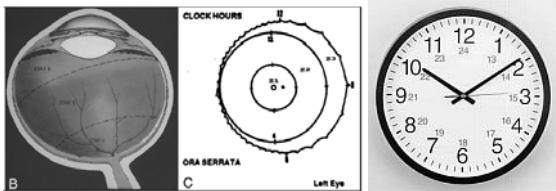
Stages (1-5): describes *severity* of disease

Plus disease: dilation/tortuosity of vessels, prominent iris vessels, pupillary rigidity

Prethreshold disease: significant ROP in Zone I or stage 2 + Plus dz or extensive Stage 3 disease

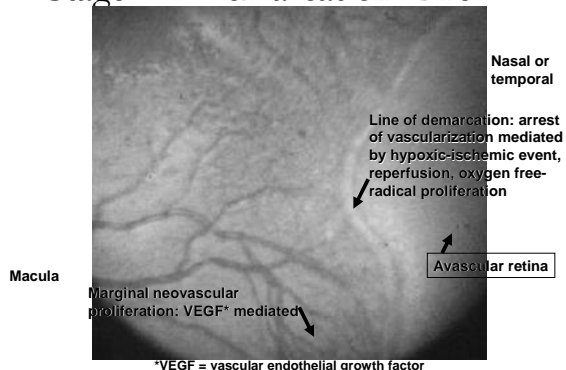
Threshold disease: extensive prethreshold (5 contiguous clock hours/ 8 total CH) + Plus dz

ZONES

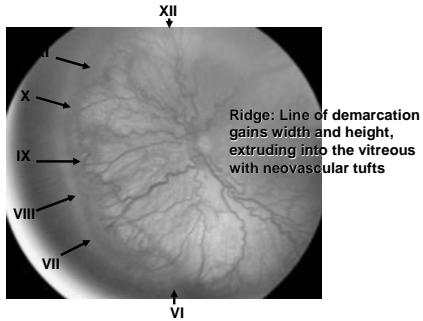


ZONE I: most posterior/ central, contains essential structures for vision (optic nerve, macula), any disease is significant
ZONE III: anterior/ peripheral, disease severity depends on extent of involvement (i.e. # clock hours)

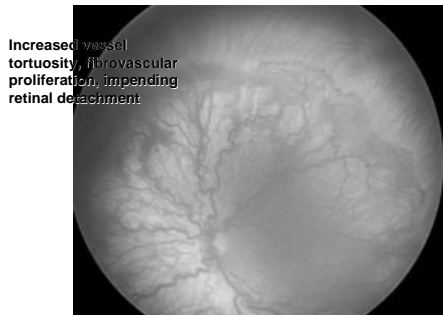
Stage 1 – Demarcation Line



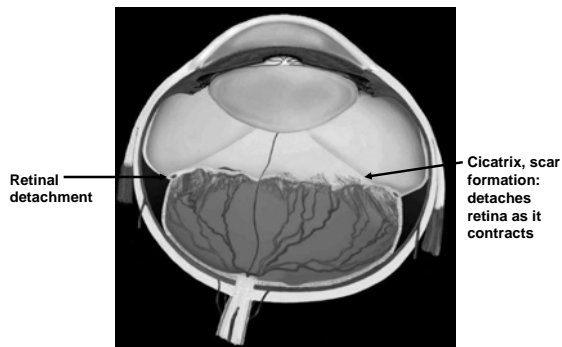
Stage 2 - Ridge

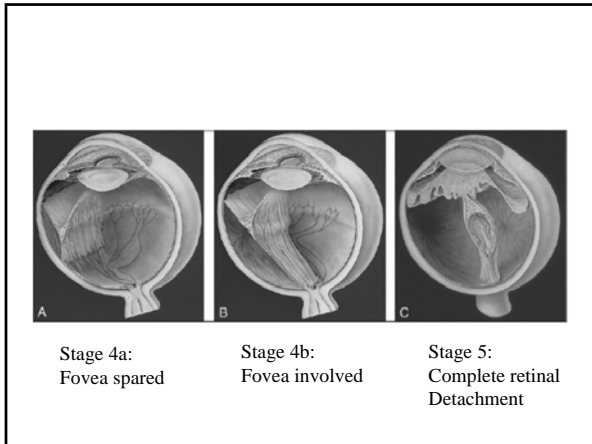


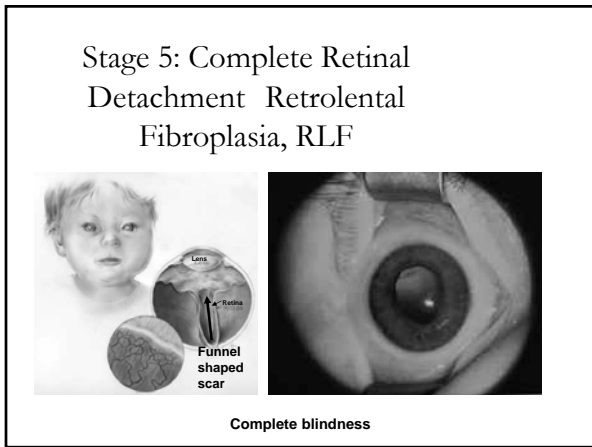
Stage 3 – Fibrous Expansion of Ridge

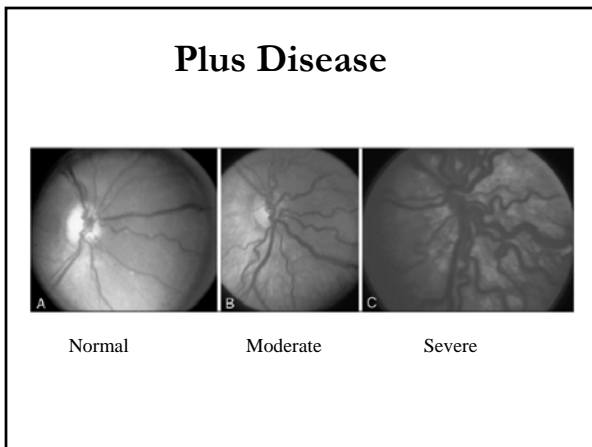


Stage 4 – Partial Retinal Detachment









Prevention of ROP

- **Vitamin E (a-tocopherol) anti-oxidant pharmacologic prophylaxis delays the onset and lessens severity, but doesn't prevent ROP.**
 - Consider in infants w/ ROP & documented deficiency
 - Aim to maintain *normal* levels (10-20 mcg/ml)
- **The Trial of Light Reduction for Reducing Frequency of ROP (Light-ROP): no difference in ROP for those with restricted ambient light exposure**
- **Steroids don't have any effect on ROP presentation or severity.**

Prevention of ROP

- **The only salutary therapy to prevent ROP onset and severity is assiduous oxygen monitoring and titration of F_{iO_2} (keep PaO_2 50-60, SaO_2 88-94%, and avoid swings in $PaCO_2$)**

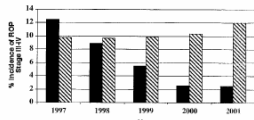


Fig. 2. Incidence of ROP stages 3 to 4 for infants with birth weights of 500 to 1500 g at CSMC (■) and VON (▨) for the years 1997 to 2001. (Rates are calculated as described in "Methods.")

Declines in ROP rates and severity have been reported from centers after instituting practice guidelines and education about oxygen use in the NICU

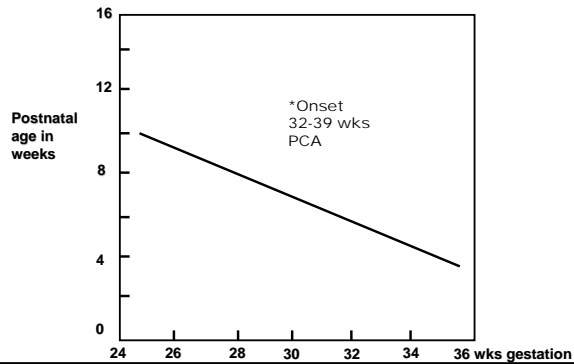
From Chow et al, *Pediatrics* 2003

Epidemiology and Risk Factors

- Increased risk in multiple births, complicated NICU course (i.e. high FiO_2 exposure)
- Decreased risk and severity in black infants compared other racial groups
- Risk inversely related to GA/ BW

Birthweight	Risk for ROP (%)	Risk for Threshold
500-750	90	15
751-999	78	7
1000-1250	47	2

Timing of ROP Development by GA



CNMC Screening Protocol

- Screening Eye Exam for all infants <32 wk GA, <1500g regardless of O2 use, other high risk pts per NICU team
- Initial Eye Exam:

Wk Gest	Week of Age	Day of Life
23-26	5-6	35-42
27-32	4	28

- Based on AAP Guidelines (*Pediatrics* 2001;**108**:809):
 - $\leq 28w$ or $\leq 1500g$ @ 4-6 wks, 31-34wk
 - ELBW<1000g @ 5-6 wks

Treatment of ROP

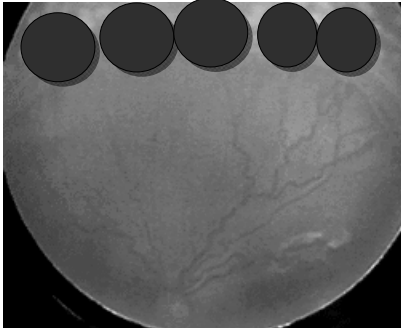
Treatment of Threshold ROP

- Cryo-surgery
- Laser surgery

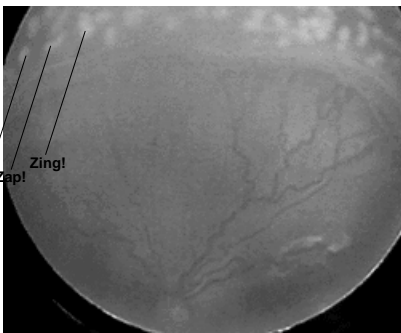
Treatment of Stage 4 and 5 ROP

- Scleral buckle
- Vitrectomy

Cryo-surgery: 8-10 big ablative craters along the line of demarcation, eliminates abnormal vessels before scar tissue laid leading to detachment



Laser Treatment: 500-1500 tiny ablative “stitches,” same purpose as cryo, more exact and most common treatment currently used

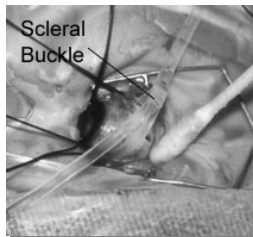


Promotes re-vascularization of ridge line

Scleral buckle and Vitrectomy

Scleral Buckle:

- Silicone band placed around eye
- Preserves the shape of the globe within the orbit for cosmetic effect
- Keeps vitreous gel from pulling on scarred retina



Vitrectomy: remove vitreous and replace with saline to maintain shape of globe and allow retina to flatten against eye wall

Outcome

- ROP was the most common cause of blindness in the U.S. from using unmonitored O₂ in incubators during the 1950's & 1960's.
- Now with improved screening, early intervention for threshold disease, and judicious O₂ use, overall risk for blindness in VLBW decreasing (4% to <2%)
- Cryotherapy or laser decreases severe visual impairment in patients with threshold disease from 50% to 20% (AAP and American Academy of Ophthalmology Joint Statement, *Pediatrics* 1997; 100: 273-274)

Outcome

- Stage 1-2 peripheral disease zones II-III regresses and is probably a benign condition.
- Stage 3, zone 1 "rush" disease is disastrous for severe macular vision impairment in the ELBW population.
- Preterm infants still have increased risk for amblyopia, strabismus, refractive errors, glaucoma even if ROP has regressed- need for optho f/u in 1st year of life

The End
