

## Retinopathy of Prematurity

Retinopathy of Prematurity (ROP) has been an interest of mine for the past 28 years. I want to provide the ophthalmic community with an update on this disease; what we have learned, where we are now and where we are going.

At the University Of Louisville School Of Medicine, we have been privileged to be a part of several multicenter clinical trials studying the natural history and treatment of ROP, starting with the CRYO-ROP study in 1986, and continuing with the STOP-ROP study, the ETROP study, and the e-ROP study. Through these studies, we have learned that ROP needs to be treated with laser therapy when premature infants have "plus disease" associated with abnormal retinal vascular development. Because treatment provides a proven benefit, screening for ROP is now the standard of care for premature infants in all intensive care units throughout the United States. I am extremely proud of the pediatric ophthalmologists in this community who have taken on the monumental task of screening dozens of infants each week in intensive care units throughout Louisville. With the aid of Terry Lewis, RN, Rahul Bhola MD, Craig Douglas MD, Peggy Fishman MD and John Franklin MD have born this task with steadfast dedication, and I honestly can't remember a patient who has not been treated in a timely manner or who has had permanent visual loss from ROP in the past several years.

What's new with ROP? A recent comparison study, soon to be published in Ophthalmology, found that over the last 25 years, the average gestational age of infants at risk for ROP has dropped from 28 weeks to 27 weeks, and the birth weight has

dropped from 950 grams to 850 grams. This is because the survival of low birth weight premature infants has gradually increased over the last two decades, due to several factors, including antenatal steroids, the use of surfactant, computer controlled ventilators, and better parenteral nutrition. Nonetheless, the incidence of ROP remains the same, with 60% of infants developing some ROP, and 10% needing treatment. Although smaller birth weight infants are surviving, disease becomes most severe at 36 weeks gestational age, a figure that hasn't changed in 25 years. The burden of screening infants at risk remains high – and now that we are in the digital age, wouldn't it be possible to have some type of automated screening? We were part of the e-ROP study that asked this very question, by performing digital retinal photography of premature infants with the "RetCam", and comparing these images to a clinical examination performed the same day (Figure). The result? It works great --- but it doesn't work!! RetCam screening had a sensitivity of 98% and a specificity of 80%; the negative predictive value was 99%. While this sounds great --- and would be great to screen a general population for a disease – it means that 1 in 50 infants in need of treatment would be missed with RetCam screening. While this is unacceptable in the United States, it does show promise for 3<sup>rd</sup> world countries.

For many years, laser treatment of ROP has been the standard of care. This has been performed in the same manner, and with the same rationale, as panretinal

photocoagulation for diabetic retinopathy or retinal vein obstruction. Recent work by Hittner and associates compared intraocular bevacizumab (Avastin) to laser for ROP. The study results remain controversial, but they found that Avastin was superior to laser, and that there were no long term side effects to its use. Nonetheless, most pediatric ophthalmologists and retinal specialists prefer laser over Avastin for ROP, because different studies have shown that intraocular Avastin is absorbed systemically, and reduces systemic vascular endothelial growth factor. This is very worrisome in a premature infant whose vascular and central nervous system development is not complete. We are currently enrolling premature infants in a multicenter clinical trial to compare laser treatment to intraocular ranibizumab (Lucentis), which has minimal effect on systemic growth factors. Hopefully, we will find a new and better treatment for a disease that continues to threaten the most vulnerable of our patients.



Figure 1 Photographer and nurse obtaining a retinal image in the NICU

By Charles C Barr MD

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