

CONTEMPORARY UNDERSTANDING AND MANAGEMENT OF RETINOPATHY OF PREMATURITY

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Learning Objectives

After completion of this article, the reader will be able to 1) describe the physiologic, biochemical, and mechanical factors involved in the pathogenesis of retinopathy of prematurity (ROP) and ROP-related retinal detachment; 2) identify infants at risk for ROP and to recall recommendations for initiation, frequency, and duration of screening ophthalmic examinations; and 3) explain the rationale for various treatment modalities and timing of treatment for ROP.

Terry¹ described retinopathy of prematurity (ROP) in 1942. The International Classification of Retinopathy of Prematurity (ICROP, 1984² and 1987³) and the Trial of Cryotherapy for Retinopathy of Prematurity (CRYO-ROP)⁴⁻⁷ have had a profound impact on the way in which we screen, treat, and even discuss ROP. Much has changed since the ICROP and CRYO-ROP. Understanding of the pathogenesis of ROP has been refined. Survival of high-risk neonates has improved, with ophthalmologists encountering

profoundly premature infants with greater frequency. Screening and treatment approaches continue to evolve, and there have been significant advances in the management of ROP-related retinal detachment. The purpose of this article is to provide an overview of advances in ROP.

Epidemiology

In the CRYO-ROP Study,⁸ the incidence and severity of ROP was closely correlated to lower birthweight and earlier postconceptional age. As technologic advances have made possible increased survival for extremely premature infants, it would seem likely that the number of infants with ROP is likely to increase.^{9,12} Several studies have suggested, however, that the increased survival rate of high-risk neonates has not been associated with a universal increase in the incidence of ROP.¹⁰⁻¹³ This trend may reflect improvements in ventilation techniques and perinatal care, specifically the prophylactic use of surfactant¹⁴ and the maternal use of antenatal steroids.¹⁵

The improved survival rate of extremely premature infants has had a profound impact on the ophthalmic community nonetheless. Ophthalmologists in urban centers are encountering increasingly premature infants with greater frequency, and those in community hospitals may be pressed to examine premature infants for the first time. In both scenarios, experience with ROP, particularly that located in zone I, may be limited.

Clinical Features

The fundamental process underlying the development of ROP is incomplete vascularization of the retina, and the ophthalmoscopic findings stem from

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this arrested development. During normal retinal development, vessels migrate from the optic disk to the ora serrata beginning at approximately 16 weeks of gestation.¹⁶ Vasculogenesis transforms precursor cells into capillary networks. Mature vessels differentiate from these networks and extend to the nasal ora serrata by 36 weeks of gestation and to the temporal ora serrata by 39 to 41 weeks.

The location of the interruption of normal vasculogenesis is related to the time of premature birth. The clinical appearance of the various stages of ROP is related to the location of the vascular-avascular junction. Most eyes in the era of the ICROP and the CRYO-ROP study developed ROP in zone II. As a result, the clinical features and course of zone II ROP^{2,3} are those with which we became most familiar. The unique clinical features of posterior ROP are less familiar to most ophthalmologists. As a consequence of the increased survival rate of high-risk neonates, however, ROP located in posterior zone II or in zone I is now commonly encountered.

Although eyes with minimal ROP located in zone I (e.g., one clock hour) frequently behave like an eye with zone II disease, ROP may appear and behave differently when located mostly (>6 clock hours) in zone I. Progression to stage 3 may proceed directly from immature retina without an intervening demarcation line (stage 1 ROP) or ridge (stage 2 ROP). The absence of a line or ridge may render it difficult to discern the interface between vascular and avascular retina. Stage 3 ROP in zone I may have a flat, broad, velvety appearance with little fibrous component (Figure 1).¹⁷ Choroidal vascular prominence through the pale retinal pigment epithelium of the profoundly premature may convey the false sense that retinal vascularization is complete.

Pathogenesis

Retinal Neovascularization

Areas of immature peripheral retina lacking vasculature are presumed to be hypoxic. Hypoxia is a common precursor to the abnormal neovascularization seen in many retinal diseases. Michaelson's hypothesis of an angiogenic chemical messenger, so-called factor X,¹⁸ secreted in response to tissue hypoxia has led to the identification of numerous angiogenic factors, among them basic fibroblast growth factor,¹⁹ transforming growth factor- α ,²⁰ and tumor necrosis factor- α .²¹ Increasing attention, however, has been focused on vascular endothelial growth factor (VEGF), formerly called vascular permeability factor.²² Vitreous levels of VEGF are increased in pa-

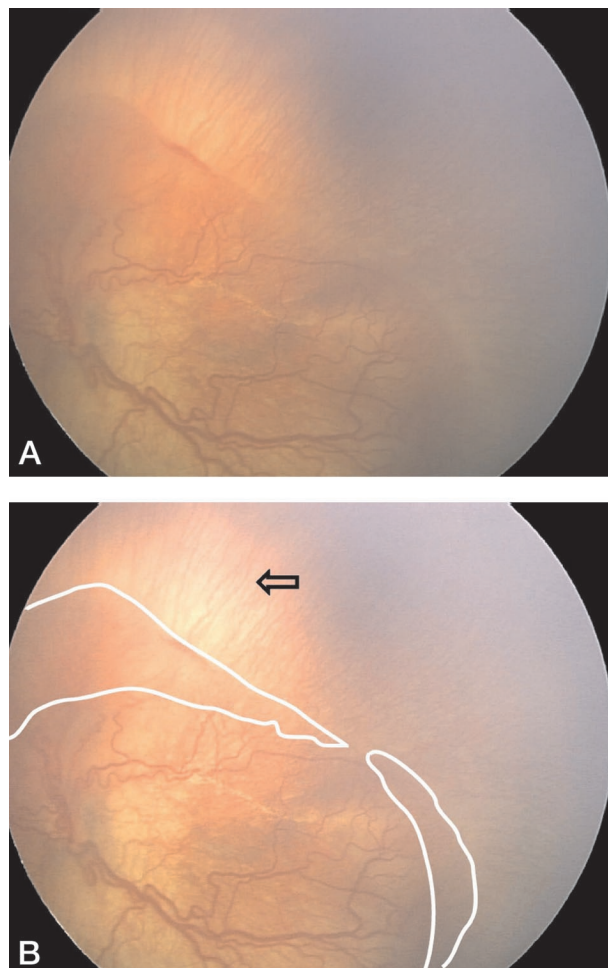


Fig. 1. A, Wide-angle fundus image of stage 3 ROP in zone I (courtesy of Christine A. Gonzales, MD, and the ROP Photographic Screening Trial [Photo-ROP] Study Group). B, Note prominent choroidal vasculature visible through pale premature retinal pigment epithelium (black arrow) and flat arcuate syncytium of stage 3 ROP (white dotted outline). The posterior aspect of the neovascular lobule is bordered by shunt vessels coursing circumferentially (courtesy of Christine A. Gonzales, MD, and the ROP Photographic Screening Trial [Photo-ROP] Study Group).¹⁷

tients with various proliferative retinopathies, including ROP, and vitreous fluid from these patients stimulates growth of endothelial cells *in vitro*.²³

A role for VEGF in ROP was suggested by data from a mouse model of ROP. In this model, VEGF is expressed in healthy postnatal retina just anterior to developing capillaries,²⁴ and vessels grow toward the advancing wave of VEGF. High levels of oxygen (corresponding to maturing, vascularized retina) decrease VEGF expression and lead to regression of retinal capillaries,^{25,26} whereas relative hypoxia induces a prompt increase in VEGF expression and may contribute to abnormal angiogenesis.²⁴

In humans, expression of VEGF has been identified in Müller cells and astrocytes.²⁷ Physiologic expres-

sion of VEGF in the healthy retina in utero likely helps to control vessel development and regression. However, inopportune changes in oxygen tension may cause abnormal upregulation or downregulation of VEGF expression. Such dysregulated VEGF expression would lead to untimely vasoobliteration or exaggerated vasoproliferation. This simplified view is supported clinically by studies in which fluctuations in oxygen levels lead to more severe ROP than overall oxygen tension.²⁸ Additionally, in one study, serum levels of VEGF were significantly higher in infants with stage 3 and threshold ROP than in those with less severe disease. The peak difference occurred at 36 weeks postconceptional age,²⁹ which coincides with the median onset of the active neovascularization of threshold disease.

A role for insulinlike growth factor I (IGF-I) has also been suggested by Hellstrom et al.³⁰ In the murine model of ROP, IGF-I is essential for normal retinal vascularization, apparently through promoting endothelial cell survival in complement with VEGF. Clinical correlation of the hypothesis that subnormal levels of IGF-I may contribute to ROP was provided by a prospective study of plasma IGF-I levels in premature infants. In infants without ROP, plasma IGF-I levels reached 30 ng/mL significantly more rapidly (mean, 19 days) than in infants with ROP (mean, 58 days). In the latter group, ROP did not develop until IGF-I levels were greater than 30 ng/mL. The authors concluded that the development of ROP was strongly associated with a prolonged low plasma level of IGF-I, followed by an increase to a threshold level of IGF-I.

Systemic Factors

Retinopathy is only one of many devastating complications of premature birth. Other systemic abnormalities that afflict these infants include bronchopulmonary dysplasia, anemia, cardiac defects, sepsis, necrotizing enterocolitis, intraventricular hemorrhage, cerebral palsy, and neurodevelopmental delay. As with ROP, these associated conditions are more prevalent and more serious in infants of lower birthweight. Moreover, the severity of neonatal ROP is a marker for functional disability later in life.³¹

A relationship between oxygen levels and ROP has been suspected for one-half a century.¹ In recent years, results of experiments with animal models and epidemiologic studies have brought the complexity and paradox of this relationship to light. Pursuant to Michaelson's proposal that progressive oxygen deficit within the retina during normal differentiation can induce angiogenesis in neighboring vessels in 1948,¹⁸

supplemental oxygen was administered to premature infants in the 1950s in an effort to relieve the putative stimulus for retinal neovascularization. This practice was abandoned after the Cooperative Study of Retrolental Fibroplasia disclosed a threefold risk of ROP in neonates without lung disease who had been given prolonged oxygen supplementation.³² However, the concept of a hypoxic stimulus for neovascularization remained biologically plausible, and the issue of supplementary oxygen regained attention. This renewed interest was based in part on several case-control studies, in which infants developing severe ROP had hospital courses complicated by lower arterial oxygenation and greater fluctuation in blood oxygen levels.^{33,34}

The Supplemental Therapeutic Oxygen for Prethreshold ROP (STOP-ROP) study was a multicenter clinical trial begun in 1994 to determine the efficacy and safety of supplemental oxygen administered to premature infants to reduce the progression to threshold ROP.³⁵ Six hundred forty-nine premature infants with prethreshold ROP in at least one eye were randomized to a conventional arm (with pulse oximetry targeted at 89% to 94% oxygen saturation) or to a supplemental arm (96% to 99% oxygen saturation). The progression to threshold ROP was lower in the supplemental arm (41% versus 48%), but not to a statistically significant degree. Subgroup analysis did show, however, that infants without plus disease and without severe lung disease may benefit from supplemental oxygen (32% progression in the supplemental arm versus 46% progression in the conventional arm).

Several authors have suggested that candidemia may be independently associated with severe ROP in babies weighing less than 1,000 g (2 lb, 3 oz).^{36,37} A recent large cohort study of 449 infants, however, failed to show a strong correlation and suggested instead that much of the observed association of these two clinical conditions is linked more to young postconceptional age.³⁸

Hospital nursery lighting is an additional variable that has been suspected to contribute to ROP. In the recent Light Reduction in Retinopathy of Prematurity (LIGHT-ROP) study, involving 361 infants weighing less than 1,251 g, a reduction in exposure to ambient light did not alter the incidence of ROP.³⁹

Genetic factors may play a role in the development of severe ROP in a subset of premature infants. Prompted by the observation that some clinical features of ROP noted in near-term and full-term infants may resemble those seen in familial exudative vitreoretinopathy, the X-linked form of which is associated with mutations in the Norrie disease (ND) gene,⁴⁰ Shastry et al⁴¹ investigated a cohort of 16 premature

infants with ROP for mutations in the ND gene. Missense mutations were found in four, all of whom had advanced disease, and in none of the parents or 50 healthy controls. A larger study showed the presence of ND mutations in 2% of infants with ROP.⁴²

Refining the Definition of Threshold Disease

The determination of threshold ROP in the CRYO-ROP study sought to define that severity of ROP for which a given eye had an equal chance of spontaneous regression or progression to unfavorable outcome (defined anatomically as the presence of a macular fold, retinal detachment involving zone I, or obscuration of the posterior pole by cataract or retrolental fibrosis and later defined as Snellen equivalent of 20/200 or worse). Although initially based only on clinical estimation, threshold disease had become accepted as the point at which treatment should be administered. It is currently defined as stage 3 ROP in zone I or II occupying at least five contiguous clock hours or eight noncontiguous clock hours of retina.⁴³ For eyes with zone II ROP, this estimation proved fairly precise; 62% of untreated eyes with threshold ROP went on to an untoward visual outcome. However, the estimation of a 50/50 threshold for eyes with zone I ROP was off the mark; untreated zone I eyes with threshold ROP had a 90% chance of untoward outcome.⁴⁴ Although the number of such eyes was small, the data suggested that the definition of threshold ROP used for zone II eyes may not be appropriate for zone I eyes.

Because zone I eyes almost always progress to threshold,⁴⁵ the question for such eyes and high-risk zone II eyes would appear not to be whether but when to treat earlier. Until recently, criteria for early treatment were lacking. This issue was investigated in the multicenter study of Early Treatment for Retinopathy of Prematurity (ETROP),⁴⁶ in which eyes with prethreshold ROP (also known as moderately severe ROP; any zone I ROP less than threshold; or zone II stage 2 with plus disease (dilation and tortuosity of posterior pole retinal vessels in at least 2 quadrants meeting or exceeding that of a standard photograph), or zone II stage 3 ROP without plus disease, or zone II stage 3 ROP with fewer than 5 contiguous or 8 cumulative clock hours with plus disease) were randomized to early treatment once they attained 15% risk of unfavorable outcome or more. Comparison between untreated eyes, high-risk prethreshold eyes treated early, and high-risk eyes treated at threshold demonstrated that retinal ablative therapy is beneficial for 1) any eye that has any stage of ROP in zone I with plus disease, 2) stage 3 ROP in zone I with or

without plus disease, and, 3) stage 2 or 3 ROP in zone II with plus disease.⁴⁶

Evidence-Based Screening

Natural history data from the CRYO-ROP and LIGHT-ROP studies were combined to speak to the question of when to begin and conclude screening for acute ROP.⁴⁷ The study included the 4,099 infants with a birthweight less than 1,251 g prospectively screened in the CRYO-ROP (23 study centers, January 1, 1986 to November 30, 1987) and the 361 infants with a birthweight less than 1,251 g and gestational age less than 31 weeks screened in the LIGHT-ROP study (3 study centers, July 1, 1995 to March 31, 1997).³⁹

Retinal findings indicative of poor outcome (namely prethreshold ROP, threshold ROP, plus disease, or stage 3+ disease) were seen in only 1% of infants before 31 weeks of postmenstrual age and in only 1% of infants after 46.3 weeks of postmenstrual age. Therefore, for most eyes in the CRYO-ROP and LIGHT-ROP studies, the time window for development of serious ROP (prethreshold or worse) was between 30.9 weeks and 46.3 weeks of postmenstrual age or between 4.7 and 18.7 weeks of chronologic age. Retinal findings indicative of minimal risk of poor outcome (namely vascularization into zone III without previous ROP or full retinal vascularization) were seen in 99% of infants by 45.9 weeks of postmenstrual age.

The study investigators suggest that screening examinations be initiated at 31 weeks of postmenstrual age or at 4 weeks of chronologic age for infants born before 27 weeks of postmenstrual age⁴⁷ and be continued until 45 weeks of postmenstrual age or progression of retinal vascularization into zone III. Many neonatal intensive care units have higher birthweight criteria, based on the concern that at-risk infants may be missed.⁴⁸ Results of the ETROP place appropriate emphasis on the importance of timely identification of prethreshold ROP. In the ETROP, infants were followed on a weekly basis after developing zone II, stage 2 ROP or if they had retinal vessel immaturity with vessels ending in zone I without ROP in that zone. Infants with low-risk prethreshold disease received follow-up twice weekly.⁴⁶ Summary guidelines for screening of premature infants in our neonatal intensive care units are presented in Table 1.

The Future of Screening

Although the CRYO-ROP study unquestionably showed the value of screening at-risk infants in preserving vision, manpower issues, costs associated with

Table 1. Screening

Whom to screen	<ul style="list-style-type: none"> • All infants with a birth weight <1,500 g (3 lbs, 4 oz) • All infants born at postmenstrual age of 32 weeks or earlier • All infants weighing between 1,500 and 2,000 g (4 lbs, 6 oz) requiring supplemental oxygen, or with an unstable clinical course and who are thought to be at high risk
Initial examination window	<ul style="list-style-type: none"> • By 31 weeks' postmenstrual age or 4 weeks' chronological age, whichever is later
When to follow up	<ul style="list-style-type: none"> • Weekly: Retinal vessel immaturity with vessels ending in zone I but no ROP in that zone <p style="text-align: center;">or</p> <p>Low risk prethreshold ROP*</p> <ul style="list-style-type: none"> • Every 2 weeks: less than prethreshold ROP in zone II • Treat: High risk prethreshold ROP
How long to examine	<ul style="list-style-type: none"> • Attainment of 45 weeks' postmenstrual age without the development of prethreshold ROP or worse • Progression of retinal vascularization into zone III without previous zone II ROP • Full vascularization (to or within 1 disk diameter of the ora serrata) on 2 occasions

* Low risk prethreshold ROP: Stage 1 or 2 ROP in zone I without plus disease, stage 2 or stage 3 ROP in zone II without plus disease, or stage 2 or stage 3 ROP with plus disease less than high-risk prethreshold in zone II.

** High-risk prethreshold ROP: Any stage of ROP in zone I with plus disease (dilation and tortuosity of posterior pole retinal vessels in at least 2 quadrants meeting or exceeding that of a standard photograph), stage 3 ROP in zone I with or without plus disease, and, stage 2 or 3 ROP in zone II with plus disease.

ROP, retinopathy of prematurity.

repeated transport of infants to remote tertiary centers for periodic ophthalmic surveillance, and the specter of significant medicolegal liability associated with ROP are but a few of the barriers to achieving the goal of universal screening. Most ophthalmologists strive to do the best they can.

Telemedicine (i.e., on-site acquisition of clinical data relayed to a remote site for interpretation) offers an opportunity to conquer some of these barriers. One can imagine a trained technician acquiring digital fundus images from at-risk infants in a neonatal intensive care unit, followed by transmission to a regional reading center. Trained certified graders could provide timely and cost-effective input into ROP management, identifying infants requiring on-site examination or treatment. Although technology enabling complete imaging of the peripheral retina and posterior pole of infants is currently lacking, interval technologies are available. Pursuant to a successful proof-of-principle project,⁴⁹ a multicenter study is underway to evaluate whether digital fundus images evaluated remotely effectively complement on-site management of ROP.⁵⁰

Digital fundus imaging would positively affect ROP-related clinical trials. The paradigm of a dedicated reading center with certified fundus image graders has become the gold standard for the conduct of ophthalmic clinical trials. To date, however, all large ROP trials have gathered data by requiring examiners to draw the retinal findings as noted during clinical examination. Neither the examiner nor study center

has an opportunity to study an image of the fundus. Although simplicity is an advantage to this approach, fundus imaging with evaluation by dedicated graders is far superior to the indirect ophthalmoscopic observations of busy clinicians. Photographic documentation of treatment is also essential to distinguish true therapeutic failure from poor outcome caused by incomplete treatment.

Treatment of Retinopathy

Convenient portable units for indirect laser photocoagulation became available shortly after the advent of the CRYO-ROP study. Although the merit of cryopexy versus laser retinopexy for ROP has been hotly debated, laser is the current standard for treating ROP. Ng et al⁵¹ and Connolly et al⁵² recently reported long-term structural and functional outcomes using laser superior to those obtained with cryotherapy. The difference is perhaps most dramatic in eyes with posterior ROP; favorable anatomic results have been reported in 83% of eyes treated with laser,⁵³ whereas cryotherapy, by contrast, provided favorable outcomes in only 25% of eyes with zone I disease.⁵⁴

The conventional treatment pattern is best described as nearly confluent with burns placed 0.5 to 1 burn widths apart (Figure 2). Complications of laser treatment include anterior segment ischemia (Figure 3),^{55,56} cataract, and burns of the cornea, iris, or tunica vasculosa lentis. Indications for using cryopexy in-

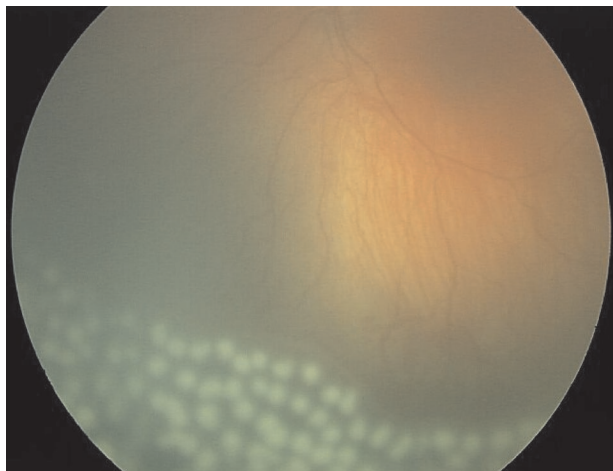


Fig. 2. Near-confluent laser ablation with burns spaced 0.5 burn widths apart up to, but not including, the ridge.

stead of laser in the management of ROP include poor fundus visibility (vitreous hemorrhage or anterior segment problems), lack of availability of laser, and lack of treating physician familiarity with indirect laser retinopexy.

Retinopathy of Prematurity-Related Retinal Detachment

Although retinal ablation is effective in most cases of threshold ROP, a significant number of these eyes progress to retinal detachment. Detachment is often seen associated with areas of incomplete peripheral ablation (skip areas) or in eyes with inexorably pro-

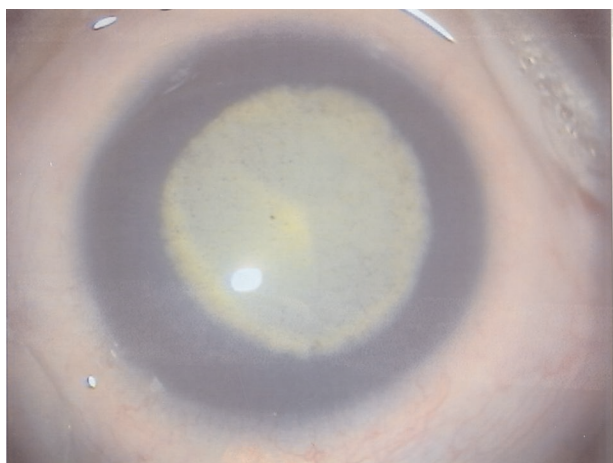


Fig. 3. The right eye of a patient with zone II threshold retinopathy of prematurity treated 4 weeks earlier using a diode laser (1,400 spots, 240 mW, 200 msec). There is a dense cataract with pigment on the anterior lens surface. Also present, though not apparent in this photograph, were posterior synechiae, a shallow anterior chamber with iridocorneal touch nasally, and mild corneal edema.

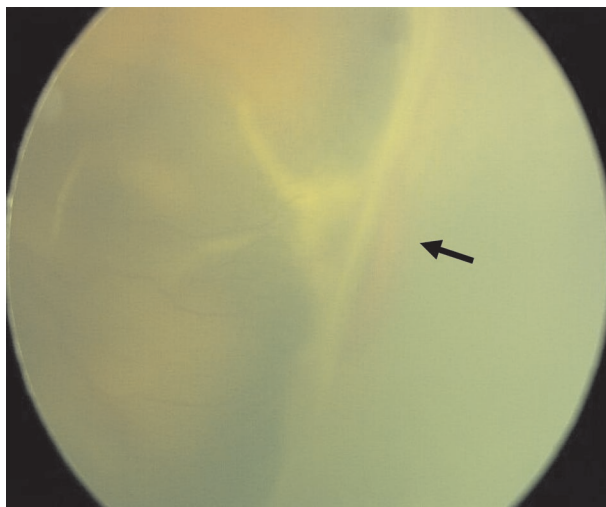


Fig. 4. Contraction of proliferation intrinsic to the circumferential ridge, resulting in a radial fold.

gressive, usually postequatorial (posterior zone II or zone I) disease.

Evolution

Contraction of neovascularization along the ridge and growth into the overlying vitreous precede tractional retinal detachment. Condensation of vitreous into sheets and strands act as a scaffold for further extension of the fibrovascular tissue. Traction along the retinal surface and contraction of the posterior hyaloid face contribute to distortion of posterior pole architecture. The configuration of the retinal detachment in ROP depends primarily on the location of the ridge and the orientation of vectors of vitreoretinal traction. Tractional forces are exerted in the following ways.

Intrinsic to Retina

This vector consists of proliferation intrinsic to the ridge itself (Figure 4). It is the tractional vector not removable surgically. Contraction of this circumferential vector results in a radial fold. It can be addressed by scleral buckle alone when it is the sole tractional vector located near or anterior to the equator.

Ridge to Lens

The most common and easily conceptualized traction vector, it is also the most important to interrupt surgically and often extends circumferentially from the ridge toward the mid peripheral lens (Figure 5).



Fig. 5. Proliferation extending anteriorly from the ridge toward the lens.

Ridge to Ridge

This vector extends as a sheet across the mouth of the developing funnel-shaped retinal detachment (Figure 6).

Ridge to Ciliary Body

This vector extends from the ridge anteriorly toward the ciliary body (Figure 7).

Ridge to Retina

This vector extends from the elevated ridge back toward the portion of the retina just anterior to the original location of the ridge.

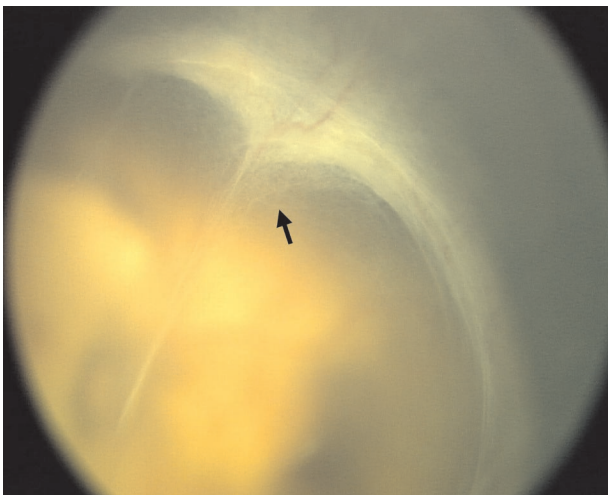


Fig. 6. Sheet of proliferation originating from the ridge and extending across the mouth of the funnel-shaped retinal detachment toward the contralateral ridge.

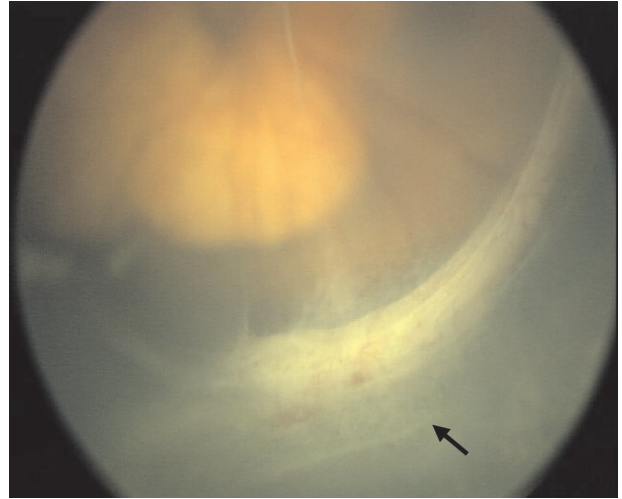


Fig. 7. Sheet of proliferation originating from the ridge extends anteriorly toward the ciliary processes in the inferior portion of the image.

Disk Stalk

There are three variants of the proliferative tissue extending from the optic disk: epiretinal sheet extending along the retinal surface to the ridge, typically very adherent to the retina, and seen in eyes with a ridge located very posterior to the equator; transvitreal stalk extending to the ridge, usually seen in eyes with an equatorial ridge; and traction extending transvitreally to the ridge-to-ridge sheet, usually seen in eyes with a ridge located anterior to the equator (Figure 8).

Some or all of the above components are present in ROP-related retinal detachments. The configuration of the detachment is determined by the relative force vector contribution of tractional component.

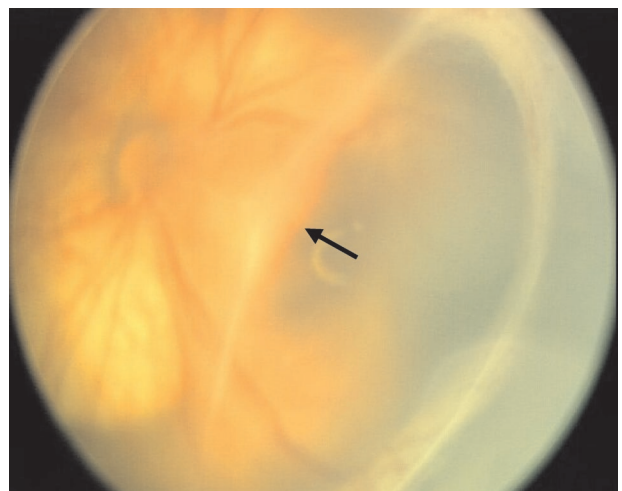


Fig. 8. Central T-shaped stalk extending transvitreally from the optic disk (out of focus) anteriorly to join with the ridge-to-ridge sheet.

Surgical Management

The advanced stages of ROP (stages 4A, 4B, and 5) are poorly understood. Common misconceptions are that macula-sparing (stage 4A) partial retinal detachments are largely benign, that surgery should be deferred until the macula is detached, that scleral buckle is the preferred retinal reattachment procedure, and that useful vision cannot be obtained in eyes with total (stage 5) detachments.

Retinopathy of prematurity-related detachments may appear stable in the first few weeks or months after peripheral retinal ablation. However, the stability of neither partial detachment⁴⁴ nor visual acuity⁵⁷ is predictable on the basis of retinal appearance in infants with ROP. This is particularly true for untreated eyes⁴⁴ or those with incomplete peripheral retinal ablation. Visual outcome of eyes with even partial ROP-related retinal detachment is generally poor by 4.5 years of age.^{8,58}

Anatomic and pathogenetic issues that are unique to the surgical management of ROP must be kept in mind. These include the incomplete development of the pars plana, the relatively large crystalline lens, and the diversity of tractional forces described above.

Awareness of all tractional vectors and alleviation of all traction are crucial to optimize surgical outcome.

The goal of intervention for ROP-related retinal detachments varies with the severity of the detachment. The goal for extramacular retinal detachment (stage 4A ROP) is an undistorted or minimally distorted posterior pole, total retinal reattachment, and preservation of the lens and central fixation vision. Scleral buckle^{59,60} and vitrectomy⁶¹ have been performed to manage stage 4A ROP. Disadvantages of scleral buckle for stage 4A ROP are the dramatic anisotropic myopia⁶² and the second intervention required for transection or removal so that the eye may continue to grow. More importantly, however, not all tractional forces can be alleviated with scleral buckling alone. Vitreous surgery can interrupt progression of ROP from stage 4A to stage 4B or 5 by directly addressing transvitreal traction resulting from fibrous proliferation. In experienced hands, lens-sparing vitrectomy allows primary retinal reattachment in at least 90% of eyes with stage 4A ROP. Early visual outcomes also appear encouraging. In a cohort of 11 consecutive eyes of children able to cooperate with Teller visual acuity testing (mean age, 2.5 years), Snellen equivalent was 20/80 or better in 8 eyes (73%).⁶³

Surgery for traction retinal detachments involving the macula (stage 4B ROP) is performed to minimize

retinal distortion and prevent total detachment (stage 5). Surgery for stages 4B and 5 ROP is performed to provide ambulatory vision. In earlier studies, visual outcome for retinal detachment beyond stage 4A was poor.⁶⁴ More recent reports have shown that form vision can be obtained by vitrectomy for stage 5 ROP.⁶⁵

Maximal recovery of vision after the insult of macula-off retinal detachment and interruption of visual development in infants may take years.

Adult Retinopathy of Prematurity

As infants afflicted with ROP have matured, the ophthalmic community has gained experience with adult ROP. Early nuclear sclerotic cataract, glaucoma,⁶⁶ exudative retinopathy,⁶⁷ and rhegmatogenous retinal detachment⁶⁸ are a few of the sequelae of ROP prompting the need for lifelong ophthalmic monitoring of formerly premature adults. Rhegmatogenous retinal detachments in adults with ROP may be challenging to repair because of irregular tears, atrophied peripheral retina, and abnormalities of the vitreoretinal interface, especially in areas of originally non-vascularized retina. Scleral buckling with large elements supporting the vitreous base, which is often posteriorly displaced, or combination of vitrectomy with scleral buckling may aid in primary success.

Conclusions

The body of information germane to caring for ROP from infancy to adulthood continues to grow. It is hoped that greater knowledge of the pathophysiology of ROP at the cellular level will afford new and more effective therapeutic strategies. Pharmacologic stabilization of aberrant angiogenesis may be one approach. High-quality evidence-based clinical data serve as a guide as to which children should be screened and when. Digital fundus imaging has the potential to revolutionize ROP screening efforts and the conduct of ROP-related clinical trials. We look to prospective studies for guidance as to whether ROP should be treated earlier in zone I and high-risk zone II eyes. Surgical intervention offers the potential for preservation of vision for eyes with ROP-related retinal detachment, particularly if addressed before macular distortion or detachment.

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