Identification and Treatment of Retinopathy of Prematurity: Update 2017

Medha Sharma, MD,*† Deborah K. VanderVeen, MD*†

*Boston Children’s Hospital, Boston, MA
†Harvard Medical School, Boston, MA

Education Gap

Understanding of the pathophysiology of retinopathy of prematurity (ROP) is needed to accurately identify at-risk infants and ensure timely screening. Schedules and strategies for ROP screening are geared toward the detection of vision-threatening ROP.

Abstract

With increased survival of very premature infants in the United States and across the world, retinopathy of prematurity (ROP) remains a leading cause of preventable childhood visual impairment and blindness. Premature birth requires that retinal maturation take place in a physiologically abnormal environment, leading to retinal injury and dysregulated growth and development. Although the pathophysiology of ROP is understood to involve exposure to extrauterine hypoxia and hyperoxia, multiple international studies have failed to identify the optimal approach to preventing ROP. Clinical efforts therefore center on optimizing screening and identification of ROP and on improving ophthalmologic interventions to modify the course of vision-threatening disease.

Objectives

After completing this article, readers should be able to:

1. Understand pathophysiology and stages of retinopathy of prematurity (ROP) development.
2. Define US screening criteria for ROP and identify at-risk infants.
3. Define type 1 ROP, the ROP severity that warrants consideration of treatment.
4. Have an awareness of tools that aid in detecting at-risk infants and methods used to identify type 1 ROP.

AUTHOR DISCLOSURE

Drs Sharma and VanderVeen have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

ABBREVIATIONS

- e-ROP: Telemedicine Approaches for the Evaluation of Acute-Phase Retinopathy of Prematurity
- ETROP: Early Treatment for Retinopathy of Prematurity
- IGF-1: insulinlike growth factor 1
- ROP: retinopathy of prematurity
- RW-ROP: referral-warranted ROP
- TW-ROP: treatment-warranted retinopathy of prematurity
- VEGF: vascular endothelial growth factor
INTRODUCTION

Retinopathy of prematurity (ROP) is a retinal vascular disease found in premature infants, and was first described by Terry in 1942 as “retrolental fibroplasia” due to the appearance of a complete retinal detachment behind the lens. (1) Although many causes were investigated, it was not until the mid-1950s that a randomized multicenter trial showed a clear association between increased incidence of ROP and increased duration of exposure to oxygen. (2) Decades of research have helped optimize management of oxygen supplementation for premature infants, with goals to maximize survival but minimize complications of ROP, pulmonary disease, and other morbidities. Early studies did not show increased mortality in infants with oxygen curtailment or a relationship between ROP development and the concentration of oxygen administered; however, more recent studies found a higher mortality rate among infants given a lower target oxygen saturation range (85%–89% vs 91%–95%). (3)

As advances in neonatal care have increased the survival of very preterm infants in the United States and other countries, ROP has become a leading cause of preventable childhood blindness throughout the world. (4)

EPIEDEMOLOGY

Of the more than 1.5 million children who are blind worldwide, approximately 30,000 children are estimated to be blind because of ROP. In developed countries, severe ROP is typically only found in infants with low birthweight and very low gestational ages at birth, (5) but older, heavier infants can develop severe ROP in low and middle income countries. In the United States, a query of the National Inpatient Sample found that almost 16% of premature infants with a hospital stay of more than 28 days developed ROP, with a primary association of low birthweight. (6)(7) Three large multicenter trials (Cryotherapy for Retinopathy of Prematurity study, Early Treatment for Retinopathy of Prematurity [ETROP] study, and Telemedicine Approaches for the Evaluation of Acute-Phase Retinopathy of Prematurity [e-ROP] study) enrolling infants with birthweights less than 1,251 g showed similar rates of any ROP (65.8%, 68%, 63.7%, respectively) and timing of onset of ROP (all during 34 weeks’ corrected gestational age). The ETROP randomized trial found that among infants with ROP, 36.9% developed moderately severe (“prethreshold”) ROP. (8) Similar associations of higher rates of ROP and severe ROP in infants born at lower gestational ages and with lower birthweights have been found in European populations. (9)(10) In some middle-income countries, variable rates of ROP are reported, which may be attributed to variable survival rates of the most premature infants, variations in early neonatal care, and limited resources for detection and treatment of ROP. For example, India is a country with 26 million births annually, with approximately 2 million children born with birthweights less than 2 kg and risk of ROP even in heavier newborns. (11)

PATHOPHYSIOLOGY OF RETINOPATHY OF PREMATURITY

Vascularization of the retina typically is not complete until near term, so that the normal process of retinal vascular development is interrupted by preterm birth. ROP is an oxygen-regulated process, and develops in 2 phases. (12)(13) In the first phase, the relative hyperoxia of the extrauterine environment results in vasoconstriction and cessation of normal vascular development, and the second phase occurs when a pathologic compensatory mechanism with aberrant neovascularization ensues. If the second phase leads to a significant amount of fibrovascular proliferation and is left untreated, then exudative, tractional, or combined type retinal detachment can occur. Vascular endothelial growth factor (VEGF) has been shown to play an important role in normal angiogenesis, and is upregulated in the second phase of ROP development. (14) VEGF is also potentiated by insulinlike growth factor 1 (IGF-1), which is deficient in infants born before completion of the third trimester of pregnancy. Optimum concentrations of VEGF and IGF-1 are crucial for normal growth and development of many tissues, including eyes, blood vessels, and brain. (15)

The pathophysiology is important when considering management of clinical care with regard to ROP. Changes in clinical care might be implemented during the first phase, before ROP develops. Screening for ROP should coincide with the second phase, to detect ROP of the severity that can lead to visual disability. Mild ROP usually resolves spontaneously and without clinically significant visual or ocular sequelae, but more severe ROP must be detected before unfavorable anatomic changes occur. Some variability in the pace at which ROP develops has been described in at-risk infants and populations. Screening guidelines must incorporate risk factors for the development of ROP and the schedule for screening examinations must be modified based on findings and risks.

CLASSIFICATION OF RETINOPATHY OF PREMATURITY

The International Classification of Retinopathy of Prematurity was first published in 1984, with a revised publication in 2005. (16)(17) Briefly, the location of ROP is divided into
3 retinal zones, with zone 1 being the most posterior and representing the least mature vascularization, zone 2 being intermediate, and zone 3 representing the temporal crescent of immature retina after the nasal part of the retina has developed complete vascularization. The severity of ROP is categorized into 5 stages: stage 1 is a flat “demarcation line” of abnormal fibrovascular tissue at the junction of the vascular and avascular retina; stage 2 is a ridge of fibrovascular tissue; stage 3 represents increasing volume of retinal and extraretinal neovascularization; stage 4 indicates partial retinal detachment; and stage 5 is total retinal detachment. The extent of disease is described in the number of clock hours of ROP (ranging from 1–12, interrupted or contiguous). Increased dilation and tortuosity of posterior retinal vessels is described as “plus disease,” which is an ominous sign of active and progressive disease. More severe disease is characterized by higher stage of ROP in a lower zone of ROP and presence of plus disease. In the new classification, a more severe form of retinopathy found in extremely low birthweight infants (aggressive posterior ROP, formerly known as “rush disease”) is described, which involves central flat intraretinal neovascularization with plus disease. Aggressive posterior ROP can progress very quickly to stage 5 ROP and blindness, so it must be recognized early. Poor vision typically results from ROP that causes macular distortion or detachment of the retina (including the macula), so detection and treatment is needed before this occurs.

Current treatment recommendations are based on the findings from the ETROP study. (18) This study randomized eyes with high-risk prethreshold ROP to receive treatment earlier than or at the conventional timing of treatment as defined in the Cryotherapy for Retinopathy of Prematurity study. (19) The primary outcome of this study was visual outcome at 9 months’ corrected age, with a secondary outcome being retinal structural outcome. A risk analysis model was used to select eyes for inclusion if the risk for adverse outcome was significant, and clinical characteristics were used to reclassify treatment-warranted ROP (TW-ROP) as type 1, for which treatment should be considered, or type 2 (eyes that should be followed and treated only if type 1 ROP develops). Type 1 ROP includes in zone 1, any ROP with plus disease or stage 3 ROP without plus disease, and in zone 2, stage 2 or 3 ROP with plus disease. The figure demonstrates examples of type 1 ROP in zone 1, and stage 3 ROP in zone 2 (Figure).

RETINOPATHY OF PREMATURITY SCREENING

Purpose of Screening
The goal of any ROP screening program is to detect vision-threatening ROP. ROP is a preventable cause of blindness, but timely diagnosis and treatment by an ophthalmologist with expertise in ROP is needed. Neonatologists and pediatricians play a critical role in the early care of premature infants, and should be aware of screening guidelines and risk factors for ROP. Structured registries and tracking systems are needed to ensure that all at-risk infants are screened and followed according to their ROP risk. Furthermore, regional variations in ROP presentation and risk exist, and screening guidelines that are regionally appropriate should be understood and implemented. (20)

Guidelines for Screening
The joint guidelines for ROP screening in the United States were updated and published in 2013. (21) Infants born at less than or equal to 30 weeks’ gestation or with birthweights of less than or equal to 1,500 g should be screened for ROP, as well as older or heavier newborns who have had a complicated medical course, at the discretion of the neonatologist. The timing of the first examination is based on the infant’s gestational age at birth, so that the first examination is

**Figure.** Digital imaging of type I retinopathy of prematurity (ROP) using Retcam shuttle (Clarity Medical Systems, Pleasanton CA). A. Zone 1 ROP with flat intraretinal neovascularization (arrow) and plus disease. B. Zone 2 stage 3 ROP (arrow, with hemorrhage), preplus disease.
generally performed by 31 weeks for infants born at less than or equal to 27 weeks of gestation, and 4 weeks after birth for infants born at greater than or equal to 28 weeks of gestation. Guidelines for follow-up examinations are outlined to ensure that infants with ROP, particularly posterior (zone I) ROP, or those with stage 2 or greater ROP, are seen in 1 week (or sooner) until the ROP regresses. ROP screening is typically performed at the bedside by an ophthalmologist with experience in ROP screening using indirect ophthalmoscopy.

As survival of premature infants increases around the world, differences in prenatal and available neonatal care can affect the susceptibility of these infants to, as well as the severity and course of, ROP. Due to differences in presentation time and neonatal care from one country to another, screening according to US guidelines might not be appropriate for detecting all infants at risk in middle income countries, so screening recommendations should be suited to the population. In developing countries, severe or rapidly progressive ROP may occur in older or heavier infants, so that routine screening cutoffs may be up to 34 weeks' gestational age at birth, and birthweight to 2,000 g, in addition to presence of various other medical or systemic diagnoses or exposures. For example, in India, further guidelines include screening for exposure to oxygen after 30 days, history of respiratory distress syndrome, sepsis, multiple blood transfusions, multiple births, apneic episodes, intraventricular hemorrhage, and in these cases, screening should be considered even for infants born at less than 37 weeks' gestation or less than 1,700 g birthweight. ROP screening practices ideally should be based on population-specific data such as that available in India, (22) but determination and implementation of locally appropriate guidelines remains a struggle in some areas. The Table shows currently established country or regional guidelines, with many additional countries following either US or UK criteria (Table).

Method of Screening

Although ROP screening should be performed by an ophthalmologist who is trained and experienced in ROP, digital imaging is becoming more common as an adjunct to the bedside examination or at times instead of the bedside examination. Several level I studies have shown the usefulness of digital imaging in screening for severe or referral-warranted ROP (RW-ROP). (23)(24)(25)(26)(27) Although digital images may not detect the presence of mild or peripheral ROP, there is a high sensitivity to detect ROP that meets type 1 treatment criteria. (28) A system must be in place for timely interpretation of such images. Follow-up imaging should probably occur more frequently (even weekly), with this understanding, and a plan for examination or treatment in place if significant ROP is detected. Digital imaging may also be useful for screening in underserved areas; however, a limitation for areas with limited resources is the cost of equipment needed to acquire good-quality retinal images. The e-ROP study further demonstrated that a telemedicine system using nonphysician imagers and nonphysician trained readers for detection of RW-ROP (defined as zone I disease, stage 3 disease or worse, or plus disease) is valid, safe, and cost-effective. (29) A secondary analysis of e-ROP data was performed to develop a predictive model for TW-ROP based on the trained readers' evaluation of digital wide-field retinal images taken at 34 weeks' postmenstrual age or earlier, along with gestational age and medical status, including respiratory support and the rate of weight at the first image session. The image evaluation findings of pre-plus disease, stage and zone of ROP, and presence of blot retinal hemorrhage at the first imaging session strongly predicted the development of TW-ROP, which may also be a useful indicator for identifying high-risk infants. (30)

Additional screening tools have been developed, which take into account infant factors other than gestational age and birthweight. (31) The most common postnatal factor incorporated into ROP screening algorithms is a measure of postnatal weight gain, which is thought to act as a surrogate for overall infant medical status. Several algorithms have been developed, which similarly can provide additional information about risk of an infant developing significant ROP, or perhaps more importantly, the low risk for development of severe ROP in infants of higher gestational age, birthweight, and good (physiologic) postnatal weight gain. These algorithms can be a useful complement to the current ROP screening protocols, and can often identify at-risk infants very early in the postnatal course, often weeks before standard screening examinations. Because fewer than 10% of currently screened infants in the United States develop TW-ROP, the use of a screening tool that could identify an infant as low risk could potentially eliminate some examinations, which can be stressful, time-consuming, costly, and probably unnecessary. Although several of the postnatal weight gain algorithms have been validated in NICU populations in the United States and Canada, the sensitivity in other countries has varied. (32) Many institutions use a tiered or combination approach by applying traditional screening guidelines and a weight-gain algorithm, with either digital imaging or bedside indirect ophthalmoscopy.
NeoReviews

Screening after Discharge from the Neonatal Intensive Care Unit

Although the course of ROP is usually determined during the NICU stay, significant ROP can develop after discharge, and infants need to be followed until ROP regresses. The mean age of infants who received treatment in the ETROP trial for high-risk prethreshold ROP was 35.2 ± 2.3 weeks’ postmenstrual age (range, 30.6–42.1 weeks) and 10.0 ± 2.0 weeks’ chronologic age. Because of this variability, it is conceivable that an infant discharged early would require later treatment, though this is uncommon. Laser ablation of the peripheral avascular retina is standard therapy for ROP, though over the past few years, treatment with intravitreal injection of anti-VEGF agents has become more common, particularly for zone 1 or posterior zone 2 disease, or for aggressive posterior ROP. (33) Based on the mode of therapy, differences in disease regression and management have been seen, which affect ophthalmologic follow-up. With laser therapy, a response is seen within 1 to 2 weeks, and recurrences that require treatment are seen within a few weeks. With anti-VEGF therapy, disease regression is seen quickly, with anti-VEGF therapy, disease regression is seen quickly, with a response seen within 1 to 2 weeks, and recurrences that require treatment are seen within a few weeks. Because of this variability, it is conceivable that an infant discharged early would require later management, though this is uncommon. Laser ablation of the peripheral avascular retina is standard therapy for ROP, though over the past few years, treatment with intravitreal injection of anti-VEGF agents has become more common, particularly for zone 1 or posterior zone 2 disease, or for aggressive posterior ROP. Based on the mode of therapy, differences in disease regression and management have been seen, which affect ophthalmologic follow-up. With laser therapy, a response is seen within 1 to 2 weeks, and recurrences that require treatment are seen within a few weeks. With anti-VEGF therapy, disease regression is seen quickly, with a response seen within 1 to 2 weeks, and recurrences are seen within a few weeks. With anti-VEGF therapy, disease regression is seen quickly, with a response seen within 1 to 2 weeks, and recurrences are seen within a few weeks.

Finally, other types of visual disability and ocular problems are found in the premature population, even in the absence of a history of significant ROP. (34) Promoting continued ophthalmologic screening evaluations and management after discharge from the NICU. Some of these problems are ocular, and others are associated with

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>BIRTHWEIGHT (G)</th>
<th>GA (WEEKS)</th>
<th>OTHER CRITERIA</th>
<th>INITIAL SCREENING</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>&lt;1,500</td>
<td>&lt;30</td>
<td>Older or heavier infants with unstable clinical course, at the discretion of the neonatologist</td>
<td>&lt;27 weeks’ GA, screening at 31 weeks’ PMA, &lt;27–30 weeks’ GA, screening at 4 weeks’ chronologic age</td>
</tr>
<tr>
<td>UK</td>
<td>&lt;1,250</td>
<td>&lt;31</td>
<td>Infants with birthweight of 1,251–1,501 or GA of &lt;32 weeks</td>
<td>&lt;27 weeks’ GA, screening at 30–31 weeks’ PMA, screening at 27–32 weeks’ GA, screening at 4–5 weeks’ chronologic age</td>
</tr>
<tr>
<td>Germany</td>
<td>&lt;1,500</td>
<td>&lt;32</td>
<td>32–36 weeks if artificial oxygen ventilation for &gt;3 days</td>
<td>5th week chronic age for &lt;27 weeks’ GA, screening at 31 weeks’ PMA</td>
</tr>
<tr>
<td>Sweden</td>
<td>N/A</td>
<td>&lt;31</td>
<td>Older infants if generally ill or have several comorbidities</td>
<td>4 weeks’ chronic age, but no earlier than 31 weeks’ PMA</td>
</tr>
<tr>
<td>Australia</td>
<td>&lt;1,250</td>
<td>&lt;31</td>
<td>Unstable course or prolonged oxygen requirements at the discretion of the responsible neonatologist</td>
<td>4 weeks’ chronic age, but no earlier than 31 weeks’ PMA</td>
</tr>
<tr>
<td>India</td>
<td>&lt;1,750</td>
<td>&lt;34</td>
<td>Screening even for older and heavier infants if high-risk factors present (&gt;37 weeks or &gt;1,700 g birthweight)</td>
<td>4 weeks’ chronic age, but for GA &lt;28 weeks or weight &lt;1,200 g, screening at 2–3 weeks after birth</td>
</tr>
<tr>
<td>China</td>
<td>&lt;2,000</td>
<td>≤34</td>
<td>Any infant, irrespective of birthweight or GA, if ventilated for &gt;1 week or received supplemental oxygen &gt;30 days</td>
<td>4–6 weeks’ chronic age or at 32–34 weeks’ PMA</td>
</tr>
<tr>
<td>Canada</td>
<td>≤1,250</td>
<td>≤30</td>
<td>More mature infants with severe and complex neonatal clinical course</td>
<td>&lt;26 weeks, screening at 31 weeks, chronic age, &lt;27 weeks, screening at 4-5 weeks’ chronic age</td>
</tr>
<tr>
<td>South Africa</td>
<td>&lt;1,500</td>
<td>&lt;32</td>
<td>1,500–2,000 g birthweight with risk factors such as a family history of ROP, cardiac arrest, multiple (&gt;2) blood transfusions, exchange transfusion, or severe HIE</td>
<td>4–6 weeks’ chronic age or 31–33 weeks’ PMA (whichever is later)</td>
</tr>
<tr>
<td>Mexico</td>
<td>≤1,750</td>
<td>≤32</td>
<td>More mature infants at the discretion of the neonatologist</td>
<td>4–6 weeks’ chronic age</td>
</tr>
<tr>
<td>Argentina</td>
<td>≤1,500</td>
<td>≤32</td>
<td>&lt;37 weeks if unstable clinical course</td>
<td>4–6 weeks’ chronic age</td>
</tr>
<tr>
<td>Brazil</td>
<td>≤1,500</td>
<td>≤32</td>
<td>Screen early if other systemic risk factors</td>
<td>4–6 weeks’ chronic age</td>
</tr>
</tbody>
</table>

GA=gestational age; HIE=hypoxic-ischemic encephalopathy; PMA=postmenstrual age; ROP=retinopathy of prematurity.

TABLE. Regional ROP Screening Guidelines
neurologic impairment. Diagnoses that are commonly seen among the premature infant population include refractive errors, strabismus, nystagmus, amblyopia, visual field deficit, visual processing deficit, reduced contrast sensitivity, and cortical visual impairment. For children who develop severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result. Visual acuity measures at 6 years of age for children enrolled in the ETROP trial showed that of eyes with a favorable anatomic outcome, only 34.6% had normal vision of 20/40 or better, and 40.7% had severe ROP, it is important to remember that even with timely treatment and a favorable anatomic outcome, normal vision does not always result.

References


# Identification and Treatment of Retinopathy of Prematurity: Update 2017

Medha Sharma and Deborah K. VanderVeen

*NeoReviews* 2017;18;e84

DOI: 10.1542/neo.18-2-e84

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>including high resolution figures, can be found at:</td>
<td><a href="http://neoreviews.aappublications.org/content/18/2/e84">http://neoreviews.aappublications.org/content/18/2/e84</a></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>References</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>This article cites 34 articles, 7 of which you can access for free at:</td>
<td><a href="http://neoreviews.aappublications.org/content/18/2/e84#BIBL">http://neoreviews.aappublications.org/content/18/2/e84#BIBL</a></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subspecialty Collections</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>This article, along with others on similar topics, appears in the following collection(s):</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Permissions &amp; Licensing</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:</td>
<td><a href="http://classic.neoreviews.aappublications.org/site/misc/Permissions.xhtml">http://classic.neoreviews.aappublications.org/site/misc/Permissions.xhtml</a></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reprints</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Information about ordering reprints can be found online:</td>
<td><a href="http://classic.neoreviews.aappublications.org/site/misc/reprints.xhtml">http://classic.neoreviews.aappublications.org/site/misc/reprints.xhtml</a></td>
</tr>
</tbody>
</table>
Abnormal Doppler scans, as noted in the case, signified underlying placental dysfunction.

References

Correction

In the section “Pathophysiology of Retinopathy of Prematurity,” the third sentence mistakenly contained the term “relative hypoxia,” which instead should have been “relative hyperoxia.”

The third sentence should read, “In the first phase, relative hyperoxia of the extraterine environment results in vasoconstriction and cessation of normal vascular development, and the second phase occurs when a pathologic compensatory mechanism with aberrant neovascularization ensues.”

The online version of the article has been corrected. The journal regrets the error.
Identification and Treatment of Retinopathy of Prematurity: Update 2017
Medha Sharma and Deborah K. VanderVeen

NeoReviews 2017;18:e84
DOI: 10.1542/neo.18-2-e84

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://neoreviews.aappublications.org/content/18/2/e84

An erratum has been published regarding this article. Please see the attached page for:
http://neoreviews.aappublications.org/content/18/3/e200.full.pdf