

# Cataract and Phthisis Bulbi After Laser Photoablation for Threshold Retinopathy of Prematurity

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- **PURPOSE:** To describe the visual and structural outcome of eyes that developed a dense cataract after laser photoablation for threshold retinopathy of prematurity.
- **METHODS:** A retrospective review of eight consecutive infants who developed dense cataract(s) after bilateral laser photoablation for threshold retinopathy of prematurity. Of the 10 eyes with cataract, five eyes were treated with a diode laser and five with an argon laser. The stage and zone of the retinopathy of prematurity, number of burns applied, time of onset of the cataract, clinical findings at the time of cataract surgery, and the course after cataract surgery were reviewed.
- **RESULTS:** Six eyes had zone 1 disease and four had zone 2 disease. The mean number of burns applied per eye was  $2532 \pm 856$  (range, 1400 to 4500). A cataract was diagnosed a median of 13 weeks (range, 1 to 28 weeks) after laser photoablation. Nine of the 10 cataracts were sufficiently dense to preclude a view of the fundus. All 10 eyes had clinical signs suggestive of an inflammatory or ischemic process that included one or more of the following findings: corneal edema, pupillary membrane, iris atrophy, depigmentation of ciliary processes, pigment on the anterior lens surface, posterior synechiae, hyphema, and shallow anterior chamber. Nine eyes underwent cataract surgery. Five of the 10 eyes had retinal detachment ranging in severity from stage 4A to stage 5 at the time of cataract surgery. Nine of the 10 eyes progressed to phthisis bulbi and no light perception.
- **CONCLUSIONS:** A dense cataract developing in the eye of an infant after laser photoablation for threshold retinopathy of prematurity is associated with a poor

visual prognosis. The constellation of associated clinical findings appears to be most consistent with anterior segment ischemia. (*Am J Ophthalmol* 2000;129:585-591. © 2000 by Elsevier Science Inc. All rights reserved.)

**L**ASER PHOTOCOAGULATION OF THE AVASCULAR RETINA is generally an effective treatment for threshold retinopathy of prematurity.<sup>1-10</sup> Compared with cryotherapy for retinopathy of prematurity, it is associated with a lower rate of retinal detachment,<sup>1-9</sup> less myopia<sup>9,10</sup> and less postoperative lid edema and conjunctival chemosis.<sup>11</sup> In addition, when laser photocoagulation is administered by a transpupillary approach, a conjunctival incision is not necessary. However, laser retinal photoablation in eyes with retinopathy of prematurity may be associated with an increased risk of cataract formation. Whereas only 2% of infants treated with cryotherapy for threshold retinopathy of prematurity develop a visually significant cataract,<sup>12</sup> as many as 6% of infants with threshold retinopathy of prematurity develop a visually significant cataract after transpupillary laser photoablation.<sup>13</sup> Two types of cataracts have been described after transpupillary laser photoablation in infantile eyes. The first type consists of focal opacities (either punctate or vacuolated) at the capsular or subcapsular level that are visually insignificant and often resolve spontaneously.<sup>14,15</sup> The second type consists of total lens opacification that completely obstructs the visual axis.<sup>16-20</sup> The latter type has generally been treated with a lensectomy and anterior vitrectomy. Some of these eyes have been reported to progress to retinal detachment after cataract surgery, but for many the long-term outcome has not been reported. A cataract also develops frequently in eyes with stage 4 or 5 retinal detachment.<sup>21,22</sup> These cataracts differ from the two types of cataract described above in that their onset is later and they occur as a sequela of retinal detachment or vitreoretinal surgery. We report the long-term visual and structural outcomes in eight consecutive infants (10 eyes) who developed cataract shortly after laser photoablation for threshold retinopathy

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**TABLE 1.** Clinical Findings in Eyes Developing Cataract

Patient No.	Eye(s) With Threshold ROP	Zone	Type of Laser	No. of Burns (RE/LE)	Adjusted Gestational Age When Treated With Laser (weeks)	Interval Between Laser Therapy and Cataract Diagnosis	Eye(s) With Cataract	Type of Cataract	Age at Cataract Surgery (months)
1	Both eyes	I	Diode	4500/4500	32	12	RE	Total	5.5
2	Both eyes	II	Diode	3009/3010	38	2	LE	Total	4
3	Both eyes	I	Argon	2225/2225	27	1	Both eyes	Total	3
4	Both eyes	II	Diode	1400/1600	38	3	RE	Total with rent in posterior lens capsule	4
5	Both eyes	RE-I/II LE-I	Argon	3000/3000	38	4	LE	Partial	3
6	Both eyes	I	Diode	3000/2600	35	3	LE	Total	3.5
7	Both eyes	I	Argon	1775/2055	36	1	Both eyes	Membranous	4.5
8	Both eyes	RE-I LE-II	Diode	NA	32	28	LE	Total	13.5

NA = not available; ROP = retinopathy of prematurity.

of prematurity. Nine eyes progressed to phthisis bulbi after cataract surgery. We propose a possible mechanism for the pathogenesis of this phenomenon.

## METHODS

WE CONDUCTED A RETROSPECTIVE REVIEW OF A CONSECUTIVE series of eight infants (10 eyes) who developed a dense cataract after bilateral transpupillary laser photoablation for threshold retinopathy of prematurity for which a 1-year or longer follow-up was available. Nine eyes (seven infants) were treated with transpupillary laser photoablation by six different retinal surgeons at centers located in the southeastern United States. One eye was treated by an ophthalmology resident under the supervision of a retinal surgeon. Five eyes were treated with argon laser and five with diode laser (Table 1). In addition to receiving laser photoablation of the posterior retina, patient 3 also received cryotherapy of the anterior retina. Before laser treatment, the infants were not noted to have any lens abnormalities. The mean gestational age of the eight infants was 26 weeks (range, 23 to 30 weeks) and the mean birth weight was 797 ± 200 gm (range, 615 to 1230 gm). Except for patient 5, who had prethreshold disease, all patients had threshold retinopathy of prematurity as defined by the International Committee for the Classification of Retinopathy of Prematurity<sup>23</sup> at the time they underwent laser photoablation. Both eyes were treated in all eight patients.

Before cataract surgery, biomicroscopy was performed using a hand-held slit lamp. In five of the eight patients, intraocular pressure was measured using pneumotonom-

etry. B-scan ultrasonography was performed on all patients preoperatively except for patient 6, who had only a partial cataract. All lensectomies were performed by a pediatric ophthalmologist (Drs Lambert and Drack) or by a retinal surgeon (Dr Capone) at the Emory Eye Center. A two-port approach was used through the limbus. A vitreous cutting instrument was placed through one port while an infusion cannula was placed through the second port. After aspirating the lens, a primary posterior capsulotomy and anterior vitrectomy was performed except in patient 2 in whom the posterior capsulotomy and anterior vitrectomy were delayed for 3 days so the retina could be evaluated in the interim by a retinal surgeon. One eye (patient 8) also underwent primary intraocular lens (IOL) implantation. Postoperatively, patients were treated with topical corticosteroids, antibiotics, and a cycloplegic agent. Four patients were followed at the Emory Eye Center, and four patients were followed by a local pediatric ophthalmologist or retinal surgeon.

## RESULTS

SIX EYES HAD ZONE 1 DISEASE, ONE EYE HAD POSTERIOR zone 2 disease, and three eyes had zone 2 disease. The median adjusted gestational age at the time of laser photoablation was 34.5 weeks (range, 27 to 38 weeks). The mean number of burns per eye was 2532 ± 856 (range, 1400 to 4500) with a power ranging from 240 to 430 mW and a duration ranging from 150 to 200 msec. A cataract was diagnosed in these eight patients a median of 3 weeks (range, 1 to 28 weeks) after laser photoablation (Table 1). Eight of the 10 cataracts were diagnosed 4 weeks or less

**TABLE 2.** Clinical Findings at the Time of Cataract Surgery

Patient No.	Pupillary Membrane	Iris Atrophy	Pigment on Anterior Lens Capsule	Posterior Synechiae	Corneal Edema	Depigmentation of Ciliary Processes	Shallow Anterior Chamber	Intraocular Pressure	B-scan Findings
1	+	+	-	+	+	-	+	RE:12	Retina attached both eyes
2	-	+	+	+	+	-	-	RE:22 LE:8	Retina attached both eyes
3	-	+	+	-	+	-	+	RE:10 LE:9	Stage 4A retinal detachment both eyes
4	-	+	+	+	+	-	+	NA	Retina attached both eyes Choroidal thickening RE
5	-	-	-	+	-	+	-	NA	Stage 4B retinal detachment both eyes*
6	-	-	-	-	+	-	-	RE:15 LE:15	Retina attached both eyes
7	+	+	-	-	-	-	-	NA	Stage 5 retinal detachments both eyes
8	+	-	-	+	+	+	+	RE:20 LE:20	Retina attached both eyes

NA = not available.  
\*Ultrasonography not performed; retinal detachments diagnosed by indirect ophthalmoscopy.

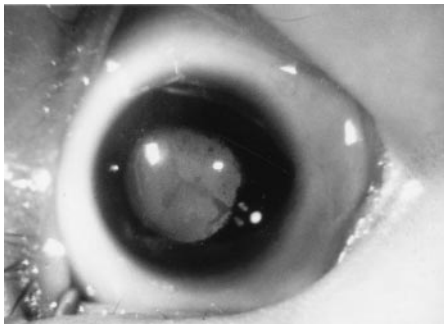
after laser photoablation. In most instances patients were followed at weekly intervals during the immediate postoperative period. The two patients (patients 1 and 8) who developed a cataract after the first postoperative month may have had a cataract for a longer period of time because they were being followed less frequently. Patient 1, however, had been examined 2 weeks before the onset of cataract, and no lens abnormalities were noted, and patient 8 had been examined 2 months before the onset of cataract and no lens abnormalities were noted. Two patients developed bilateral cataracts, whereas six patients developed a unilateral cataract. Seven of the eyes had total cataract, one eye had a partial cataract, and two eyes had a membranous cataract. Cataract surgery was performed on nine of the 10 eyes. A variety of anterior segment abnormalities suggestive of an inflammatory or ischemic process were noted at the time of cataract surgery in these eyes (Table 2). These abnormalities included pupillary membrane (n = 3), iris atrophy (n = 5), pigment on the anterior lens capsule (n = 3), posterior synechiae (n = 5), corneal edema (n = 6), depigmentation of the ciliary processes (n = 2), and shallow anterior chamber (n = 4) (Figure 1). Each eye had one to five of these abnormalities. In addition, a hyphema was noted during the first postoperative examination of three patients after laser photoablation. In all three eyes the hyphema had cleared by the time cataract surgery was performed.

The intraocular pressure was reduced preoperatively in two cataractous eyes and elevated in one cataractous eye compared with their fellow eyes. There was no difference

in the interocular intraocular pressure in two other patients.

The retina detached in five of the 10 eyes before cataract surgery. Two eyes had stage 4A detachment, one eye had a stage 4B detachment, and two eyes had stage 5 detachment. Two patients (patients 3 and 7) had bilateral retinal detachment. In five eyes, lens material leaked into the anterior chamber as soon as an opening was created in the anterior lens capsule, indicating liquefaction of the lens. The membranous cataract in the one eye of patient 7 was so fibrotic that an opening could not be created in the cataract either with a vitreous cutting instrument or with intraocular scissors. The fellow eye of patient 7 did not undergo cataract surgery.

The patients were followed for a median of 2.0 years (range, 1 to 5 years) after cataract surgery. Nine of the 10 eyes had no light perception. The one eye with vision (patient 6) wore a contact lens, but was amblyopic. Five of the eight patients underwent additional surgeries: vitrectomy and membrane stripping (n = 4), pupillary membranectomy (n = 6), posterior capsulotomy and anterior vitrectomy (n = 1), synechiolysis (n = 1), and strabismus surgery (n = 1) (Table 3). At last follow-up, nine of the 10 eyes were phthisical and most wore prosthetic shells. All eyes were microphthalmic with corneal diameters ranging from 6 to 9 mm. The only eye without phthisis bulbi (patient 6) had a corneal diameter of 9 mm, whereas the fellow phakic eye had a corneal diameter of 11 mm. In no case was an interocular difference in corneal diameter



**FIGURE 1.** The right eye of patient 4 at 4 months of age. The patient had zone 2 threshold retinopathy of prematurity treated 4 weeks earlier in this eye using a diode laser (1400 spots, 240 mW, 200 ms). There is a dense cataract with pigment on the anterior lens surface, posterior synechiae, a shallow anterior chamber with iridocorneal touch nasally, and mild corneal edema. A large rent was found in the posterior lens capsule during cataract surgery.

noted before laser photoablation therapy. One eye also developed extensive iris neovascularization (patient 8).

## DISCUSSION

WE REPORT THE DEVELOPMENT OF CATARACT IN 10 EYES after laser photoablation for threshold retinopathy of prematurity. In eight of the 10 eyes the cataract developed during the first month after laser photoablation. Five of these eyes had retinal detachment at the time of cataract surgery, and all but one eye went on to develop phthisis bulbi. Clinical findings were present in all of these eyes, suggestive of an earlier inflammatory or ischemic process.

The number of laser burns administered to the eyes in this series was greater than in other series.<sup>2,5,7</sup> It is the treatment philosophy at our institution that photoablation of the peripheral avascular retina should be confluent. This philosophy derives from the confluent ablation standard established in the Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) Study,<sup>3,8,12</sup> as well as from clinical series supporting the contention that eyes with threshold retinopathy of prematurity treated with a confluent laser pattern fare more favorably than eyes that have undergone less dense treatment (Ferrone et al, oral presentation, American Academy of Ophthalmology, November 10, 1998). Four of the patients were treated at our institution using this treatment philosophy. The mean number of burns used per eye is similar to what we typically used for eyes with such posterior disease. In other series that have reported using fewer laser burns per eye, nonconfluent photoablation was used with gaps of one-quarter to one-half burn width between each burn.<sup>2,7,11</sup> This difference in technique may partially explain the greater number of burns per eye in our series. A second possible reason for the

high number of laser burns used in this series is the higher percentage of eyes with zone 1 and postequatorial zone 2 disease in this series compared with other series that have reported using fewer laser burns per eye.<sup>2,5,7</sup>

A Medline search revealed clinical reports of 16 infants who developed cataract(s) after transpupillary laser photoablation for threshold retinopathy of prematurity.<sup>13-19</sup> Cataracts were visually insignificant in six of these patients, and in three patients they resolved spontaneously. The remaining 10 patients had total cataract(s) and underwent cataract surgery. Nine of these 16 patients developed bilateral cataract. Many of these patients also developed corneal edema, hyphema, and a shallow anterior chamber soon after laser photoablation. Five of the eyes were reported to progress to inoperable retinal detachment, even though the retinas were reported to be attached in all but one patient at the time of cataract surgery. Long-term follow-up was not available for three of these patients. In 1997, Gold<sup>19</sup> surveyed 285 North American pediatric ophthalmologists regarding the method they used to treat threshold retinopathy of prematurity and whether a cataract was noted after treatments. The respondents reported 68 children who developed a cataract after treatment for threshold retinopathy of prematurity: 42 after argon laser photoablation, 21 after diode laser photoablation, and five after cryotherapy. One-half of the cataracts were judged to be visually significant, but the long-term outcome of these eyes and the laterality of the cataracts was not surveyed.

The visual prognosis of a unilateral infantile cataract, even with prompt surgery, is generally poor. This is usually because of a delay in initiating treatment or to poor compliance with contact lens wear or patching therapy of the fellow eye.<sup>24</sup> Retinal detachment is a rare complication of infantile cataract surgery, and when it does occur, it usually occurs decades later.<sup>25,26</sup> In a large series of children who underwent cataract surgery reported by Parks and associates,<sup>27</sup> only one of 174 eyes developed retinal detachment and no eye developed phthisis bulbi.

What is the etiology of the cataracts that develop in children with threshold retinopathy of prematurity, and why do they have such a poor outcome? Focal lens changes noted intraoperatively during transpupillary laser therapy are likely the result of focal thermal effects of the laser beam (Table 4). These changes have been reported to occur with both diode and argon laser treatments, and they resolve spontaneously in one-half of cases.<sup>14,15</sup> Similar lesions have also been reported in adults after laser treatments for subretinal neovascularization or diabetic retinopathy.<sup>28,29</sup>

There are several possible etiologies for the total cataracts that have been reported by us and by others after both argon and diode transpupillary photoablation in infants with threshold retinopathy of prematurity. The associated clinical findings of pupillary membranes, iris and ciliary process atrophy, pigment on the anterior lens surface,

**TABLE 3.** Additional Ophthalmic Surgeries and Visual Outcomes in Eight Infants With Laser-induced Cataract

Patient No.	Follow-up Interval Since Lensectomy (years)	Subsequent Surgeries	Anatomical Outcome	Visual Outcome
1	5	<ul style="list-style-type: none"> <li>● Membranectomy ×2</li> <li>● Vitrectomy/membrane peeling</li> </ul>	Phthisis bulbi RE	NLP RE
2	2	<ul style="list-style-type: none"> <li>● Posterior capsulotomy/anterior vitrectomy</li> </ul>	Phthisis bulbi LE	NLP LE
3	2	<ul style="list-style-type: none"> <li>● Vitrectomy/membrane peeling both eyes</li> <li>● Synechiolysis</li> </ul>	Phthisis bulbi both eyes	NLP both eyes
4	2	None	Phthisis bulbi RE	NLP RE
5	1 1/2	None	Phthisis bulbi LE	NLP LE
6	2	<ul style="list-style-type: none"> <li>● Strabismus surgery</li> </ul>	Microphthalmia LE	Amblyopia LE
7	2	None	Phthisis bulbi both eyes	NLP both eyes
8	1	<ul style="list-style-type: none"> <li>● Membranectomy ×4</li> <li>● Vitrectomy/membrane stripping</li> </ul>	Phthisis bulbi LE	NLP LE

NLP = no light perception.

**TABLE 4.** Types of Cataract in Infants After Laser Photocoagulation for Retinopathy of Prematurity

Type of Cataract	Proposed Mechanism	Type of Laser	Latent Period Before Cataract Develops	Associated Findings	Natural History
Capsular or subcapsular punctate opacities	Thermal injury	Argon or diode	None	Posterior synechiae	May resolve after 2–4 weeks
Vacuolar	Optical interface phenomenon	Diode	None	None	May resolve over 6 weeks
Total	Anterior segment ischemia	Argon or diode	Usually 1 to 4 weeks, but it can be as long as 6 months	<ul style="list-style-type: none"> <li>● Corneal edema</li> <li>● Shallow anterior chamber</li> <li>● Pupillary membrane</li> <li>● Pigment on anterior lens surface</li> <li>● Iris atrophy</li> <li>● Hyphema</li> <li>● Posterior synechiae</li> <li>● Iris neovascularization</li> </ul>	Commonly progresses to stage 5 retinal detachment and/or phthisis bulbi
Total	Associated with detached retina or after vitreoretinal surgery	—	Months or years after retinal detachment or vitreoretinal surgery	<ul style="list-style-type: none"> <li>● Angle-closure glaucoma</li> <li>● Shallow anterior chamber</li> <li>● Corneal opacification</li> <li>● Posterior synechiae</li> </ul>	Stable unless angle-closure glaucoma develops

posterior synechiae, corneal edema, hyphema, and a shallow anterior chamber suggest an inflammatory or ischemic etiology. The two most likely etiologies are phacoantigenic uveitis or anterior segment ischemia. In support of phacoantigenic uveitis, patient 4 had a rent in the posterior lens capsule at the time of cataract surgery, and the lens material was noted to be liquefied in some eyes. Moreover, microperforations that were not appreciated intraoperatively may have been present in other cases. Both the rapid

onset of these cataracts after photoablation and the associated iridocyclitis support this etiology.

There is also a body of clinical and experimental literature that supports anterior segment ischemia as a cause of the findings we observed. Anterior segment ischemia has been reported in patients after pan-retinal photocoagulation,<sup>30–32</sup> scleral buckling surgery,<sup>33</sup> strabismus surgery,<sup>34–36</sup> and cyclocryotherapy.<sup>37</sup> It is typically associated with the same findings we observed in our series,

namely, corneal edema, iris atrophy, posterior synechiae, and cataract. The most compelling evidence, however, comes from a rabbit model of anterior segment ischemia developed by Freeman and associates.<sup>38</sup> They produced anterior segment ischemia in six of 10 rabbit eyes by administering diathermy in a double row along the course of the long posterior ciliary arteries from the equator to the ora serrata as the overlying medial and lateral rectus muscles were retracted. On the first postoperative day, diffuse corneal edema was noted. By the fourth postoperative day, the cornea had a ground glass appearance. The cornea then generally cleared in 3 to 4 weeks, revealing posterior synechiae, pigment on the anterior lens capsule, and a mature cataract. In two eyes, however, the onset of the cataract was delayed for 6 months. All six of these eyes developed phthisis bulbi. However, if the same diathermy treatment was applied to only one long posterior ciliary artery, the only clinical sign that developed was transient hypotony. Anterior segment ischemia did not develop in the 10 eyes that received cryotherapy along the course of both long posterior ciliary arteries. The clinical course of the eyes in our series closely approximates the clinical course reported in these rabbit eyes.

Histopathologic studies of monkey and cat eyes after argon and diode transpupillary photocoagulation have demonstrated that laser burns not only produce necrosis of the outer retina, but can also produce thermal injuries to the inner sclera<sup>39</sup> and to the ciliary nerves as they course through the suprachoroidal space.<sup>40</sup> Assuming that thermal injury to the long posterior ciliary arteries can produce anterior segment ischemia in some infantile eyes after transpupillary photoablation, there are several possible treatment alternatives that should be employed to minimize or eliminate these injuries. First, the least amount of energy necessary to create a discrete grey white burn could be used, particularly in the 3 o'clock and 9 o'clock meridians, where the long posterior ciliary arteries course through the suprachoroidal space.<sup>41</sup> This may minimize thermal injury to the long posterior ciliary arteries without compromising the effectiveness of the treatment for retinopathy of prematurity. Second, a scatter pattern rather than a confluent pattern of laser spots could be administered along the 3 o'clock and 9 o'clock meridians. However, this may result in a higher rate of retinal detachment (Ferrone et al, oral presentation, American Academy of Ophthalmology, November 10, 1998). Third, laser photoablation could possibly be staged, particularly in eyes with posterior disease. However, this may also result in a higher rate of retinal detachment. Finally, cryotherapy could be used instead of laser photocoagulation to treat the horizontal meridian, because freezing causes less damage to ocular vessels than photocoagulation.<sup>42</sup> It seems unlikely that using a transscleral delivery system for laser photocoagulation would have any advantage over a transpupillary deliver system if the pathogenesis of these cataracts is related to thermal injury to the long posterior ciliary

arteries.<sup>43,44</sup> In addition, transcleral laser treatment generally requires a conjunctival incision for posterior disease and is associated with more postoperative conjunctival and eyelid edema.

If an infantile eye with threshold retinopathy of prematurity develops corneal edema and iridocyclitis in the postoperative period after laser photocoagulation, it would seem prudent to treat this eye with the frequent instillation of topical corticosteroids. Although immediate cataract surgery is usually recommended in an infant with a dense unilateral cataract, it may be preferable to defer cataract surgery if there are objective signs of anterior segment ischemia, because cataract surgery may accelerate the process of these eyes becoming phthisical. Given the poor prognosis and the possibility that concurrent intraocular lens implantation may induce further inflammatory changes, primary intraocular lens implantation should be avoided. The high incidence of retinal detachment in these eyes may arise from a synergistic effect of the anterior segment ischemia on the progression of the retinopathy of prematurity. Although retinal detachment surgery may be beneficial in some cases, such eyes generally fare poorly.

In summary, most total cataracts that develop in infants with threshold retinopathy of prematurity after laser photocoagulation likely arise secondary to anterior segment ischemia. This complication may be preventable either by lightly treating the 3 o'clock and 9 o'clock meridians with laser photocoagulation or by using cryotherapy instead of laser photocoagulation along these meridians.

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