

RETINOPATHY OF PREMATURITY: LATE COMPLICATIONS IN THE BABY BOOMER GENERATION (1946–1964)

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ABSTRACT

Purpose: To report the natural history and late complications of retinopathy of prematurity (ROP) in members of the baby boomer generation (1946–1964).

Methods: Retrospective observational series of 86 eyes from 47 adult ROP patients (aged 45 to 56 years) who did not receive treatment as infants. Posterior segment pathology, refractive status, lens status, and visual acuity were evaluated.

Results: Seventy-six eyes (88.4%) had posterior segment pathology due to ROP, including 22 (25.6%) with retinal detachments. The rates of myopia and cataract formation were 90.7% and 83.7%, respectively. Visual acuity was 20/200 or worse in 43 eyes (51.2%) and 20/60 or better in 35 (41.7%).

Conclusions: There are significant late complications of ROP underscoring the importance of lifelong follow-up.

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INTRODUCTION

Prior to the 1940s, retinopathy of prematurity (ROP) was an unknown disease because severe prematurity was often fatal. The period between the 1940s and the introduction of treatment in the 1980s resulted in a cohort of baby boomers with ROP that escaped initial treatment. Although the disease continues to affect infants of especially low birth weight and gestational age,¹ effective treatment is now available with cryotherapy or laser.²⁻⁴ Complications of ROP include myopia, early development of cataracts, iris neovascularization, glaucoma, retinal pigmentation, retinal folds, dragging of the retina, lattice-like degeneration, retinal tears, and rhegmatogenous and exudative retinal detachments.⁵⁻¹⁰ This report presents a review of baby boomers with ROP born during a time when neither a generally accepted form of treatment nor the definitive international classification of ROP was available.^{11,12}

METHODS

The study population included patients aged 45 years or older diagnosed as having ROP as infants. After approval by the institutional review board was received, patients' charts were reviewed for birth weight, gestational age, present age, gender, posterior segment pathology, prior surgery, refractive error, phakic status, glaucoma, and best-corrected visual acuity.

RESULTS

Forty-seven referral patients with ROP were identified. There were 86 eyes (eight were enucleated). Thirty-three patients (70.2%) were female and 14 were male (29.8%), suggesting that females may have had a greater tendency to survive than did males (Table 1). However, this observation is not statistically significant. Earlier reports of ROP have found that males outnumbered females three to two.¹³ By comparison, a database review of Jefferson Hospital's neonatal intensive care nursery (babies weighing 1,250 gm or less born between June 1995 and August 2003) revealed the survival of 182 males and 173 females, an almost gender-neutral survival rate. Both genders had a 24.1% prevalence of stage 3 ROP. Forty-four males with stage 3 ROP (98%) survived, and 42 females with stage 3 ROP (93%) survived.

Our study population had a mean age of 49.9 years with a range of 45 to 56 years. Birth weights (known in 36 patients) ranged from 680 to 2,438 gm with a mean of 1,251 gm. The mean gestational age (known in 32 patients) was 28.2 weeks, and the range was 20 to 36 weeks.

POSTERIOR SEGMENT FINDINGS

Seventy-six of the 86 eyes (88.4%) had posterior segment pathology due to ROP (Table 2). The remaining 10 eyes demonstrated other forms of regressed ROP. Retinal dragging was the most common posterior segment pathology, occurring in 29 of the 86 eyes (33.7%).

Retinal detachments occurred in 22 eyes (25.6%). Five were exudative and 17 were rhegmatogenous. Three eyes with exudative detachments were successfully reattached using cryotherapy, scleral buckling, and vitrectomy with buckling. Two eyes treated with scleral buckling alone failed to reattach. Twelve eyes with rhegmatogenous retinal detachments were successfully buckled, and two were reattached after vitrectomy with scleral buckling. Vitrectomy was unsuccessful in one eye as was scleral buckling in two others. In all, 17 eyes (14 with rhegmatogenous detachments and three with exudative detachments) of the 22 eyes with retinal detachments (77.3%) were reattached.

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Bold type indicates **AOA** member.

Two of the failures were exudative detachments, and three were rhegmatogenous. The exact date of retinal detachment onset was known for 11 eyes. One of these was exudative and occurred at age 36 years. The average age at onset for all retinal detachments was 35 years, and the range was 14 to 51 years.

Nine eyes (10.5%) had retinal pigmentation, and eight (9.3%) had lattice-like degeneration. Retinal tears occurred in seven eyes (8.1%) and were treated with cryotherapy (five eyes) and laser (two eyes). Six eyes (7.0%) had retinal folds, and five eyes (5.8%) had posterior vitreous detachments. The prevalence of macular holes, epiretinal membranes, chorioretinal scars, and retinal pigment epithelium changes was 2.3% for each. Lacquer cracks occurred in one eye, as did a macular star (1.2%).

REFRACTIVE ERRORS

The refractive error was known for 43 of the 86 eyes (Table 2). Thirty-nine of the 43 (90.7%) showed some degree of myopia, ranging from -0.50 to -22.00 diopters, with a mean of -5.71 diopters. Fourteen eyes (32.6%) were highly myopic (≥ -6.00 diopters), 19 (44.2%) were moderately myopic (< -6.00 diopters but ≥ -2.00), and six (14.0%) were mildly myopic (< -2.00 but > 0) (Table 3). Four eyes (9.3%) were either emmetropic or hyperopic. Only 10 refractions were known for the 20 eyes that received a scleral buckle. The range for this subgroup was from -0.50 to -6.25 diopters, with a mean of -3.63 diopters.

LENS STATUS

Fourteen of the 86 eyes (16.3%) had a clear natural lens, and the remaining 72 eyes (83.7%) had a cataract or implant or were aphakic (Table 2). Stated another way, 35 patients (74.5%) had had cataract surgery on one or both eyes, whereas only 12 (25.5%) retained their natural lenses. Nuclear sclerosis was the most common type of cataract, occurring in 13 of the 29 phakic eyes (44.8%) that did not undergo cataract extraction.

CORNEA AND GLAUCOMA

Band keratopathy developed in five eyes (5.8%), and two eyes (2.3%) had opaque corneas. The remaining 79 eyes (91.9%) had clear corneas (Table 3).

Fourteen of the 86 eyes (16.3%) had some form of glaucoma. Six (7.0%) had narrow angles treated with laser peripheral iridotomy. Open-angle glaucoma occurred in five eyes (5.8%). Three eyes (3.5%) were diagnosed with neovascular glaucoma. One was treated with panretinal photocoagulation, one with a tube shunt, and one with a tube shunt in addition to panretinal photocoagulation.

BEST-CORRECTED VISUAL ACUITY

Twenty-three of 84 eyes (27.4%) had a best-corrected visual acuity (BCVA) of 20/30 or better (Table 4). Eighteen eyes (21.4%) had a BCVA between 20/30 and 20/200, and 43 eyes (51.2%) were 20/200 or worse.

TABLE 1. BIRTH WEIGHT, GESTATIONAL AGE, GENDER, AND PRESENT AGE OF 47 PATIENTS WHO WERE DIAGNOSED WITH RETINOPATHY OF PREMATURETY

| PATIENT NO. | BIRTH WEIGHT (Grams) | GESTATIONAL AGE (WK) | GENDER | PRESENT AGE (YR) |
|-------------|----------------------|----------------------|--------|------------------|
| 1 | 1474 | 26 | F | 55 |
| 2 | 1360 | 28 | M | 52 |
| 3 | 1190 | 24 | M | 51 |
| 4 | 1417 | 32 | F | 51 |
| 5 | 1701 | 30 | F | 51 |
| 6 | 1360 | 32 | F | 50 |
| 7 | 1219 | 28 | F | 50 |
| 8 | 1502 | 32 | F | 50 |
| 9 | 1077 | 20 | F | 50 |
| 10 | 1361 | 24 | F | 50 |
| 11 | 964 | 28 | M | 50 |
| 12 | 992 | 32 | F | 50 |
| 13 | 1474 | 30 | F | 49 |
| 14 | 1361 | 28 | F | 49 |

TABLE 1. (CONTINUED) BIRTH WEIGHT, GESTATIONAL AGE, GENDER, AND PRESENT AGE OF 47 PATIENTS WHO WERE DIAGNOSED WITH RETINOPATHY OF PREMATUREITY

| PATIENT NO. | BIRTH WEIGHT (Grams) | GESTATIONAL AGE (WK) | GENDER | PRESENT AGE (YR) |
|--------------------|-----------------------------|-----------------------------|---------------|-------------------------|
| 15 | 2438 | 36 | F | 51 |
| 16 | 794 | 24 | F | 54 |
| 17 | 1020 | 36 | M | 51 |
| 18 | 1588 | 26 | F | 51 |
| 19 | 1276 | 32 | F | 46 |
| 20 | 1503 | 33 | F | 46 |
| 21 | 907 | 24 | F | 46 |
| 22 | 1020 | 26 | F | 45 |
| 23 | 1474 | 32 | F | 50 |
| 24 | 1333 | 28 | M | 51 |
| 25 | 907 | 24 | M | 49 |
| 26 | ND | ND | M | 47 |
| 27 | 1474 | ND | M | 51 |
| 28 | 1162 | 28 | F | 48 |
| 29 | 907 | ND | F | 48 |
| 30 | 1361 | ND | M | 50 |
| 31 | ND | ND | M | 49 |
| 32 | 936 | 26 | F | 48 |
| 33 | ND | ND | F | 53 |
| 34 | ND | ND | M | 51 |
| 35 | ND | ND | F | 49 |
| 36 | 680 | 24 | F | 48 |
| 37 | ND | ND | F | 50 |
| 38 | 1361 | ND | F | 52 |
| 39 | ND | ND | F | 47 |
| 40 | 1559 | 28 | F | 50 |
| 41 | ND | ND | F | 52 |
| 42 | ND | ND | M | 56 |
| 43 | 1359 | ND | M | 50 |
| 44 | 716 | 24 | F | 54 |
| 45 | 822 | 24 | F | 50 |
| 46 | ND | ND | F | 48 |
| 47 | ND | 32 | M | 47 |

ND = not determined.

TABLE 2. BCVA, POSTERIOR SEGMENT FINDINGS, TREATMENT, RESULTS, REFRACTIVE ERROR, LENS STATUS, CORNEA, AND GLAUCOMA FOR EACH EYE OF THE 47 PATIENTS WITH RETINOPATHY OF PREMATURITY

| PATIENT NO. AND EYE | BCVA | POSTERIOR SEGMENT FINDINGS AND INDICATIONS FOR TREATMENT | TREATMENT/ RESULTS | REFRACTIVE ERROR* | LENS STATUS | GLAUCOMA/ TREATMENT | CORNEA/ OTHER |
|---------------------|--------|--|--------------------|-------------------|-------------|---------------------|---------------|
| 1 RE | LP | Exudative RD | VIT, SB/flat | -4.00 | Clear | | |
| 1 LE | 20/30 | Retinal tear | CT | -5.25 | Clear | | BK |
| 2 RE | 20/30 | Dragging | | -5.25 | NS | | |
| 2 LE | 20/30 | Rhegmatogenous RD, dragging | SB/flat | -3.00 | NS, PSC | | |
| 3 RE | 20/60 | Rhegmatogenous RD, dragging | SB/Flat | -5.25 | PCIOL | | |
| 3 LE | HM | Rhegmatogenous RD, dragging, ERM | VIT, SB/flat | -3.00 | PCIOL | | |
| 4 RE | 20/40 | ERM | | -10.00 | PCIOL | | |
| 4 LE | 20/40 | Retinal fold | | -10.00 | PCIOL | | |
| 5 RE | 20/400 | | | -6.00 | PCIOL | NA/LPI | |
| 5 LE | 20/400 | | | -6.00 | PCIOL | | |
| 6 RE | 20/100 | Dragging, retinal pigment | | -2.50 | PCIOL | | |
| 6 LE | CF | PVD | | -2.50 | PCIOL | | |
| 7 RE | 20/50 | Rhegmatogenous RD, PVD | SB/flat | -2.25 | PCIOL | | |
| 7 LE (ENUC) | | | | Balance | | | |
| 8 RE | 20/50 | Dragging | | -0.75 | PCIOL | | |
| 8 LE | CF | Dragging | | +0.25 | PCIOL | | |
| 9 RE | 20/30 | Dragging, lattice-like degeneration | | -14.50 | PCIOL | | BK |
| 9 LE (ENUC) | | | | Balance | | | |
| 10 RE | 20/70 | Dragging | | +10.00 | Aphakic | | |
| 10 LE | 20/70 | Dragging | | 0 | PCIOL | NA/LPI | |
| 11 RE | 20/30 | Rhegmatogenous RD, dragging, PVD | SB/flat | -5.25 | PSC | | |
| 11 LE | 20/20 | Dragging | | -3.00 | PSC | | |
| 12 RE | 20/20 | Rhegmatogenous RD | SB/flat | -1.00 | NS | | |
| 12 LE | CF | Retinal tear | CT, PRP | -0.75 | PCIOL | NVG/PRP | |
| 13 RE | 20/30 | Dragging, retinal pigment | | -2.00 | PCIOL | | |
| 13 LE | 20/60 | Dragging, retinal pigment | | -4.25 | PCIOL | | |

TABLE 2. (CONTINUED) BCVA, POSTERIOR SEGMENT FINDINGS, TREATMENT, RESULTS, REFRACTIVE ERROR, LENS STATUS, CORNEA, AND GLAUCOMA FOR EACH EYE OF THE 47 PATIENTS WITH RETINOPATHY OF PREMATUREITY

| PATIENT NO. AND EYE | BCVA | POSTERIOR SEGMENT FINDINGS AND INDICATIONS FOR TREATMENT | TREATMENT/ RESULTS | REFRACTIVE ERROR* | LENS STATUS | GLAUCOMA/ TREATMENT | CORNEA/ OTHER |
|----------------------------|-------------|---|---------------------------|--------------------------|--------------------|----------------------------|----------------------|
| 14 RE | 20/200 | Exudative RD, dragging, retinal tear | CT/flat | -1.00 | NS | | |
| 14 LE | 20/40 | Dragging, retinal tear | CT | -1.25 | NS | | |
| 15 RE | 20/400 | Rhegmatogenous RD, PVD, lacquer cracks, macular hole | SB/flat | -5.75 | Clear | | |
| 15 LE | 20/30 | PVD | | -6.00 | Clear | | |
| 16 RE | HM | | | -14.00 | Aphakic | | BK |
| 16 LE | LP | Dragging, retinal fold | | Balance | Aphakic | POAG | |
| 17 RE | 20/25 | Dragging | | -8.25 | PCIOL | | |
| 17 LE | 20/400 | Exudative RD | SB/flat | Balance | PCIOL | | |
| 18 RE (ENUC) | | | | Balance | | | |
| 18 LE | 20/40 | Rhegmatogenous RD | SB/flat | -0.50 | PCIOL | | |
| 19 RE | 20/25 | Retinal pigment | | -4.50 | Clear | | |
| 19 LE | 20/25 | | | -6.50 | Clear | | |
| 20 RE | 20/100 | Chorioretinal scar | | -5.00 | NS | | |
| 20 LE | CF | Rhegmatogenous RD, macular hole | SB/flat | -6.25 | NS | | |
| 21 RE (ENUC) | | | | Balance | | | |
| 21 LE | HM | Macular star | | -6.00 | PCIOL | | |
| 22 RE | CF | | | -4.75 | NS | | |
| 22 LE | CF | Retinal tear | Laser | -3.75 | NS | | |
| 23 RE | CF | Dragging | | +13.75 | PCIOL | | |
| 23 LE | LP | Rhegmatogenous RD, dragging | SB/detached | Balance | Aphakic | | |
| 24 RE | HM | Rhegmatogenous RD | SB/flat | | PCIOL | | |
| 24 LE | 20/25 | Dragging | | | PCIOL | | |
| 25 RE | NLP | Retinal fold | | | Aphakic | NA/LPI | Opaque |
| 25 LE | NLP | No view (cornea opaque) | | | Aphakic | NA/LPI | Opaque |
| 26 RE | 20/40 | Rhegmatogenous RD | SB/flat | | PCIOL | | |
| 26 LE | NLP | Phthisis | | | Clear | | |
| 27 RE | 20/20 | Lattice-like degeneration | | | Clear | | |
| 27 LE | 20/30 | Lattice-like degeneration | | | Clear | | |

TABLE 2. (CONTINUED) BCVA, POSTERIOR SEGMENT FINDINGS, TREATMENT, RESULTS, REFRACTIVE ERROR, LENS STATUS, CORNEA, AND GLAUCOMA FOR EACH EYE OF THE 47 PATIENTS WITH RETINOPATHY OF PREMATURITY

| PATIENT NO. AND EYE | BCVA | POSTERIOR SEGMENT FINDINGS AND INDICATIONS FOR TREATMENT | TREATMENT/ RESULTS | REFRACTIVE ERROR* | LENS STATUS | GLAUCOMA/ TREATMENT | CORNEA/ OTHER |
|---------------------|---------|--|--------------------|-------------------|-------------|---------------------|---------------|
| 28 RE | 20/30 | Lattice-like degeneration | | | PCIOL | | |
| 28 LE | 20/25 | Lattice-like degeneration | | | PCIOL | | |
| 29 RE | Unknown | Dragging | | | PCIOL | | |
| 29 LE | Unknown | Dragging | | | PCIOL | | |
| 30 RE | 20/30 | Dragging | | | Clear | | |
| 30 LE | 20/70 | Dragging | | | Clear | | |
| 31 RE | 20/400 | | | | PCIOL | NVG/TS/PRP | |
| 31 LE (ENUC) | | | | | | | |
| 32 RE | HM | Chorioretinal scar | | | PCIOL | | Nystagmus |
| 32 LE | CF | Exudative RD | SB/detached | | NS | | Nystagmus |
| 33 RE | LP | Rhegmatogenous RD | VIT/detached | | Aphakic | | |
| 33 LE | 20/40 | | | -5.50 | Clear | | |
| 34 RE | 20/20 | Retinal tear | Laser | | PCIOL | | |
| 34 LE (ENUC) | | | | | | | |
| 35 RE | 20/40 | Retinal pigment | | | PCIOL | | |
| 35 LE | 20/30 | | | | PCIOL | | |
| 36 RE | NLP | RPE changes | | | Clear | | |
| 36 LE | 20/200 | | | | PCIOL | | |
| 37 RE | 20/200 | Lattice-like degeneration | | -13.50 | NS | NA/LPI | |
| 37 LE | 20/80 | Lattice-like degeneration | | -22.00 | NS | NA/LPI | |
| 38 RE | HM | Retinal pigment, retinal fold | | | PCIOL | | |
| 38 LE | NLP | Retinal pigment | | | Aphakic | NVG/TS | BK |
| 39 RE | 20/400 | Exudative RD | SB/detached | | Aphakic | | |
| 39 LE | NLP | | | | Aphakic | POAG | BK |
| 40 RE (ENUC) | | | | | | | |
| 40 LE | 20/300 | Dragging, retinal pigment, retinal tear | CT | | PCIOL | | |

TABLE 2. (CONTINUED) BCVA, POSTERIOR SEGMENT FINDINGS, TREATMENT, RESULTS, REFRACTIVE ERROR, LENS STATUS, CORNEA, AND GLAUCOMA FOR EACH EYE OF THE 47 PATIENTS WITH RETINOPATHY OF PREMATUREITY

| PATIENT NO. AND EYE | BCVA | POSTERIOR SEGMENT FINDINGS AND INDICATIONS FOR TREATMENT | TREATMENT/ RESULTS | REFRACTIVE ERROR* | LENS STATUS | GLAUCOMA/ TREATMENT | CORNEA/ OTHER |
|---------------------|--------|--|--------------------|-------------------|-------------|---------------------|---------------|
| 41 RE | 20/200 | Dragging, lattice-like degeneration | | -11.50 | NS | | |
| 41 LE (ENUC) | | | | | | | |
| 42 RE | 20/400 | | | | PCIOL | | |
| 42 LE | 20/25 | Rhegmatogenous RD | SB/flat | | PCIOL | POAG | |
| 43 RE | 20/30 | Rhegmatogenous RD | VIT, SB/flat | | PCIOL | | |
| 43 LE | 20/50 | Rhegmatogenous RD | SB/flat | | PCIOL | | |
| 44 RE | CF | Retinal fold | | | PCIOL | | |
| 44 LE | CF | Retinal fold | | | PCIOL | | |
| 45 RE | HM | Dragging, exudates | | | PCIOL | POAG | |
| 45 LE | HM | Dragging, exudates | | | PCIOL | POAG | |
| 46 RE | CF | | | | PCIOL | | |
| 46 LE | 20/25 | Retinal pigment | | | Clear | | |
| 47 RE | HM | RPE changes | | | Aphakic | | |
| 47 LE | NLP | Rhegmatogenous RD | SB/detached | | Aphakic | | |

BCVA = best-corrected visual acuity; BK = band keratopathy; CF = counting fingers; CT = cryotherapy; ENUC = enucleation; ERM = epiretinal membrane; HM = hand motion; LE = left eye; LP = light perception; LPI = laser peripheral iridotomy; NA = narrow angle; NS = nuclear sclerosis; NVG = neovascular glaucoma; PCIOL = posterior chamber intraocular lens; POAG = primary open-angle glaucoma; PRP = panretinal photocoagulation; PSC = posterior subcapsular cataract; PVD = posterior vitreous detachment; RD = retinal detachment; RE = right eye; RPE = retinal pigment epithelium; SB = scleral buckle; TS = tube shunt; VIT = vitrectomy.

*Refractive errors are shown in spherical equivalents.

TABLE 3. SPHERICAL EQUIVALENTS OF EACH EYE OF THE 43 PATIENTS WITH RETINOPATHY OF PREMATUREITY WHERE A CURRENT REFRACTION WAS AVAILABLE

| SPHERICAL EQUIVALENT OF REFRACTIVE ERROR | NUMBER OUT OF 43 KNOWN REFRACTIONS |
|--|------------------------------------|
| ≥ -6.00 | 14 (32.6%) |
| ≥ -2.00 and < -6.00 | 19 (44.2%) |
| Between 0 and -2.00 | 6 (14.0%) |
| ≥ 0 | 4 (9.3%) |

TABLE 4. BEST-CORRECTED VISUAL ACUITY (BCVA) OF EACH OF THE EYES OF THE 47 PATIENTS WITH RETINOPATHY OF PREMATURITY

| BCVA | NUMBER OUT OF 84 KNOWN VISUAL ACUITIES |
|---------------------|--|
| ≥20/30 | 23 (27.4%) |
| <20/30 to ≥20/60 | 12 (14.3%) |
| <20/60 to ≥20/100 | 6 (7.1%) |
| <20/100 to ≥20/400 | 12 (14.3%) |
| Counting fingers | 11 (13.1%) |
| Hand motion | 9 (10.7%) |
| Light perception | 4 (4.8%) |
| No light perception | 7 (8.3%) |

TABLE 5. BEST-CORRECTED VISUAL ACUITY (BCVA) RELATED TO POSTERIOR SEGMENT PATHOLOGY IN EACH OF THE EYES WITH RETINOPATHY OF PREMATURITY

| BCVA | DRAGGING* | RETINAL DETACHMENT (22 EYES) | RETINAL TEAR (7 EYES) | RETINAL PIGMENT (9 EYES) | RETINAL FOLD (6 EYES) |
|---------------------|-----------|------------------------------|-----------------------|--------------------------|-----------------------|
| ≥20/30 | 9 | 5 | 2 | 3 | 0 |
| <20/30 to ≥20/60 | 4 | 5 | 1 | 2 | 1 |
| <20/60 to ≥20/100 | 4 | 0 | 0 | 1 | 0 |
| <20/100 to ≥20/400 | 3 | 4 (3 were ERD) | 2 | 1 | 0 |
| Counting fingers | 2 | 2 (1 ERD) | 2 | 0 | 2 |
| Hand motion | 3 | 2 | 0 | 1 | 1 |
| Light perception | 2 | 3 (1 ERD) | 0 | 0 | 1 |
| No light perception | 0 | 1 | 0 | 1 | 1 |

ERD = exudative retinal detachment.

*27 of 29 visual acuities known.

DISCUSSION

Eight eyes (9.3%) of the patients in this study were enucleated. Unfortunately, neither the status nor the indications for enucleation were known. These eyes may represent the terminal consequences of ROP.

All of the 86 eyes available for review had regressed ROP. Seventy-six eyes (88.4%), however, had some residual posterior segment pathology related to a history of ROP. As in previous studies, these findings highlight the need for lifelong follow-up of patients who have been diagnosed as having ROP.⁹

Twenty-two eyes experienced a retinal detachment. Unfortunately, the exact date of occurrence was available for only 11 eyes. Interestingly, the average age at onset for this group was 35 years, with a range of 14 to 51 years. Twenty of the eyes with a retinal detachment were treated with a scleral buckling procedure. An earlier series demonstrated the efficacy of scleral buckling alone in the treatment of stage 4B and 5 ROP.¹⁴ Sixteen of the 20 patients who underwent a scleral buckle procedure for retinal detachment had attached retinas at the time of review, for a success rate of 80.0%. Two of the unsuccessful cases were exudative retinal detachments. Other studies report the successful combination of vitrectomy and scleral buckle in treating retinal detachments associated with ROP.^{9,10} Two rhegmatogenous retinal detachments and one exudative detachment in this report were successfully treated with a vitrectomy combined with scleral buckling.

Previous studies have also demonstrated a correlation between the degree of ROP and the presence of myopia.^{6,15-17} The degree of

ROP for each patient in the present study is not known. Despite regression of disease, 90.7% of the eyes (where refractive information was available) were found to be myopic at the time of review. Holström and coworkers demonstrated three different patterns of myopia in a population of 6-month-olds.¹⁸ Twenty-four of 37 eyes (64.9%) were found to have persistence of or progression of myopia at 6 months of age. Our study also demonstrates a high incidence of myopia in adults with ROP. The refraction was known for half the eyes with a buckle. The mean of -3.63 diopters for this group compared with the -5.71 diopters for the entire study cohort suggests that the rate and degree of myopia for most were due to causes other than scleral buckling alone, although a buckle may induce higher myopia.

Five eyes developed band keratopathy, and two had opaque corneas due to other causes. Only one of the eyes with band keratopathy was associated with other anterior segment pathology such as neovascularization (Table 3, patient 38, left eye). A report by Schulenburg and coworkers¹⁹ described one patient who developed bilateral band keratopathy in a series of 69 infants at risk for ROP. This patient had bilateral obliterated anterior chambers.

The early development of cataracts has long been recognized as a complication of ROP.^{7,20} In this report, only 14 eyes (16.3%) had a clear natural lens.

Glaucoma is another recognized threat to vision in infants with ROP, even with the retina attached.⁵ Smith and Schivitz²¹ reported three cases of acute angle-closure glaucoma occurring in patients with ROP. All were treated successfully with use of miotics and either surgical or laser iridotomy. These outcomes suggested pupillary block as the mechanism. Six of our patients had narrow angles warranting peripheral iridotomies.

In this review, there was no correlation with posterior segment disease such as retrolental membranes in eight of the 14 cases of glaucoma. Three eyes developed neovascular glaucoma. This was presumed to be due to stimulation of angiogenic factors from avascular retina leading to neovascularization of the anterior segment. Two eyes were treated with panretinal photocoagulation in an effort to halt the process of neovascularization.

BCVA is the most important measure of outcome. In this study, BCVA was measured by using a standard Snellen chart. Unfortunately, 51.2% of the eyes in this retrospective review had a BCVA of 20/200 or less. However, good BCVA is still possible despite ROP, as demonstrated by Ferrone and coworkers²² in their series of patients with marked posterior segment changes secondary to ROP. We had similar results. For example, 13 of 27 eyes (48.1%) with retinal dragging and known BCVA had a visual acuity of 20/60 or better (Table 5). Ten of 22 eyes (45.5%) with retinal detachments had a BCVA of 20/60 or better. None of these eyes harbored exudative retinal detachments. Three of seven eyes (42.9%) with retinal tears had a visual acuity of 20/60 or better. Eyes with only retinal pigmentary change and no other ROP finding were the most likely to achieve good visual function. Five of nine eyes (55.6%) with retinal pigmentary changes had visual acuity of 20/60 or better. In contrast, only one of six eyes (16.7%) with retinal folds had a BCVA of 20/60 or better. This group of eyes had the poorest visual prognosis.

ROP may be a devastating eye disease occurring in premature infants. This review reports late complications in a population who did not receive initial treatment in infancy. Developments in treatment, such as cryotherapy and laser photocoagulation, have lessened these vision-threatening complications, but lifelong follow-up is still required.

REFERENCES

1. Campbell PB, Bull MJ, Ellis FD, et al. Incidence of retinopathy of prematurity in a tertiary newborn intensive care unit. *Arch Ophthalmol* 1983;101:1686-1688.
2. The natural ocular outcome of premature birth and retinopathy. Status at 1 year. Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Arch Ophthalmol* 1994;112:903-912.
3. Multicenter Trial of Cryotherapy for Retinopathy of Prematurity: ophthalmological outcomes at 10 years. *Arch Ophthalmol* 2001;119:1110-1118.
4. Tasman W. Late complications of retrolental fibroplasia. *Ophthalmology* 1979;86:1724-1740.
5. Hartnett ME, Gilbert MM, Hirose T, et al. Glaucoma as a cause of poor vision in severe retinopathy of prematurity. *Graefes Arch Clin Exp Ophthalmol* 1993;231:433-438.
6. Choi MY, Park IK, Yu YS. Long term refractive outcome in eyes of preterm infants with and without retinopathy of prematurity: comparison of keratometric value, axial length, anterior chamber depth, and lens thickness. *Br J Ophthalmol* 2000;84:138-143.
7. Knight-Nanan DM, Algawi K, Bowell R, et al. Advanced cicatricial retinopathy of prematurity—outcome and complications. *Br J Ophthalmol* 1996;80:343-345.
8. Maly E. Frequency and natural history of retinopathy of prematurity (ROP). A prospective study in a Swedish city 1986-1990. *Acta Ophthalmol Suppl* 1993;52-55.
9. Kaiser RS, Trese MT, Williams GA, et al. Adult retinopathy of prematurity: outcomes of rhegmatogenous retinal detachments and retinal tears. *Ophthalmology* 2001;108:1647-1653.
10. Sneed SR, Pulido JS, Blodi CF, et al. Surgical management of late-onset retinal detachments associated with regressed retinopathy of prematurity. *Ophthalmology* 1990;97:179-183.
11. Multicenter trial of cryotherapy for retinopathy of prematurity. Preliminary results. Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Arch Ophthalmol* 1988;106:471-479.
12. An international classification of retinopathy of prematurity. The Committee for the Classification of Retinopathy of Prematurity. *Arch Ophthalmol* 1984;102:1130-1134.

13. Kinsey VE, Zacharias L. Retrolental fibroplasia: incidence in different localities in recent years and a correlation of the incidence with treatment given the infants. *JAMA* 1949;139:572-578.
14. Greven C, Tasman W. Scleral buckling in stages 4B and 5 retinopathy of prematurity. *Ophthalmology* 1990;97:817-820.
15. Nissenkorn I, Yassur Y, Mashkowski D, et al. Myopia in premature babies with and without retinopathy of prematurity. *Br J Ophthalmol* 1983;67:170-173.
16. Quinn GE, Dobson V, Kivlin J, et al. Prevalence of myopia between 3 months and 5 1/2 years in preterm infants with and without retinopathy of prematurity. Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Ophthalmology* 1998;105:1292-1300.
17. Knight-Nanan DM, O'Keefe M. Refractive outcome in eyes with retinopathy of prematurity treated with cryotherapy or diode laser: 3 year follow up. *Br J Ophthalmol* 1996;80:998-1001.
18. Holmström M, el Azazi M, Kugelberg U. Ophthalmological long-term follow up of preterm infants: a population based, prospective study of the refraction and its development. *Br J Ophthalmol* 1998;82:1265-1271.
19. Schulenburg WE, Prendiville A, Ohri R. Natural history of retinopathy of prematurity. *Br J Ophthalmol* 1987;71:837-843.
20. Gold RS. Cataracts associated with treatment for retinopathy of prematurity. *J Pediatr Ophthalmol Strabismus* 1997;34:123-124.
21. Smith J, Shivitz I. Angle-closure glaucoma in adults with cicatricial retinopathy of prematurity. *Arch Ophthalmol* 1984;102:371-372.
22. Ferrone PJ, Trese MT, Williams GA, et al. Good visual acuity in an adult population with marked posterior segment changes secondary to retinopathy of prematurity. *Retina* 1998;18:335-338.

PEER DISCUSSION

DR TERRI L. YOUNG. This is a retrospective chart review of 47 adult patients (or 86 eyes) with a history of retinopathy of prematurity (ROP) evaluated in an academic retina service. The purpose of the study was to report the natural history and late complications of ROP in members of the "baby boomer" generation, defined by the authors as those individuals born within the years 1946-1964. These patients had not received interventional treatment at the time of development of their presumptively severe ROP, nor were they necessarily monitored for ROP progression as a neonate. Specific anatomical ocular and functional determinants were catalogued, consisting of posterior segment pathology, lens status, refractive error, and visual acuity.

The authors noted posterior segment pathology in 85% of eyes- 25% of eyes had retinal detachments. One could presume that the 8 enucleated eyes had retinal detachments as well, increasing the percentage of eyes in that category.

The reported visual acuities of 51.2% with 20/200 or worse and 41.7% with 20/60 or better levels were actually determined in 84 eyes instead of 86 eyes. The rate of myopia reported at 90.7% is discrepant. Information was actually used on 43 eyes, rather than 86, so the denominator is skewed. The assessment is indeterminate as most of these eyes were pseudophakic or aphakic, and pre-surgical refractive errors were not used. Additionally, as stated in the report, only 10 refractions were known for the 20 eyes that underwent a scleral buckle procedure. It was unclear how virgin refractive errors could be recorded, and how a high percent myopic refractive error could be accurately determined for this cohort given this background.

Other general considerations for the authors would be to include the interval dates of data acquisition, provide some indication of follow-up time period, consider other contributing factors for decreased visual acuity apart from retinal derangement, i.e. optic atrophy, amblyopia, and central visual impairment, and to consider whether there is a difference in ophthalmic outcomes in those patients born in the latter "baby boomer" years where neonatal nursery practice had started to shift to less oxygen use after the studies in the early to mid 50's showed a high correlation of what was termed then "retrolental fibroplasia" with uncontrolled oxygen administration.

The literature is chock-full of studies that emphasize the need for continued ophthalmic evaluation throughout life in patients with severe and near-severe ROP development, primarily because of known later complications of associated glaucoma and retinal detachment.¹⁻⁴

The best study to date is the recently published 15-year outcome study by the Cryotherapy for Retinopathy of Prematurity Cooperative Group.² Between 10 and 15 years of age, new retinal folds, detachments, or obscured view of the posterior pole occurred in 4.5% of treated and 7.7% of control eyes. This study found new retinal detachments even in eyes with relatively good structural findings at age 10 years, emphasizing the importance of long-term regular follow-up in eyes that experience threshold ROP. This is the best model, in my opinion for excellent study-design, and provides valuable longitudinal data. There was an invited commentary by Allistair Fiedler accompanying this article, which essentially states that these patients should always be considered high risk, and should have regularly scheduled ophthalmic evaluations for life.³

The closest study I could find to match this one in terms of having a cohort with largely unknown neonatal clinical information was a UK study by O'Connor et al in 2002.⁴ This was a retrospective study of 505 infants that weighed less than 1700 grams at birth. This cohort was traced at 10-12 years of age to determine how low birth weight alone and ROP might influence their ophthalmic outcome. Two very important features about this study relative to the baby boomer review are the use of age-matched controls (they recruited 169 11-year-olds born at term and examined under the same condition), and the expanded outcome measures assessed. This included visual function tests such as visual acuity, contrast sensitivity, stereo acuity, perimetry, and color vision. Ocular component measurements included refractive state, the presence of strabismus, and anatomic outcomes.

The present study underscores the necessity for prospective large population studies (usually multi-center), with standardized case and appropriately matched controls, and standardized parameter assessments.

REFERENCES

1. Tasman W. Late complications of retrolental fibroplasias. *Ophthalmology* 1979; 86:1724-1740.
2. Palmer EA, Hardy RJ, Dobson et al, et al. 15-year outcomes following threshold retinopathy of prematurity: final results from the multicenter trial of cryotherapy for retinopathy of prematurity. *Arch Ophthalmol* 2005; 123: 311-318.
3. Fiedler AR. Premature for life. *Arch Ophthalmol* 2005; 123: 392-394.
4. O'Connor AR, Stephenson T, Johnson A, et al. Long-term ophthalmic outcome of low birth weight children with and without retinopathy of prematurity. *Eye* 2000;14:23-29.

DR M. EDWARD WILSON. Since these birth years also encompass the time when oxygen was sometimes indiscriminately reduced in these babies, how many of these individuals, now in their 40s and 50s, have hypoxic, or anoxic brain injuries such as cerebral palsy? I think there was an increase incidence at least in the later years in this group. Do you have a theory as to why, after cataract surgery in these patients, that the capsule would become phimotic or opacify more readily? Were those in the patients who had had vitrectomies?

DR EDWARD L. RAAB. Since many of us in pediatric ophthalmology do not routinely graduate our patients at a certain age cutoff, when should we be advised to transfer these particular patients to the care of a vitreoretinal specialist?

I have a comment about the use of the term "legal blindness". This is not a term that applies to individual eyes. Legal blindness is an administrative definition for a patient seeing as a whole, that is, the better eye, in effect, is seeing at less than a certain level. We should avoid describing an eye as legally blind, although patients do this frequently

DR EVELYN A. PAYSSE. Some of the patients we now see that are extremely premature never fully vascularize their peripheral retina, sometimes in Zone 2 or Zone 3. After we follow them until they are 48 to 52 weeks post-conception, we finally pronounce that these infants have arrested vascular development. We feel that these infants may be indeed at increased risk of retinal detachment as they get older due to this poor vascularization. Would you comment on those patients? Do you feel that these patients are prone to late rhegmatogenous retinal detachments or are they at increased risk for any other retinal disorder? I would also like to know the etiology of the late exudative retinal detachments that you found in your patients?

DR MORTON S. COX. In your exudative group you mentioned treatment and perhaps vitrectomy and endolaser. How were these patients treated, and what was the outcome?

DR ELIAS I. TRABOULSI. I have only operated on one of these patients, a premature patient with a cataract and only one eye. A few months after the surgery she developed a dense posterior capsular and anterior vitreal proliferation. She had been buckled and not vitrectomized and the posterior capsule opacity was mistaken for a retinal detachment since it was so thick. Eventually, the capsule was opened and the vision came back very nicely. I'm trying to tie that to the concept of "premature for life". These patients may have a sub-set of cells that remain in their eye because they were born prematurely with different properties. These cells might have disappeared, if the eye had been allowed to proceed to maturity. Maybe over time you would have the proliferation of these cells in the anterior vitreous, behind the capsule, or around the capsule or even posteriorly and this could produce the late retinal detachment, and other vitreoretinal interface type of problems that lead to folds or tears. We might consider obtaining vitreous samples from these patients at the time of surgery and evaluate the sample with cell markers that might be present in immature cells, or precursor cells, or stem cells or other types of cells that would be more prevalent in fetal life rather than in adult life. That might give us a clue as to why these late complications happen in these patients.

DR DOUGLAS R. ANDERSON. What you have presented is a natural history of under care. It's not a natural history, but at least a history of what happened to people during this period of time 50 years ago, and with the treatment modalities that were available at that time. How might this compare with those born prematurely in the present day with regard to current standards of neonatal care with regard to present-day ophthalmic care, and also taking into account that babies with lower birth weight now can survive easier than at the time earlier in history. Hopefully there have been improvements in medical care.

How do you compare centers that have a special expertise in neonatal care and ophthalmic care for retinopathy of prematurity, with the average care that actually is delivered within the country in communities without physicians highly experienced or expert in the care of these problems?

On another subject, I do not think there is such a thing as legal blindness, in a universal sense, except in context of a particular situation. Every agency has its own definition of when a person is considered blind, for the purpose of some entitlement, whether that entitlement is to receive talking books, or special transportation, or a deduction on their income taxes, and so on. The definitions of "blindness" for particular entitlements, although they may be similar, are not always the same between agencies. There is no single definition of what legal blindness is. In scientific reports, it might be appropriate to say certain individuals in one or both eyes met, or did not meet, a particular criterion, perhaps one that we often use – namely 20/200 acuity – without using the ambiguous term "legal blindness."

DR WILLIAM S. TASMAN . Dr Young made some good suggestions such as looking at optic neuropathy, central visual impairment, and amblyopia as other causes of visual loss. We could not assess the contributions of these conditions in our database, but we certainly acknowledge that these entities may be responsible for the impaired vision of some individuals.

The suggestion that boomers born later might have had a different outcome than those born earlier could not be confirmed. We chose to take the group as a whole and did not look at subgroups with regard to outcome, since the subgroup numbers would be quite small.

Dr Young in her discussion points out that the rate of myopia we reported at 90.7% is discrepant since the information was actually based on 43 eyes. This was clearly stated in the manuscript and there was no indication that it was 86 eyes. She then goes on to say that the assessment was indeterminate as most of these eyes were pseudophakic or aphakic and pre-surgical refractive errors were not used. Most of these eyes were virgin myopes, and even in those eyes that were pseudophakic we were still able to document that they were myopic. She then points out that the best study to date is the published 15-year outcome study by the Cryotherapy for Retinopathy of Prematurity Cooperative Group. While that is an excellent study, those subjects are only 10-15 years of age. Our group was middle-aged and there was no source available such as the Cryo ROP Group. Our present study, Dr Young points out, underscores the necessity for prospective large population studies, usually multicentered, with appropriately matched controls and standardized parameter assessments. In an ideal world that may be true, but I personally would not like to see my tax dollars go to a study on baby boomers who were premature.

Dr Doug Anderson wondered how our results might compare with those born prematurely today with regard to neonatal care and state of the art ophthalmic care. Clearly, lower birth weight babies are surviving today and we do have laser therapy available. I believe there are centers that specialize in neonatal care and ophthalmic care for Retinopathy of Prematurity that do an excellent job compared to others where only average care is available. Dr Anderson also brings up a question about the definition of when a person is considered blind for the purpose of some entitlement. We agree that there is no single definition of legal blindness.

Dr Paysse asked if we feel that adults with ROP are prone to late rhegmatogenous retinal detachments or are they at increased risk for any other reason. Some of them have lattice like degeneration, which may predispose to detachment. I do not think the fact that they have an avascular zone of retina is necessarily a contributing factor. The late exudative retinal detachments are usually related to vitreous traction (a result of the ROP) in some area of the peripheral retina that leads to exudation.

Dr Cox asked how we treat the exudative group. Our preferred method of intervention is vitrectomy and endolaser occasionally with an encircling procedure as well.

Dr Traboulsi raised an interesting thought about why these patients may have premature clouding of their capsules and speculated that proliferation of cells in the anterior vitreous may in some way contribute to detached retina.

Dr Raab wondered when to transfer from pediatric care to a retina specialist. Our experience has been like his, a conjoint effort between the pediatric ophthalmologist and the retina specialist. I agree that the onus is more on the retina specialist to emphasize to the parents the importance of the long-term follow-up.