Glaucoma in Children: Are We Making Progress?

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Background: Glaucoma in children presents difficult clinical challenges. Even when appropriately treated, blindness can occur. Design: Retrospective interventional case series and literature review. Methods: All clinical records of children seen by the author with a diagnosis of glaucoma established before 16 years of age were reviewed from 1977 to 2003. Glaucoma was classified as primary infantile, aphakic, syndrome-related, and secondary. The best-corrected visual acuity, refractive error, configuration of the optic nerve cup, and perimetry were recorded. The intraocular pressure (IOP) for each visit was recorded. IOP measurements of 19 mm Hg or less were considered “good.” The percentage of “good” readings was calculated for each eye. Representative visual acuities, refractive errors, IOP, disk configuration, and perimetry were recorded at 6, 12, 18, and 24 years of age for each patient. The admitting ophthalmologic diagnosis for each child at the Western Pennsylvania School for Blind Children was recorded from 1887 to 2003. Results: One hundred twenty-six children (204 eyes) were studied: infantile glaucoma, 52 eyes; aphakic glaucoma, 40 eyes; syndrome associated, 69 eyes; and secondary glaucoma, 43 eyes. The mean follow-up was 11.6 years (1 to 30 years). Overall, 60 (29.4%) of 204 eyes had a 6/12 (20/40) or better corrected visual acuity at the most recent visit. The percentage with this acuity remained stable throughout the follow-up period. Eyes with infantile glaucoma had the best acuity, and 40% had 6/12 (20/40) or better. Amblyopia was common and responded to treatment. Eyes with aphakic glaucoma had the worst acuity with only 10% achieving 6/12 or better. These eyes had a bimodal onset of glaucoma; eyes with an early onset had an angle closure configuration and eyes with a delayed onset had an open angle. Early cataract removal and microcornea were risk factors for glaucoma. If the IOP was maintained at 19 mm Hg or less (good) on 80% of the determinations over time, the optic nerve cup compared with the diameter of the optic nerve (C/D ratios) were stable. Eight patients had multiple, good quality, visual fields performed over 3 to 15 years. If the patients had “good” IOP on 70% of the measurements, the visual fields remained stable. A historical perspective of glaucoma control was gained by looking at the admitting diagnosis at the Western Pennsylvania School for Blind Children. From 1910 to 1970, an average of 9.2 children blind due to glaucoma were admitted each decade. From 1971 to 2003, there were only three children with glaucoma admitted over 30 years. Conclusion: Removal of congenital cataracts should be delayed until 3 to 4 weeks of age. Consideration should be given for using 19 mm Hg or less to measure the success of glaucoma treatment in children. Treatment of amblyopia is as important as IOP control in children. Imaging technology such as optical coherence tomography and measurement of central corneal thickness may play an important future role in the assessment of children with suspected or known glaucoma.

RECOGNITION OF FRANK D. COSTENBADER, MD

Frank D. Costenbader, MD, was the first ophthalmologist who had the courage and foresight to limit his practice to treating children and eye problems related to children. What seems to be a logical extension of ophthalmology for those of us today must have been a courageous, thinking “out-of-the-box” step for Dr. Costenbader.12

In the 1930s and early 1940s pediatric ophthalmology did not exist. Dr. Costenbader, after 10 years of practice, made the decision to devote his career solely to the care of infants and children, a decision that members of AAPOS have also made.

Dr. Costenbader was a true advocate for children, an educator, and a man with vision. At the start of his practice, fellowships, as we know them, did not exist. Preceptorships were the way of educating ophthalmologists who would care for children. Marshall M. Parks, MD, was selected as Dr. Costenbader’s first preceptee. This mentoring process was strengthened by establishing the Department of Ophthalmology at Children’s Hospital in Washington, DC. In 1963, a formal training program in
pediatric ophthalmology was established at the Children’s Hospital Medical Center. Many of our membership are graduates of this program.2

In honor of Dr. Costenbader’s efforts, the Costenbader Alumni Society was established and it continues to advance education, foster scholarship, and provide advocacy for children and their related eye conditions.

Unfortunately, I have never had the honor of meeting Dr. Costenbader. However, I feel as if I have known him through his publications and the informal recounting of Drs. Parks and O’Neill, and many others.

INTRODUCTION

All of us have been exposed to children with vision-threatening problems and glaucoma may be one of the most vexing of these. Over the 28 years that I have been in practice, we have witnessed some major advances in the diagnosis and treatment of childhood glaucoma. For example, we now have automated perimetry, ophthalmic imaging, optical coherent tomography (OCT), (Carl Zeiss Meditec, Inc. Dublin, CA.) corneal pachymetry, and the Tono Pen™ (Mentor, Norwell, MA) to improve our diagnostic capabilities.

We have seen the replacement of miotics and epinephrine derivatives with more effective beta-blockers and selective alpha-agonists. Prostaglandin analogs and topical carbonic anhydrase inhibitors are now available for expanded medical treatment options.

Surgical treatment has been enhanced by better understanding of the anatomy of the filtration angle in primary infantile glaucoma, refinement of guarded filtration procedures, supplementation of filtration with 5-fluorouracil and mitomycin-C, the addition of stelicate tube to plate-shunts, with and without pressure regulating valves, and improvement in cyclodestructive procedures using the Nd: YAG laser, the diode laser, or endocyclophotocoagulation (ECP).

The recent prospective studies of glaucoma in adults, Ocular Hypertensive Treatment Study (OHTS), The Early Manifest Glaucoma Trial (EMGS), Collaborative Normal Tension Glaucoma Study (CIGTS), and the Advanced Glaucoma Intervention Study (AGIS), have provided us with information on the course of glaucoma in adults.3-12 From these studies, and others,13-15 we have learned that, in adult’s eyes that have ocular hypertension, the risk for progression to unilateral blindness over 15 years in untreated patients was 1.5 to 10.5% and in treated patients it was only 0.3 to 2.4%.6 There is a high correlation between the level of intraocular pressure (IOP) and loss of visual field.4,13 We have also learned that the worse the initial condition of the eye is with respect to glaucoma damage, the lower the IOP needs to be to prevent further blindness.15 Lower IOP is associated with reduced progression of visual field deterioration.4 In adults treated with anti-metabolite-assisted filtration, a reduction of the mean preoperative IOP from 26 mm Hg to a mean of 11 mm Hg resulted in stable visual fields for 5 years in 95% of treated patients.12 Over 6 years, patients in the EMGT study showed that each higher or lower millimeter of mercury of IOP on follow-up was associated with an approximate 10% increase or decrease in progression as measured by perimetry and photographic disk criteria.5 Treatment for open-angle glaucoma in adults is effective. It results in lower rates of progression than control groups, but treatment does not necessarily guarantee a lack of progression of glaucoma related damage.5 The prospective studies in adults have shown that the central corneal thickness should be considered when assessing the IOP.7 Patients with thin corneas have a greater risk for developing glaucoma damage.7 We have also learned that glaucoma is an intraocular pressure-sensitive optic neuropathy and that, over relatively short periods, 4 to 8.5 years, even small differences in the IOP at the low end of the treated IOP range may be critical.9

Similar prospective collaborative studies do not exist for children. Glaucoma is relatively uncommon, and it is unlikely that similar studies will be initiated for children. We must therefore use data obtained from studies of adults to guide us in the treatment of children. The anticipated longer life expectancy, the uncommon occurrence, the difficulty in examination, and the challenge of measuring treatment effect early in life conspires to make management of glaucoma in children difficult.

The hypothesis for this presentation is that advances in diagnosis and treatment have improved the outcome in children with glaucoma over the past three decades. I would like to test the hypothesis by examining changes in the population at the Western Pennsylvania School for Blind Children and also share with you the experience that I have gained over the years. More than this, I wish to challenge our young ophthalmologists to become interested in this topic and to stimulate them to seek new and more effective treatments for children with glaucoma.

Glaucoma in children is a large topic to cover. I will focus on the classification of glaucoma, evaluation techniques, and new treatment modalities. I will present data from a longitudinal study of a cohort of our patients with primary infantile, secondary, syndrome-related, and aphakic glaucoma and give some recommendations for target pressures to seek in this population. Finally, I will close with results of our effort to control childhood glaucoma in our region.

PATIENTS AND METHODS

In preparation for this presentation, I have reviewed my reprint files on glaucoma. After submitting the protocol for this retrospective study to the University of Pittsburgh Institutional Review Board and receiving approval for this study, I reviewed the clinical records of examinations of 126 patients (204 eyes) with childhood glaucoma. A diagnosis of glaucoma was established by at least two of the following criteria: (1) repeated IOP measurements over 22
mm Hg; (2) cupping of the optic nerve consistent with glaucoma; and (3) visual field loss consistent with glaucoma. Clinical records were eliminated if glaucoma was diagnosed after age 16, if the glaucoma occurred as a result of trauma, if there were insufficient data such as fewer than three visits, or if a patient was evaluated for a second opinion or in consultation. Fifty-two eyes had primary infantile glaucoma, 40 had aphakic glaucoma, 69 eyes had syndrome-associated glaucoma, and 43 had secondary glaucoma. These children have been followed for an average of 11.6 years (range 1 to 30).

A review of the admitting ophthalmologic diagnosis of all children admitted to the Western Pennsylvania School for Blind Children from 1887 to 2003 was conducted. The five most common diagnoses were tabulated in 10-year intervals over 116 years.

Definition and Classification

What is glaucoma? Current thinking holds that glaucoma is a pressure-sensitive, neurodegenerative disease of the optic nerve, associated with retinal ganglion cell death and subsequent axonal loss and nerve damage as reflected by cupping of the optic nerve, loss of visual field, and, in its later stages, blindness. In children, the causes for glaucoma are multiple; the onset is variable, and the treatments and outcomes are different. Glaucoma may be associated with conditions that are life-limiting. Studies reported often leave us with incomplete information: they use inconsistent terminology, different age and diagnostic criteria, and they often study a mixture of conditions that cause glaucoma and select variable levels of intraocular pressure for diagnosis and measuring treatment effect. Some studies report acuity results for eyes, and others report the acuity in the best eye for a patient. To learn more about this condition, we must develop uniform agreement on the nomenclature, classification, and reporting standards so we can better study and compare conditions that cause glaucoma in children. John Flynn, MD, and others made a great contribution to the study of retinopathy of prematurity by developing the International Classification of retinopathy of prematurity (ROP). We must develop a classification system that is universally accepted and clinically meaningful and at the same time recognizes the different etiology and mechanisms that cause glaucoma in children. There are many classifications offered that fulfill this need: Schaffer-Weiss; Hoskins, deLuise, and Anderson; Allen Beck; Pickering, Wong, Dickens, and Hoskins; Papadopoulos and Khaw; and Freedman and Walton have all offered classifications of glaucoma that are useful to the clinician. Table 1 represents a synthesis of these classifications. This categorization is clinically useful in counseling parents, planning procedures, and comparing results. For example, treatment results achieved for primary infantile glaucoma will differ depending on the age at onset. It was Dr. Costenbader who was one of the first to recognize that treatment and results will be different depending on the age at the time of onset of glaucoma. Treatment results will also differ regarding the extent of progression at the time of diagnosis and the condition that causes glaucoma. Results will be very different when comparing to glaucoma in a child with Sturge Weber syndrome to one treated for primary infantile glaucoma. Separation of aphakic glaucoma into early onset, frequently with an angle closure mechanism, and delayed onset, usually with an open-angle configuration, will influence the method of treatment and the results achieved. Glaucoma associated with syndromes has responses to treatment that vary with the syndrome. When confronted with a child with a recognized syndrome, the clinician is well advised to seek out current information that is specific for that particular condition.

For analysis and reporting purposes, I have divided our cohort of patients into four groups: primary infantile; aphakic glaucoma; syndrome-associated glaucoma; and secondary glaucoma. Children with traumatic glaucoma have been excluded.

Evaluation of Children

In addition to standard questions about light sensitivity, clouding of the cornea, enlargement of the eye, and pre-
and perinatal events, we should include questions regarding exposure to topical steroids. Ohji, Kinoshita, Ohmi, et al have described pressure elevations as high as 30 mm Hg after only 2 weeks of topical 0.1% dexamethasone. Over the past three decades, knowledge of the genetics and hereditary patterns has increased exponentially from prior understanding of the “multifactorial” inheritance patterns. Middle Eastern populations show an increased predilection for primary infantile glaucoma. The mapping of chromosomes with study of the chromosome loci for individual conditions such as Axenfeld–Rieger syndrome and aniridia is now common. A comprehensive list of these discoveries is beyond the scope of this study, but undoubtedly, there will continue to be advances as these investigations progress. One must be constantly vigilant in reviewing descriptions of new entities that have an association with glaucoma.

**Diagnostic Measures**

In 1980, Parks made the observation that a myopic change in the refraction was helpful in following children with infantile glaucoma. Egbert and Kushner and others have made a similar observation in children with aphakia. We have observed that the change in the fit of a previously well-fit rigid gas-permeable contact lens in aphakic eyes can also suggest a pressure elevation.

Optic nerve cupping that is asymmetric can suggest glaucoma. Reversal of cupping in young children occurs with control of IOP. Quigley explained the cupping by damage and loss of nerve fibers, and the enlargement of the scleral canal with increases in the IOP, because relatively elastic connective tissue present in the optic nerve head in the first year of life. The scleral canal enlargement can in turn exaggerate the apparent size of the cup. Chaturvedi, Hedley-Whyte, and Dreyer demonstrated a reduction of the magnocellular cell density in the lateral geniculate body with cupping in adults. It is probable that reversal of the cupping in children is not associated with an increase in number or recovery of the damaged retinal ganglion cells.

The OHTS has shown that a decrease in central corneal thickness is a risk factor for glaucomatous optic nerve damage since application tonometry tends to understate the IOP when the cornea is thicker. We should begin to include measurement of central corneal thickness in the evaluation of children suspect of having glaucoma. Applanation tonometry is inaccurate if the cornea is either much thicker or much thinner than “normal.” The normal central corneal thickness for an adult cornea is 0.554 ± 0.022 mm. Payse has studied 198 eyes in 108 normal children and has found that values for central corneal thickness are similar to the adult population. In a study on the relationship of central corneal thickness to IOP, Muir, Jin, and Freedman found that the central cornea thickness of normal children used as controls was 0.559 ± 0.39 mm. Thick corneas can lead to artificially high measurements of the intraocular pressure. Muir, Jin, and Freedman have associated ocular hypertension with an increased central corneal thickness in children. We have found this true in children with aphakia. We have measured the central corneal thickness in normal eyes and the aphakic eyes of children with cataracts and glaucoma (Table 2). We have found that this subset of aphakic eyes to have very thick corneas. The mean thickness for the fellow phakic eyes was 0.594 mm and for the aphakic eyes were 0.655 mm. Both of these values are well above the expected central corneal thickness for children. The thickened corneas can lead to inaccurate measurements of IOP and could explain the frequency of ocular hypertension in this subgroup. In a prospective study, Egbert, Wright, Dahlhauser, et al found that, of 62 children who had bilateral cataract surgery, 4.5% had glaucoma and 45% had ocular hypertension. After removal of unilateral cataracts, glaucoma was present in 12.5% of eyes and ocular hypertension was found in 32% of eyes. John W. Simon, MD, has made similar observations (John W. Simon, personal communication).

With prolonged increased IOP, we have observed that the scleral canal in young children undergoes symmetric enlargement. In eyes of older children, the internal rim of the optic nerve develops increased expansion along the vertical axis of the optic nerve as is seen in adults. The pattern of associated loss of visual field using Goldmann perimetry parallels that of adults, with changes in the arcuate area followed by nasal field loss, and with progression, loss to a remaining temporal island of vision.

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*Glaucoma.
automated perimetry is difficult in children under 8 years of age. When possible, however, this is the preferred method to use. We have been able to obtain quality-automated perimetry in most cooperative children with steady fixation starting at age 9 or 10 years of age.

In the last decade, measurement of the nerve fiber layer with optical coherent tomography (OCT, Carl Zeiss Meditec, Inc., Dublin, CA) and Heidelberg retinal tomography (HRT, Heidelberg Engineering, GmbH, Dossenheim, Germany) have provided a capability of detecting glaucoma damage to the nerve fiber layer before it is detected on perimetry. Children can cooperate in these studies when they are age 10 and older. Normative values for children are being established. The reproducibility and standardization of the technique need to be established.

Ultrasound biomicroscope evaluations of the opaque anterior segment are available, but this author has not found this technology helpful in assessing glaucoma in children. On the other hand, the use of loupes and a handheld slit-beam projector developed by David Walton, MD, has provided an excellent means of assessing the filtration angle and the depth of the chamber in children.

Traditional comprehensive evaluations are conducted under anesthesia. We usually obtain pressure readings with the Perkins applanation tonometers (Keeler, London, UK), the Tono Pen, and the Schiotz tonometers. Jaafar and Kazi have shown that some young and uncooperative children can be safely sedated with chlorohydrate without influencing the IOP.

**Treatment: Medical**

Medical treatment of glaucoma includes use of oral and topical pressure-lowering medications. Over the last 30 years, effective agents have been introduced, including nonselective and selective beta-blocking agents, prostaglandin analogs, topical carbonic anhydrase preparations, and alpha-agonists. Most medications we use are not approved for use in children. The drugs of first choice are a beta-blocking agent such as Timolol Maleate 0.25 or 0.5%, administered twice a day. Alternatively, a prostaglandin analog such as bimatoprost, travoprost, or latanoprost can be used. These are usually used once a day in the evening. Acetazolamide 5 to 10 mg/Kg orally each day, or its topical form, dorzolamide or brinzolamide, used twice daily, are helpful supplements to lower the intraocular pressure. Drug combinations are available for convenience.

Medications must be used with caution in children. The beta-blocking agents may have cardiovascular effects and may aggravate asthma. The safety of topical brimonidine, an alpha II agonist, in young children is a concern. Enyedi and Freedman have reported bradycardia, hypotension, and difficulty arousing some children and extreme fatigue after receiving Alphagan (Allergan, Irvine, CA). Although effective, this agent should only be used with caution in older children, if at all. Prostaglandin analogs may cause disruption of the blood aqueous barrier, cystoid macular edema, and changes in the color of the iris and skin. Oral preparations of carbonic anhydrase inhibitors have been associated with potassium loss, which may become a problem with use for prolonged periods, or when used in conjunction with oral corticosteroids. Carbonic anhydrase inhibitors can also cause hematopoietic toxicity and aplastic anemia. When these agents are used over time, appropriate monitoring of the blood count and serum potassium should be considered.

**Treatment: Surgical**

Surgical treatment of glaucoma has evolved over the past three decades. The use of guarded filtration, the trabeculectomy operation, has had only fair success in children.\(^69\)\(^-\)\(^72\) After introduction of the guarded filtration procedure, it was quickly adopted to treat refractory glaucoma in children. Initial reports were not encouraging. Within weeks to months, the initial success is often lost with reduction of the size of the filtration bleb and closure of the internal scleral ostium. Cataracts can form as a result of the operation. Gressel, Heuer, and Parrish have reported success in young patients, but only 33% of the patients had developmental glaucoma. Sturmer, Broad-\(^69\)\(^5\) way, and Hitchings reported use of a trabeculectomy in a “young” population; however, the youngest patient in this series was 11 years old.\(^73\) Others have used trabeculotomy or have combined trabeculectomy with a trabeculotomy procedure with lasting and satisfactory control of the IOP.\(^16\)\(^,\)\(^17\)\(^,\)\(^76\)

Around 1990, the use of supplemental antimetabolites combined with filtering procedures was introduced.\(^77\)\(^-\)\(^81\) These agents provided suppression of the fibrotic response and improved the success of filtration. The need for performing frequent (daily) subconjunctival injections of 5-fluorouracil was a drawback. The use of a single application of mitomycin-C (MMC), applied on the sclera at the time of the procedure, was quickly accepted. Mitomy-\(^82\)\(^5\)cin-C has increased the duration and success of the filtration procedure. Overfiltration, thin or leaking blebs and endophthalmitis have been some concerning complications reported following use of MMC.\(^83\)\(^-\)\(^94\) With mitomycin-C, bleb infection rates have been as high as 8%. In another report, the risk for endophthalmitis was 2.1% and the risk for infection was greater if the filter was placed at the inferior limbus rather than at the superior limbus. Even with these risks, these procedures have permitted control of the intraocular pressure in the eyes of children with complicated forms of glaucoma.

Others have favored use of tubes inserted into the anterior or posterior chamber that shunt aqueous to plates that are sutured to the sclera near the equator of the globe. Some shunts have pressure-sensitive valves to reduce hypotony following insertion. Aqueous shunts are relatively effective for treating infants with recalcitrant glaucoma. A comparison of the mitomycin-C-enhanced
filters to unenhanced tube to plate-shunts showed the aqueous shunt devices had a significantly greater success for control of glaucoma during the first 2 years of life. Wilson, Mendis, Smith, et al reported lower IOP levels in adults with the trabeculectomy procedure when compared with the Ahmed valve implant (New World Medical, Inc., Ranchero Cucamonga, CA) in adults. The plate implants appear to have decreasing effect with time. We have also observed this. Many of our implants begin to fail after 3 to 5 years. A cystic cavity forms around the plate and the pressure begins to rise. Hypotony, infection, hemorrhage, and retinal detachment complicate both the trabeculectomy supplemented with MMC and the tube to plate-shunt procedures.

The goniotomy procedure will be discussed later in the section on primary infantile glaucoma. The goniotomy operation is principally used to treat infantile glaucoma. It has also been used to prophylactically treat eyes with aniridia, and glaucoma related to uveitis in children.

There will be eyes that will not have a lasting satisfactory pressure response to medical treatment or the procedures designed to filter or to shunt the aqueous from the eye. In these situations, the ciliary body is incrementally ablated. This has been performed with transscleral cyclophotocoagulation applied to the conjunctiva overlying the ciliary body. The use of the diode laser and the continuous-mode ND:YAG laser can also be used to accomplish this in a less traumatic, and less painful, manner. These procedures are performed without direct visualization of the treated ciliary processes. The ciliary processes can be treated with direct visualization by endocyclophotocoagulation. This procedure requires incision near the limbus to introduce the endoscope and photocoagulator. With all ablative procedures, hypotony and insufficient effect are common complications. Eyes will frequently require retreatment.

Primary Infantile Glaucoma

The incidence of primary infantile glaucoma is 1:10,000 to 20,000 live births in Western countries and as high as 1:2500 in the Middle East. Eighty percent of affected children develop signs of glaucoma within the first year of life.

Theories for the mechanism causing this form of glaucoma have evolved. The presence of a nonpermeable “Barkan” or translucent membrane covering the trabecular meshwork and the anterior mesodermal cleavage defects has been reassessed. Ten eyes of children with infantile glaucoma were studied and compared with 40 normal infant eyes. Schlemm’s canal was present in all specimens, but in the eyes with glaucoma, there were decreased vacuoles adjacent to the wall of the canal. The insertion of the anterior ciliary body and iris sometimes overlapped the trabecular meshwork. The transparent sheet of tissue that was overlying the filtration angle was found by electron microscopy to be a thickened layer of normally perforated uveal meshwork. There are thickened trabecular beams and the iris has traction on it produced by these trabecular beams. This traction prevented the normal posterior migration of the ciliary body and the iris root. This was corrected by the goniotomy procedure. Tawara and Inomata offer an alternative explanation for elevation of the IOP in eyes with primary infantile glaucoma. Their observations, with light and electron microscopy, suggested that the thick and compact tissue observed in the trabecular meshwork was associated with immature development and they asserted that this may be one of the primary causes of increased IOP.

Any infant with epiphora, blepharospasm, light aversion, and an enlarging cornea associated with Haab striae and optic nerve cupping should be considered as having primary infantile glaucoma. Wallace and Plager have provided us with age-adjusted horizontal corneal diameter values which should be used when evaluating children. Myopia of 3 D or more occurs in two-thirds of the eyes and 24% have 2 D or more of astigmatic correction. Costenbader and Kwitko, in a review of 77 eyes with congenital glaucoma, suggested a separate classification for eyes that have glaucoma diagnosed in the nursery. This subclassification is justified, as the eyes of children who are diagnosed in the nursery require twice the number of procedures when compared with “older children” who were diagnosed between 5 days to 36 months.

I have had the opportunity to follow some children with a corneal haze for a week or two who then have had resolution of corneal cloudiness. These children were later diagnosed as having primary infantile glaucoma. The cloudiness of the cornea in some children may occur in cycles and may be accompanied with fluctuations in the IOP. With elevation of the IOP, breaks in Descemet’s membrane occur permitting aqueous to enter the stroma of the cornea causing hydrops. This is accompanied by a mild inflammatory response and a subsequent decrease in the intraocular pressure. The break or breaks in Descemet’s membrane leave a scroll of Descemet’s membrane or Haab striae. When Descemet’s becomes continuous again, the aqueous barrier is reestablished, and the hydrops clears. If measured, the IOP either may be normal or will return to an increased level.

Treatment of primary infantile glaucoma is surgical. Medications are used to control pressure and to clear the cornea in preparation for surgery. Surgical treatment includes a goniotomy, trabeculotomy, or trabeculectomy, or a combination of these procedures.

The goniotomy procedure used to treat primary infantile glaucoma in children was initially used to treat adults with primary open-angle glaucoma. The trabecular tissue, just below Schwalbe’s line, is incised to increase facility of outflow and decrease the intraocular pressure. Several authors have advocated goniotomy for treatment of infantile
Glaucoma.

Goniotomy has a success rate of 94% in the series by Hoskins, Shaffer, and Hetherington. Trabeculotomy ab externo, using a Harms’ probe (Katina products, Denville, NJ), has been proposed by Allen and Burian and Harms and Dannheim and has been advocated by McPherson and others for treatment of primary infantile glaucoma. Trabeculotomy is also the procedure of choice if the angle structures are not sufficiently visible to perform a goniotomy. A long-term (9.5 years mean follow-up) study of patients treated with trabeculotomy for infantile glaucoma showed that 59.5% of eyes achieved a visual acuity of 6/12 (20/40) or better.155

Beck and Lynch have used 6-O Prolene (Ethicon, New Brunswick, NJ) introduced circumferentially into Schlemm’s canal for 360 degrees and then pulled centrally to perform a trabeculotomy. This procedure was found to have a slightly better outcome than goniotomy in the Atlanta population. Goniosurgery has been used successfully to treat glaucoma-complicated childhood uveitis. The Nd:YAG laser has been used to perform angle surgery, but the technique has not had wide acceptance.158,159

Success in treatment of primary infantile glaucoma will be determined by the age at onset and the ability to deliver a safe and effective procedure. The earlier the onset of the glaucoma, the more difficult it is to control. Schaffer studied 577 consecutive goniotomies. Control of the IOP had a success rate of only 30% if the glaucoma was present at birth or after age 2 years. The success of the goniotomy procedure increased to 94% if the eye was treated between 1 month and 2 years. Haas recorded a 77% cure rate; failure results from the extent of the deformity of angle structures and individual patient characteristics.

When control is successful, the visual outcome can be good. Morgan, Black, Ellis, et al reported 58% of their patients had 6/15 or better visual acuity. Taylor, Ainsworth, Evans, et al reported that of 117 patients studied over 20 years, 48% had 6/12 or better of visual acuity. Trabeculectomy can produce similar results. O’Reilly, Lanigan, and O’Keefe reported excellent results with trabeculectomy for infantile glaucoma; 83% of their patients achieved 6/12 (20/40) or better visual acuity.

Vision loss is often due to amblyopia. Barkan suggested that the vision loss could be attributed to corneal scars and irregularities, optic nerve defects, and amblyopia. Richardson, Ferguson, and Schaffer reported that 65% of their patients had 6/15 or better visual acuity. Clothier, Rice, Dobinson, et al, and Rice suggested that amblyopia may be the most important and treatable cause for decreased acuity. Morin and Bryars attributed damage to the optic nerve as the cause for loss of vision. Biglan and Hiles reported successful treatment of amblyopia in children with infantile glaucoma. It is not surprising that amblyopia is common. Refractive errors differ by 3 or more diopters in two-thirds of the patients and 24% have 2 D or more of astigmatism.

Even when effectively treated by goniotomy, children may develop recurrent pressure elevations later in childhood or early adulthood. Following successful treatment, Broughton and Parks found that 7 of 34 eyes had an increase in IOP over the ensuing 5 years. Haas had a recurrence rate averaging 18%. Following a review of our patients with infantile glaucoma who were successfully treated with goniotomy, no patient redeveloped an increased IOP after 2 years of age.

**Aphakic Glaucoma**

Aphakic glaucoma is one of our most difficult management problems. Following removal of a cataract and successful rehabilitation of the eye, glaucoma emerges years later and will threaten vision. The onset, results of treatment, and conclusions about prevention will depend on the condition that has caused the cataract, the type of opacity, the size of the cornea, the timing of the surgery, and the frequency of additional surgical procedures. Some earlier studies of this problem have studied children and eyes with a mixture of conditions associated with cataracts that will also develop glaucoma. Conditions such as Lowe syndrome, aniridia, and trauma frequently have coexistence of cataracts and glaucoma. The mechanism for glaucoma may be specific to the condition. It is only by studying eyes that have “uncomplicated aphakia” that we can learn more about the cause or causes for this form of glaucoma.

The age at onset of pediatric aphakic glaucoma vary. Chandler and Phelps and Arafat were some of the first authors to call our attention to this problem. Simon, Mehta, Simmons, et al have studied the incidence and have found that 24% of patients developed glaucoma 6.8 years after cataract surgery. This rate increased to 41% if those with less than a 5-year follow-up were excluded. Chroussos, Parks, and O’Neill reported a 6% incidence of chronic glaucoma with a mean follow-up of 5.5 years. Magnusson, Abrahamsson, and Sjostrand studied Swedish children born with cataracts and found a 12% incidence of aphakic glaucoma. This figure represents a true incidence of this condition since the study was conducted in a fixed geographic location with centralized data collection. In this study, children who had cataract surgery were followed for a mean of 9.6 years. Early cataract surgery and microphthalsmos were found to be risk factors for glaucoma. Keech, Tongue, and Scott found an incidence of glaucoma of 11%. Surgery within the first 2 months of life was found to be a risk factor. Keech, in a later study, found a prevalence of glaucoma of 32% if cataracts were present and removed early in life, and followed for a mean of 7 years. The prevalence of aphakic glaucoma was increased if the corneal diameter is small and the cataract type is nuclear. Parks, Johnson, and Reed found a 32% prevalence of glaucoma when these findings are present. In a study of the effect that a reduced corneal diameter has on the risk for developing aphakic glaucoma, Wallace and Plager found 94% of eyes with aphakic glaucoma had age-adjusted microcornea.
It is the removal of the cataract that permits glaucoma to develop. In a study of 41 patients (58 eyes) who had cataracts present before 2.5 years of age that were not removed, Mori, Keech, and Scott found no evidence of either open-angle glaucoma or ocular hypertension. In this study, only two eyes with persistent hyperplastic primary vitreous (PHPV) developed angle closure glaucoma. Another critical observation was made by Simon and associates. They reported a patient that had bilateral cataracts and had surgery only on one eye. A pressure of 50 mm Hg was noted in this eye. The fellow, unoperated eye had normal pressures consistently. Children with bilateral cataracts do not always develop glaucoma when both eyes receive cataract surgery. Chen, Walton, and Bhatia reported 30 patients with bilateral lens extraction but aphakic glaucoma in only one eye.

Under a separate protocol, we studied 37 eyes in 24 children who had cataracts. We excluded trauma and other conditions that may be associated with glaucoma. All cataracts were documented before the first year of life and removed before age 5. Ninety-two percent of cataracts were removed before 1 year of age and 27% were removed before 1 month of age. The median age at cataract removal was 3.4 months.

**Pattern of Onset and Type of Aphakic Glaucoma**

We found a bimodal pattern of onset for aphakic glaucoma (Figure 1). Mills and Robb have made similar observations. It is important to recognize this since both the mechanism causing the glaucoma and its treatment are different within these two subgroups. The first onset peak is noticed within the first weeks to months following cataract surgery. This early-onset glaucoma is frequently associated with pupillary block, shallowing of the anterior chamber, and angle closure. We have found eyes with microcornea and those with retained lens material and eyes in which an intraocular lens haptic was placed in the ciliary sulcus to be at risk for early-onset, angle closure glaucoma. Failure to perform an iridectomy puts the eye at risk for this complication. Our observations are in agreement with Mills and Robb that the newer surgical instruments that provide us with better removal of lens cortex do not completely prevent this problem. This form of glaucoma requires prompt surgical intervention to correct goniosynechiae and to reestablish the chamber. Angle closure glaucoma can occur several years later. Simon, Mehta, Simmons, et al reported an aphakic eye that developed angle closure glaucoma more than 69 months following cataract removal.

The second form of glaucoma has an onset that is delayed and is associated with microcornea, nuclear cataracts, early surgery, and a failure of the filtration angle to develop an angle recess with an adult configuration. On gonioscopy, these eyes show an open-angle configuration with a flat iris insertion, an indistinct scleral spur, and uveal scleral meshwork. The trabecular meshwork may contain pigment and it may be difficult to identify structures within the filtration angle.

The age of onset of delayed-onset, open-angle glaucoma may occur years following the cataract. Asrani and Wilensky reported an average interval between cataract surgery and the onset of open-angle glaucoma of 12.2 years. One patient developed glaucoma 32 years after surgery. Phelps and Arafat reported a patient with open-angle glaucoma occurring 45 years after cataract surgery in childhood. It is clear that we must persist in following children who have had cataract surgery throughout their lives.

Delayed-onset open-angle glaucoma is uncommon when a lens implant has been used. Asrani, Freedman, Hasselblad, et al, in a meta-analysis of 377 eyes with primary lens implantation, found only one eye with open-angle glaucoma. They have suggested that when a primary IOL is used, there is a reduced incidence of delayed-onset glaucoma. This may be a function of eye selection for an IOL. Two risk factors for glaucoma have been avoided. Implants are infrequently placed in eyes with microcornea, and the surgery in this study was relatively delayed (mean age at surgery 5.06 years). We, however, have made similar observations in our children who have had cataract surgery and a primary implant. In our patients who developed glaucoma following implants, all had anterior chamber lens placement or placement of the lens haptic in the ciliary sulcus. No patient in our series developed delayed-onset glaucoma and had a primary implant placed within the capsule bag. Brady-McCreery, Atkinson, Kelty, et al found no glaucoma in a series of 45 eyes with posterior chamber IOLs. Aphakic glaucoma occurs many years after cataract removal. It may be that the follow-up is insufficient to see the delayed onset of glaucoma. In the infant aphakia treatment study, preliminary results showed that 2 of 12 eyes developed glaucoma. As to why this occurs,
however, remains illusive. Children with bilateral cataracts who have had one of the cataracts removed; that eye developed glaucoma, whereas the fellow eye did not.\(^{131,187}\) Several authors\(^{174,177,182}\) have noted that cataract surgery performed early in life, within the first month or even within the first year of life, has a higher risk for development of open-angle glaucoma. Rabiah has noted no difference in the risk whether the surgery is performed at 2 months or at 9 months.\(^{190}\)

It may be that the absence of the lens early in life alters or causes an arrest in development of the filtration angle, or it may be a lack of accommodation and pull of the ciliary muscles on the trabecular meshwork that in some way permits the meshwork to become compact and dysfunctional.\(^{194-197}\) It may be that some substance or “cytokine” may diffuse from the posterior eye into the anterior chamber and change the facility of outflow of the eyes.\(^{188-191}\) Because of the late onset occurring five or more years following the cataract surgery, it is not likely that inflammation, use of postoperative corticosteroids, or any other portion of the cataract surgery is the cause of this problem.

Control of delayed-onset, open-angle glaucoma is often possible with one or two topical medications and sometimes surgery. In our series, we found that surgery was needed to manage glaucoma in 6 of the 22 eyes (27%) with delayed-onset open-angle glaucoma. Chen, Walton, and Bhatia found that 57% of eyes required surgery.\(^ {187}\) Taylor, Ainsworth, Evans, et al noted that 50% of eyes with aphakic glaucoma required surgery.\(^ {162}\) Arslan and Wilen-sky found that they could control the pressure with medication alone in 63.6% of eyes.\(^ {181}\) When surgery is required, initial treatment includes use of a guarded filtration procedure with or without MMC or insertion of a tube to plate-shunt. Some eyes will resist these treatments and will require cycloablation procedures.

In delayed-onset glaucoma, we found visual acuity of 6/12 (20/40) or better in only 5 of 37 (13%) eyes. Chen, Walton, and Bhatia found that only 10% of their eyes had this level of acuity; 76% had 6/30 (20/200) or worse.\(^ {187}\) Many children with aphakic glaucoma have deprivation, strabismic, and refractive amblyopia. Amblyopia, nystagmus, and difficulty in maintaining a clear visual axis are frequently the cause of poor visual outcomes.

Current recommendations for performing cataract surgery at a very young age should be reassessed. Early surgery and prompt rehabilitation are necessary to achieve good vision and binocular function.\(^ {198-202}\) Cataracts should be removed before 17 weeks of life and preferably before 2 or 3 months of age to achieve the best chance for good visual acuity and binocular function.\(^ {198-202}\) Early surgery is important for visual development but at the same time it is a risk factor for developing delayed-onset glaucoma. The incidence of glaucoma is correspondingly high, ranging from 6 to 31%. Once glaucoma occurs, visual acuity is 6/12 (20/40) or better only 10% of the time or less, and many eyes have visual acuity less than 6/30 (20/200). Several studies have identified early cataract removal as a risk factor.\(^ {174,179,187,189,190}\) and consideration should be given to delaying surgery until 4 to 5 weeks of age, especially in eyes that have nuclear cataracts and microcornea. We currently perform cataract surgery in patients with bilateral complete cataracts after the third week of life but before the fifth or sixth week. Others have made similar recommendations.\(^ {189}\)

**Visual Function as a Function of Control of IOP**

We have studied the visual acuity, optic nerve changes, and visual fields for 30 years for children with glaucoma that was diagnosed before age 16 years. Our goal was to test the hypothesis that maintenance of the intraocular pressure at 19 mm Hg or less over time prevents damage to the optic nerve and loss of vision and visual field in children with glaucoma. We used four classifications for glaucoma: primary infantile glaucoma, aphakic glaucoma, secondary glaucoma, and syndrome-associated glaucoma.

Visual acuity was determined with best optical correction in place by age-appropriate tests beginning with the quality of fixation, Allen cards, the Sheridan–Gardner test, and Snellen acuity. The best-corrected visual acuity was recorded for the initial visit. As age and cooperation permitted, values for representative optic nerve cupping, the best-corrected visual acuity, and factors that influence it were collected at ages 6, 12, 18, and 24 years for each child. Visual acuity was considered “good” if the best-corrected visual acuity was 6/6 to 6/12 (20/20 to 20/40), “fair” if it ranged from 6/15 to 6/30 (20/50 to 20/100), and “poor” if it was 6/60 (20/200) or worse.

At the most recent visit, the best-corrected visual acuity was recorded for each patient. At this visit, for all eyes that had visual acuity of less than 6/12, a judgment was made on the cause or causes for the decreased vision.

The IOP was considered to be in “good control” if it was 19 mm Hg or less and was considered to be in “poor control” if it was 20 mm Hg or more. To assess the effect that IOP control had over time, the IOP measurements that were “good” were divided by the total number of IOP measurements for each eye throughout the entire follow-up period. These values were expressed as “percentage of IOP with good control” for each eye throughout the follow-up period for each eye.

The level of visual acuity at the most recent visit was correlated with the type of glaucoma and the percentage of IOP measurements that were “good” (19 mm Hg or less). The percentage of visits with “good” IOP control over the follow-up period was also correlated with changes in the C/D ratio.

The optic nerve cup-to-disk (C/D) ratio was recorded at the initial examination and at most follow-up visits. Representative values for the optic nerve cup-to-disk ratio were recorded for each 6-year interval during follow-up.

Visual field tests included automated (Humphrey) and manual techniques (Goldmann). Of the 126 patients, 33 had...
visual fields performed at one time during the follow-up period. Each visual field was reviewed and compared with other visual fields for quality, consistency, and time interval between tests. Patients’ tests for visual field were excluded if they had poor fixation, lack of cooperation, nystagmus, or if the field was of poor quality due to age. The visual fields were compared with the type of glaucoma, stability of visual acuity, the percentage of good IOP measurements, and the progression or regression of the optic nerve cup.

This study included 204 eyes of 126 patients with childhood glaucoma: 52 eyes had primary infantile glaucoma; 40 eyes had aphakic glaucoma; 69 eyes had syndrome-associated glaucoma; and 43 eyes had secondary glaucoma.

Visual acuity for this population showed that between 25 and 30% of all eyes with glaucoma would have “good” visual acuity, a level of visual function that would permit operation of a motor vehicle. The percentage of eyes with glaucoma, at each 6-year interval having good vision, remained stable for each of the four 6-year periods (Figures 2 and 3). On the other hand, glaucoma has a devastating impact on the vision of affected eyes. Almost half of the eyes affected become legally blind. Eyes with primary infantile glaucoma had the best visual acuity, and those with aphakic glaucoma had the worst (Figure 3).

At 6 years of age 22% of eyes had good, 31% had fair, and 45% had poor visual acuity. At 12 years of age 29% of eyes had good, 30% had fair, and 40.5% had poor visual acuity. At 18 years of age 28% of eyes had good, 21% had fair, and 50% had poor visual acuity. At 24 years of age 27% of eyes had good, 27% had fair, and 45% had poor vision. Visual acuity remained stable throughout the follow-up period.

We recorded the visual acuity at the most recent visit and compared it to the percentage of “good” (19 mm Hg or less) pressure readings throughout the study period. A weak correlation of good acuity and “good” IOP control (Pearson correlation analysis ($r = -0.341$)) was present. Glaucoma impacts the visual field in the early phases. Central vision is reduced only in the late advanced stages of the disease.

The reason for decreased visual acuity in eyes with visual acuity less than 6/12 (20/40) at the most recent examination in each glaucoma group is shown in Figure 4. Not every but some patients with decreased visual acuity had more than one reason for decreased acuity. Of eyes with decreased final vision, 96 (47%) had amblyopia as a cause, 65 (32%) had glaucoma, 36 (18%) had retinal problems, 31 (15%) had corneal defects, 23 (11%) had problems related to lens, and 8 (4%) had optic nerve disorders not associated with glaucoma.

Eyes with good IOP control should have a stable or a reduction in the C/D ratio. We attempted to identify an intersection point between good IOP control and stability of the C/D ratio to be able to say that, if IOP is controlled to this degree, one can achieve stable optic nerve C/D ratios. This intersection point in our study was near 80%. It is inferred from this that if the IOP is 19 mm Hg or less on 80% of the determinations during the follow-up period, it is likely that there will be no change in the optic nerve C/D ratio.

Eight patients had frequently performed, high-quality, consistent visual fields over a time interval ranging from 3 to 15 years. All but one patient had bilateral glaucoma (15 eyes). The visual fields were stable in all but one patient. In
this patient, the eye with aphakic glaucoma was difficult to control and had progressive loss of visual field. Seven eyes had their IOP 19 mm Hg or less (“good”) for 70% of the time throughout the study, and none of these eyes lost visual field. Of the eight remaining eyes, all but one (see patient referred to above) had stable visual fields, even though some eyes had a “good” pressure control only 45 to 60% of the time.

**Regional Measures of Success**

Are we making progress? Yes, we are! The Western Pennsylvania School for Blind Children has been in existence since 1887. Children who are blind in Western Pennsylvania have been referred for schooling at this facility. In recent years, there has been a movement to mainstream blind children with other school-age children, and this may alter the prevalence in the population to some degree. However, the pattern of blinding conditions over the past 115 years is remarkable.

Janet Simon, PhD, and I examined the principal ocular condition of each child in the school since 1887. We subdivided the top five most frequently occurring conditions into 10-year increments. We recognize that there was a variation in the ophthalmologist’s capability in establishing a diagnosis in the early decades of the 20th century when compared with recent decades. There is also a change in the population with the tendency to “mainstream” children into their regional schools. These disclaimers considered, we examined the prevalence of glaucoma in this population. In the decades starting in the 1900s, the prevalence of blindness due to glaucoma ranges from 5.4 to 11.5% of the school population. In 1961 to 1970 it represented 5.3% of the population. During the years 1971 to 1980, one of the children in the institution had glaucoma as a source of blindness and in 1981 to 1990 only two children, 1.5%, were blind due to glaucoma. Between 1991 and the year 2000, no child in the school had the principal diagnosis of glaucoma. There have been only three children enrolled with blindness due to glaucoma in the past 30 years.

I believe that the institution’s population reflects more effective treatment for glaucoma and treatment of children with cataracts and related complications. Starting in the late 1960s and early 1970s medical care had a significant effect on reducing the prevalence of glaucoma at this regional facility. Others have noted similar trends.

We are at a juncture in time where we now have an improved understanding on the causation and treatment of glaucoma in children. New instrumentation is available for more accurate diagnosis and to provide the ophthalmologist with better metrics to follow the course of this condition. Effective methods of treatment can now provide control of the intraocular pressure.

Existing classifications must be consolidated into a single standardized classification that is universally accepted. Data reporting needs to be standardized. New technology needs to be evaluated and tested for appropriateness, accuracy, and reproducibility in children. Concomitant with this, leadership must emerge to design prospective studies to answer questions about causation and outcome and to evaluate efficacy of treatment of glaucoma in children. It is only with this discipline that additional valuable information and answers will be forthcoming over the next several decades.

**References**


