PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA: A STUDY OF THE ANTERIOR SEGMENT ABNORMALITIES

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INTRODUCTION

GLAUCOMA IS AN UNUSUAL CHILDHOOD HEALTH PROBLEM, AND MAY BE CAUSED BY a large number of possible disease mechanisms (Table I). Subdivision of these causes into primary and secondary mechanisms is useful, where a primary glaucoma is one caused by an intrinsic disease of the aqueous filtration mechanism and is often of genetic origin, while a secondary glaucoma mechanism is one related to disease elsewhere in the body and/or eye. In the evaluation of a new patient with childhood glaucoma, interpretation of the anterior segment abnormalities can be difficult and findings puzzling. Not only are the possible angle abnormalities many in number of variable severity, but in addition associated congenital anomalies and changes secondary to prolonged glaucoma and surgery can be present.

It is the purpose of this paper to share observations that the author has made in the examination of children with only Primary Congenital Open Angle Glaucoma. This study will concentrate on the anterior segment abnormalities of children with this disorder found at the time the condition was recognized and present them in the perspective of what has been already written about these abnormalities. It is hoped secondarily that this material will fuel in the reader a continued interest in the careful examination of young children with glaucoma. Such information may also be of assistance in the identification and classification of children with Primary Congenital Open Angle Glaucoma (PCOAG) as well as imparting some insight into its mechanism. Selection and understanding of the results of treatment may also be aided by familiarity with this information.

METHODS AND MATERIALS

Anterior segment examinations, including gonioscopy, were carried out on 25 untreated children with PCOAG seen from 1968 to 1978 by the author. These examinations were carried out both in the office and the operating room. All examinations were performed and recorded by the author in

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TABLE I: CHILDHOOD GLAUCOMAS

I. Primary Genetically Determined Glaucoma
  A. Congenital Open Angle Glaucoma
  B. Juvenile Glaucoma
  C. Primary Glaucoma Associated with other Eye or Systemic Abnormalities
    1. Associated with Systemic Abnormalities
      a) Sturge-Weber Syndrome
      b) Neurofibromatosis
      c) Pierre-Robin Anomaly
      d) Oculocerebrorenal Syndrome
      e) Reiger's Syndrome
      f) Hepatocerebrorenal Syndrome
      g) Marfan's Syndrome
      h) Rubinstein-Taybi Syndrome
      i) Infantile Glaucoma Associated with Retardation & Paralysis
      j) Oculodental-Digital Syndrome
      k) Syndrome of Microcornea, Absent Frontal Sinuses, & Open Angle Glaucoma
      l) Mucopolysaccharidosis
      m) 13-Trisomy
    2. Associated with Ocular Abnormalities
      a) Aniridia
      b) Retinal Cavernous Hemangioms
      c) Congenital Ocular Melanosis
      d) Sclerocornea
      e) Familial Hypoplasia of the Iris
      f) Anterior Chamber Cleavage Syndrome
      g) Isolated Iridocorneal Dysgenesis
      h) Posterior Polymorphous Dystrophy

II. Secondary Glaucoma
  A. Traumatic Glaucoma
    1) Acute
      a) Angle Concusssion
      b) Hyphema
    2) Late Onset with Angle Recession
    3) A-V Fistula
  B. Intraocular Neoplasm
    1) Melanoma
    2) Melanocytoma
    3) Juvenile Xanthogranuloma
    4) Retinoblastoma
    5) Leukemia
  C. Uveitis
    1) Open Angle
    2) Angle Blockage
      a) Synechial Angle Closure
      b) Iris Bombe with Pupillary Block
  D. Lens Induced Glaucoma
    1) Subluxation—dislocation
    2) Spherophakia
    3) Phacolytic Glaucoma
  E. Glaucoma After Surgery For Congenital Cataract
    1) Lens Material Blockage of the Trabecular Meshwork
    2) Pupillary Block
    3) Phacolytic Glaucoma
    4) Chronic Open Angle Glaucoma Following Absorption of Lens Material
  F. Steroid Glaucoma
  G. Retrolental Fibroplasia

preparation for this report and the care of these children.

All intraocular pressure measurements were performed in an office setting using a Perkins hand-held tonometer. Following inspection of the cornea gonioscopy was carried out both in the office and the operating room. Koeppe gonioscopy contact lenses were utilized for all examinations combined with the use of Barkan-type biomicroscopy gonioscope equipment. Slit lamp examinations were carried out on all infants using a hand-held slit lamp and loupe. Observations from those examinations were supplemented by formal slit lamp examinations when possible in infants and routinely in children over three years of age.

DEFINITION

Primary congenital open angle glaucoma (PCOG) is the best known and most frequent type of pediatric glaucoma and usually occurs in early life. It is genetically determined and occurs in 1:10,000 births. It is more frequent in boys, is usually sporatic and bilateral, and most often shows evidence of multifactorial inheritance.[1] Occurrence in identical twins has been recorded at least nine times,[2] and steroid testing of parents suggests that this type of primary open angle glaucoma has no genetic relationship with the open angle glaucoma of late adult years.[3] The ophthalmic literature reporting experience with this disturbing problem is voluminous. By the turn of the century it was a recognized clinical entity and often described as hydrophthalmos. Pathologic studies done at that time distinguished it as a glaucoma caused by angle anomalies rather than one secondary to inflammation or corneal disease as was once suspected.[4,5] The descriptive term of buphthalmos (Oeil de boeuf) for this condition called attention to the abnormal ocular enlargement that occurs when glaucoma is uncontrolled in early life and which was the expected outcome in this condition before 1940. Loss of vision followed by blindness was a predictable future for these children. In 1925 approximately 10% of blind children had congenital glaucoma.[6]

CLASSIFICATION

Costenbader (1967) called attention to the poor response of nine patients to surgery who were found with glaucoma in the first 5 days of life, compared to those found after this time.[7] It has also been my experience that glaucoma patients seen at birth or in the first month of life respond less favorably to goniotomy surgery. Furthermore, they also possess anterior segment findings which are atypical compared to children diagnosed after

this time in their first year. Haas (1968) called attention to the poorer response to goniotomy in 69 eyes of patients diagnosed before the second month of life.[8] The success rate in this group was 55% compared to 97% in the group diagnosed after their second month.

Barkan early in his experience with goniotomy called attention to the poor results in older patients with neglected congenital glaucoma and pleaded for the early recognition and treatment of this condition. Such cases are now unusual thanks to his early efforts and the increased awareness of the pediatric medical community to the possibility of congenital anomalies. There exists however a related group of older children with PCOAG who, rather than possessing conspicuous signs of glaucoma, have signs and symptoms of this problm that are too subtle to be recognized early in life by the uninitiated. In these patients the glaucoma has been present since infancy but, rather than produce conspicuous deformity, it remains relatively occult, and is often not recognized until later in childhood or even until the adult years.

Based on these considerations and further data to be reported the following clinical classifiation of Primary Open Angle Glaucoma is proposed. I will contrast the anterior segment findings found in 25 patients belonging to these three proposed subdivisions of PCOAG.

TABLE II: PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA

Subdivisions	Age at Diagnosis	Patients
Neonatal PCOAG	0 - 4 Weeks	4
Infantile PCOAG	4 Wks - 1 Year	19
Late-Recognized PCOAG	1 Year - Adult	2
- Manifest		0
- Occult		2
Total Patients Studied:		25

RESULTS

The importance of careful study of the anterior segment in PCOAG was considered as early as 1914.[9] Following the development of practical contact lens gonioscopy in the 1920's, the clinical study of adult glaucoma made use of this new technique. The rediscovery by Otto Barkan that his gonio-trabeculotomy operation, already tried in adult glaucoma, was of real value in some types of congenital glaucoma stimulated the more careful examination and gonioscopy of these patients.[10] Successful control of this glaucoma allowed the cornea to again become functional, and appraisal of its condition then became important, both in the management of the glaucoma as well as in the consideration of the visual development of these eyes.

The pertinent anterior segment findings in 25 patients with newly recognized PCOAG studied by the author will be presented, by examination of the cornea, iris, angle, lens, and pressure data.

A. THE CORNEA IN PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA

Review

The corneal changes of congenital glaucoma have been recognized for centuries and still represent the most vivid memory of this condition for most ophthalmologists. Von Muralt first distinguished this glaucoma as a nosologic entity and, not surprisingly, both he and von Graefe in 1869 still considered enlargement of the cornea to be the primary disorder.[11,12]

Abnormal enlargement and accelerated growth of a child's cornea as indicated by its diameter from birth to two years of age, are universally accepted as highly suggestive signs of increased intraocular pressure during this period in life. The average diameter at birth is between 9.5 and 10 mm, and corneal growth is completed by one year of age, after having reached an average diameter of 11.5 mm.[13,14] The average horizontal corneal diameter in later childhood therefore is 11.5 mm. A reported review of 123 cases of PCOAG found a corneal diameter of 11 mm or less in only 24% of those patients under three months of age and only in 9% of those over three months.[15] Relative corneal enlargement, though shown to relate to the duration of abnormal intraocular pressure, shows a less certain correlation with the level of intraocular pressure.[15,16] Associated with the corneal enlargement is a generalized enlargement of the entire eye which often causes a shift of the refractive error towards myopia;[17] recognition of this change can be a helpful clinical guide whenever pressures and corneal diameters are difficult to measure in an office setting. Flattening of the cornea has been found which lessens the myopic shift that might otherwise result.[18,19] Corneal diameter asymmetry is an important sign of the unilateral occurrence or persistence of this glaucoma.

Corneal abnormalities were found in each of these 25 patients with PCOAG. Corneal opacification and enlargement occurred in greater than 90% of these patients (Table III). Corneal opacification was the most important diagnostic sign leading to the recognition of an ocular abnormality and the eventual diagnosis of PCOAG.

Ruptures in Descement's membrane due to the mechanical effect of stretching of the cornea is well known to occur secondary to glaucoma in early life, and were reported recognized in PCOAG by Haab.[21] They have been reported most often to be horizontal and sinuous, and are associated with regional corneal opacification caused by epithelial and stromal edema.[20] The late development of serious chronic corneal edema in rela-

tion to breaks in Descement's membrane caused by glaucoma in infancy punctuates the importance of these changes.[22]

The recognition of corneal epithelial cytologic abnormalities in untreated PCOAG that suggest glaucoma can add an additional dimension to the diagnostic appraisal of these patients.[23]

Findings

Each cornea of the 25 patients with PCOAG was first examined by hand slit lamp examination and nonfocal illumination in an office setting. Estimation of the corneal diameter and presence of asymmetry, and localization and quantitation of opacification could be carried out there satisfactorily. Examination of the corneas under general anesthesia followed after a short interval. Measurements of the corneal diameter, precise localization and quantitation of corneal breaks, and appraisal of corneal opacification could be carried out and recorded at that time.

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TABLE III: PCOAG—INCIDENCE OF CORNEAL ABNORMALITIES (41 EYES)

Corneal Opacification	23/25 patients	92%
Corneal Opacification	35/41 eyes	85%
Corneal Enlargement	39/41 eyes	95%
Breaks in Descement's Membrane	21/41 eyes	51%

Corneal opacification was variable in severity but most often was severe (Table IV). When mild it appeared as a diffuse bedewing or vacuolization of the corneal epithelium seen best at the time of Koeppe gonioscopy employing reflected light rather than the direct beam. When epithelial edema was more marked the view of angle and fundus could be improved by removal of a small patch of corneal epithelium even when stromal edema is also present. (A momentary application of 70% alcohol and minimal scraping was employed.)

TABLE IV: PCOAG—CORNEAL OPACIFICATION-SEVERITY (41 EYES)

Mild	14/41 eyes	34%
Severe	22/41 eyes	54%
Absent	5/41 eyes	12%

Corneal opacification was a frequent and especially conspicuous abnormality in the neonatal group (Table V). In these patients diffuse total

involvement of each cornea was present rather than patchy involvement of sudden onset as is often seen in the older infant.

TABLE V: PCOAG—CORNEAL OPACIFICATION-INCIDENCE (41 EYES)

Neonatal PCOAG	8/8 eyes	100%
Infantile PCOAG	26/29 eyes	90%
Late-Recognized PCOAG	2/4 eyes	50%

Corneal enlargement was found in nearly every patient with PCOAG (Table III). Though repeatedly mentioned in the voluminous literature of PCOAG, the standards for corneal enlargement have not been discussed. The definition of megalocornea has been addressed and there is acceptance that it may be defined as a horizontal corneal diameter of greater than 12.5 mm.[24] This represents an enlargement of 1.0 mm over the normal average childhood and adult corneal diameter as described earlier. It would seem important that enlargement not be based on some single standard but rather take into account the small cornea of the newborn and its rapid growth during the first year (Table VI).

TABLE VI: AVERAGE NORMAL INFANT HORIZONTAL CORNEAL DIAMETERS[25]

Birth	9.5 mm
6 Months	10.5 mm
1 Year	11.5 mm

Measurement of the corneal size as indicated by its diameter is difficult in the infant in the office setting. Measurements for this study were taken in the operating room using a straight edge ruler in approximation with the apex of the cornea.

Corneal enlargement studies compared the normal diameter values listed in Table VI. No cornea was considered enlarged which measured less than 1 mm above the normal for the patient's age. The incidence of corneal enlargement is recorded in Table VII and shows a near constant occurrence. The amount of corneal enlargement for each clinical group is shown in Table VIII and evidence of progressive enlargement in the infantile group is shown. The average enlargement is nearly two times the suggested minimal criteria for corneal enlargement suggested above.

TABLE VII: PCOAG—CORNEAL ENLARGEMENT (41 EYES)

Overall Incidence	39/41 eyes	95%
Neonatal PCOAG	7/8 eyes	88%
Infantile PCOAG	29/29 eyes	100%
Late-Recognized PCOAG	3/4 eyes	75%

TABLE VIII: PCOAG—AVERAGE ENLARGEMENT (41 EYES)

Neonatal PCOAG	8 eyes	2.1 mm
Infantile PCOAG	29 eyes	2.8 mm
Late-Recognized PCOAG	4 eyes	1.5 mm
Fellow Normal Eyes	9 eyes	1.5 mm

This information would suggest that one might consider enlargement of 1.0 mm away from the average corneal diameter for each age as reason for concern in respect to glaucoma, and a deviation of more than 2.0 mm as a definite abnormality. Greater enlargement of the cornea was found not only in older patients but also in those corneas which possessed breaks in Descemet's membrane (Table IX).

TABLE IX: PCOAG—CORNEAL ENLARGEMENT WITH/WITHOUT BREAKS IN DESCEMENT'S MEMBRANE (41 EYES)

Average Enlargement with breaks	21 eyes	2.6 mm
Average Enlargement without breaks	20 eyes	2.2 mm

The average corneal enlargement in the nine normal fellow eyes of children with unilateral PCOAG is reported in Table VIII. Each of those corneas was at least 1 mm greater than the expected normal value (Table VI) for the patient's age.

Breaks in Descemet's membrane were seen in half of the eyes with PCOAG studied (Table X).

TABLE X: PCOAG—INCIDENCE OF BREAKS IN DESCEMET'S MEMBRANE (41 EYES)

Overall Incidence PCOAG	21/41 eyes	51%
Neonatal PCOAG	1/8 eyes	12%
Infantile PCOAG	17/29 eyes	57%
Late-Recognized PCOAG	3/4 eyes	75%

As indicated they were seen in greater frequency in children diagnosed at longer intervals after birth (Table X). Children diagnosed before five months of age showed such breaks one-third as frequently as those diagnosed later (Table XI).

TABLE XI: PCOAG—INCIDENCE OF BREAKS IN DESCEMET'S MEMBRANE BEFORE AND AFTER 4 MONTHS OF AGE (21 EYES)

4 Months or younger	5/21 eys	24%
5 Months or older	16/21 eyes	76%

Additional evidence to support the progressive nature of the secondary corneal changes in PCOAG is the higher incidence of multiple breaks found in older infants (Table XII).

TABLE XII: PCOAG—INCIDENCE OF MULTIPLE BREAKS OF DESCEMET'S MEMBRANE (21 PATIENTS)

4 Months and younger	2/5 patients	40%
5 Months and older	12/16 patients	75%

Breaks in Descemet's membrane may be first seen in clear corneas in those children recognized after infancy, but most often are seen associated with significant local corneal opacification (Table XIII).

TABLE XIII: PCOAG—INCIDENCE OF BREAKS IN DESCEMET'S MEMBRANE WITH DEGREES OF CORNEAL OPACIFICATION (21 PATIENTS)

Clear cornea	1/5 eyes	20%
Mild Opacification	6/14 eyes	43%
Severe Opacification	14/22 eyes	64%

Breaks in Descemet's membrane are usually horizontal, and occur with about equal frequency as multiple or single occurring defects (Table XIV).

TABLE XIV: PCOAG—TYPE OF BREAKS IN DESCEMET'S MEMBRANE (21 EYES)

Horizontal	19/21 eyes	90%
Multiple	11/21 eyes	52%
Single	9/21 eyes	43%
Sinuous	1/21 eyes	5%

Breaks in Descement's membrane vary greatly in appearance. When of recent onset such a defect appears as a wavey—parallel pair of lines on the inner surface of the cornea often nearly obscured by significant stromal edema and thickening. Slit lamp examination may show evidence of posterior curling of the edges of the parted membrane away from the stromal surface. Following reendothelization of the newly created space between the breaks, clearing of the stromal opacity occurs. Decreased opacification of the band between the breaks occurs in time to such a degree that when examined later it nearly resembles the normal corneal posterior surface. There permanently remains, however, a fine striation of this surface and increased opacification at its edge for its full length.

Observations of breaks of Descemet's membrane are made by slit lamp examination and at the time of Koeppe gonioscopy. Use of a standard opthalmoscope with a plus 8 D lens best allows mapping of the breaks. They appear with this technique as dark lines and can be distinguished from the iris by their noncircumferential distribution and relative movement with rotation of the ophthalmoscope.

B. THE IRIS IN PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA

Review

The iris in PCOAG has been said to possess only minor anatomic variations from normal. It has been found to be flat, which represents a deviation from the usual moderate anterior convexity of the newborn. Surprisingly, I could find no mention of the pupil in past studies. Red radial iris stromal vessels have been described commonly. The presence of visible gray vessels has been observed and considered to be secondary to iris atrophy.[25] Circumferential vessels at the iris root have been reported frequently.

The character, shape, and position of the iris at its periphery has attracted the most attention and been reported very differently. Peripheral-radial-scallops of visible iris posterior pigment epithelium also have been reported and thought to be distinguishable from the normal visibility of such patches in the infant by their significant anterior position in the iris stroma.[26,27] Between these pigment arcades the anterior iris surface has appeared thickened with extension as bands on to the trabeculum in continuity with the uveal portion of the trabeculum.[28] The periphery of the iris may be circumferentially tented anteriorly a change made especially apparent by the anterior bending of radial vessels and anterior position of the visible posterior iris pigment layer.[29] Such forward tenting of the iris has been seen in 50% of PCOAG patients, and in 50% of these patients the forward position of radial blood vessels has been present also.[30] The smooth continuity of the anterior surface of the peripheral iris with the uveal meshwork of the trabeculum, with or without tenting, would seem to represent an important observation.

Findings

Examination of the irides of 25 patients with PCOAG was carried out. Inspection of the iris at the time of Koeppe gonioscopy under general anesthesia provided the greatest information about this structure.

The irides of these patients were found flat rather than showing convexity of their anterior stromal surfaces. The position and contour of the iris at its insertion varied greatly in proportion to the angle anomaly (Table XVI).

TABLE XVI: PCOAG—IRIS DEFECTS (41 EYES)

Anterior Stromal Opacification	0/41 eyes	0%
Peripheral Anterior Tenting	21/41 eyes	51%

No qualitative stromal abnormalities were recognized, however, visible radial peripheral blood vessels were common as was visibility of the posterior pigment epithelium. These findings were not catalogued as defects. Pupillary abnormalities were rare, but anisocoria was seen frequently when there was asymmetric enlargement of either globe secondary to glaucoma.

In the period of this study other infants were seen for evaluation of their glaucoma because of suspected PCOAG. Experience with these patients has indicated to me that careful appraisal of the iris can be of diagnostic importance in excluding other causes of primary glaucoma in childhood (Table XVII).

TABLE XVII: PRIMARY PEDIATRIC GLAUCOMA ASSOCIATED WITH IRIS ABNORMALITIES (1968 - 1978)

Disease	Cases	Iris Abnormality
Neurofibromatosis	5	Anterior insertion; ectropion uveal
Lowe's Syndrome	3	Miosis
Iridocorneal Dysgenesis	2	Megalocoria, ectropion uvea, anterior insertion
Spherophakia	2	Convexity, angle closure
Aniridia	49	Hypoplasia; angle degeneration
Anterior Chamber Cleavage Syndrome	2	Abnormal pupil; iridocorneal adhesion
Marfan's Syndrome	1	Iridodonesis; positive peripheral transillumination
Microspherophakia	2	Anisocoria, megalocornea, iridodonesis, positive transillumination

C. THE ANGLE IN PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA

Review

Detailed study of the angle in PCOAG began at the turn of the century in the pathology laboratory and present day investigations have returned there employing electronmicroscopy techniques with specimens from microsurgical procedures. First Collins (1896) then Seefelder (1906) described angle pathology consisting of abnormal trabecular tissue, abnormal attachment of the iris to the trabeculum and cornea, and abnormal insertion of the ciliary body into the trabeculum rather than into the scleral spur.[4,5] Seefelder described that the inner lamellas of the trabecular meshwork were more compressed than normal. The pathologic changes of abnormal tissue in the angle was also described by Kuyskens and correlated

with gonioscopy observations.[31] Recent transmission electronmicroscopy found granular material in the intertrabecular spaces.[32] When specimens from infant patients were examined by scanning electronmicroscopy, however, in spite of a demonstrable inner membrane suspected at surgery, no imperforate membrane could be identified.[33]

The appearance and significance of the gonioscopic findings in PCOAG has been valued very differently, and is information that has emanated only over the last thirty years. Even though Barkan in 1936 reported results with goniotomy in adults under direct vision, his initial and historic report in 1942 of 17 successful operations in infants noted that these cases were operated without gonioscopic observation.[34] In 1948 Barkan reported goniotomy results with 76 eyes but had done only 20 of these operations under direct visualization.[35] Gonioscopy examination of these patients allowed him to conclude that the angle of congenital glaucoma showed "little individual variation," and that the principal defect was the insertion of the iris at or near Schwalbe's line. In 1953 however, he reported the findings and results of surgery on 196 eyes.[36] He described for the first time the presence of a semitransparent-membraneous vertically-oriented trabeculum between the cornea and somewhat anteriorly inserted iris that appeared to be continuous with the anterior surface of the iris. He noted that the width of the trabeculum varied from child to child and even in the same eye, and described tenting of the peripheral iris for the first time.

Lister in 1952 called attention to the density and homogenity of the angle face noting that a "misty whitish tissue" obscured the trabecular and ciliary band regions.[37] In 1955 Barkan also described more "opaque" tissue of the trabeculum noted that it subdued the appearance of blood in Schlemn's canal.[38] To others the trabecular tissue has appeared normal and of no diagnostic value.[38,39]

There has been unusual unanimity in respect to Schlemn's canal which has been consistently found on pathologic examination and on gonioscopy of surgically controlled eyes.[5,40] The position of the canal usually is well anterior of the iris insertion, but may be hidden in some sectors by an abnormal anterior iris insertion and may be more narrow than normal.[41] Barkan was aided by jugular compression to produce filling of Schlemn's canal at the time of post-operative examinations.[40,41] Suction gonioscopy has been employed to produce blood in Schlemn's canal on pre-operative examinations in all of 19 consecutive infants.[42] In these cases remarkable outflow of aqueous humor was noted from Schlemn's canal when opened in conjunction with ab externo trabeculotomy surgery.

The scleral spur has been described infrequently in PCOAG, but noted by Shaffer[41] to be less prominent, and by Grant to be seen "as though

viewed through ground-glass screen."[30] The infrequent description of this structure is in marked contrast to the attention given to its near absence on pathologic examination and the possible effect of this abnormality on the facility of outflow.[43]

The ciliary body band also has been mentioned infrequently, but described by Shaffer[41] (1955) as a "shadowy gray area" seen through the anterior isis stroma, and by Lister[44] (1966) as a structure "more or less" concealed by a "fog of tissue" in the angle. Grant (1966) provides the most detailed description of this structure, noting that it is always present, and is more narrow, irregular and less clearly defined than in normal eyes.[30] More recent descriptions of the gonioscopic findings in primary congenital open angle glaucoma fail to mention this structure and suggest that the iris inserts into the trabecular area.[45-47]

Asymmetry of the angle in unilateral cases with a more severe anomaly on the affected side has been described.[42,45,48] The greater angle involvement on the clinically more involved eye may be represented by a defect present in more sectors of the angle or by a more severe anomaly circumferentially.[30]

Barkan noted the poorer prognosis for successful goniotomy in advanced cases when the diagnosis was delayed and suggested that obliteration of Schlemn's canal, seen pathologically in such eyes, might be responsible for these results, but did not correlate failure with gonioscopic findings.[40] Lister (1966) made a unique suggestion offering that "the success or failure" of goniotomy "lies in the state of the filtration angle," and suggested that cases could be discerned by gonioscopy.[4] Examples given of PCOAG patients that might be expected to do poorly were those with advanced enlargement of the globe, a positive family history for PCOAG, and those with angles showing no normal trabeculum.

Angle Findings

Although much of the examination of an infant with suspected glaucoma can be done in an office setting, careful informative gonioscopy must be done with the assistance of general anesthesia. Findings at initial examination were compared to post-operative angle findings at unoperated meridians to assure the accuracy of initial observations when helpful. Recorded gonioscopic data for each PCOAG child's eye included the anatomic features listed in Table XVIII.

Schwalbe's line was found normal in 39 of 41 eyes with PCOAG and shifted intermittently posterior in 2 of 41 eyes.

The trabecular meshwork was the most difficult angle component to qualitatively evaluate. It appeared often to possess increased opacification and in some eyes was narrowed (Table XIX).

TABLE XVIII: PCOAG—GONIOSCOPIC OBSERVATIONS (50 EYES)

1) Schwalbe's Line	:	Size and position
2) Trabeculum	:	Transparency and width
3) Scleral Spur	:	Visibility
4) Ciliary Body Band	:	Visibility and width
5) Iris Root	:	Position, stromal contour, vessel character
6) Uveal Meshwork	:	Inner surface character

TABLE XIX: PCOAG—GONIOSCOPIC FINDINGS - THE TRABECULUM (41 EYES)

Increased Opacity	21/41 eyes	51%
Decreased Width	14/41 eyes	34%
Circumferential Variability		
Opacification	2/41 eyes	5%
Width	4/41 eyes	10%

In a small number of eyes certain evidence of circumferential variation in width and opacification was found (Table XIX).

Decreased visibility or absence of the scleral spur was the most common gonioscopic abnormality in PCOAG (Table XX).

TABLE XX: PCOAG—GONIOSCOPIC FINDINGS - THE SCLERAL SPUR (41 EYES)

Absent	27/41 eyes	66%
Decreased Visibility	8/41 eyes	20%
Normal Appearance	6/41 eyes	15%

The ciliary body band, like the trabeculum, revealed defects of transparency and width and showed evidence of circumferential variation in a small number of patients (Table XXI).

TABLE XXI: PCOAG—THE CILIARY BODY BAND (41 EYES)

Absent	10/41 eyes	24%
Decreased Width	13/41 eyes	32%
Increased Opacification	20/41 eyes	49%
Circumferential Asymmetry		
Opacification	12/41 eyes	27%
Width	9/41 eyes	22%

To help discern qualitative significance of the above described angle abnormalities in PCOAG the gonioscopic findings of the better and worse eye of unilateral and asymmetric bilateral PCOAG were compared. Unilateral PCOAG were those cases with clinical glaucoma requiring operation on only one side. Asymmetric bilateral cases of PCOAG were those cases with abnormal pressure requiring operations on both sides but with a pressure increment of 10 mm Hg or more between the child's two eyes.

When the comparison was made between the eyes of unilateral cases of

PCOAG, the glaucoma eyes were found to have an equal angle anomaly or more defective angle in each of nine of the unilateral patients (Table XXII).

TABLE XXII: PCOAG—GONIOSCOPIC FINDINGS OF UNILATERAL PCOAG GLAUCOMA EYES - COMPARED TO THE NORMAL CONTRALATERAL EYE (9 EYES)

A) *The Trabeculum*		
Increased Opacification	5/9 eyes	56%
Equal Opacification	4/9 eyes	44%
B) *Scleral Spur*		
Decreased Visibility	7/9 eyes	78%
C) *Ciliary Body Band*		
Increased Opacification	6/9 eyes	67%
Equal Opacification	3/9 eyes	33%
Decreased Width	3/9 eyes	33%
Equal Width	5/9 eyes	56%

This information confirms that unilateral clinical PCOAG is often associated with an asymmetric angle anomaly worse on the glaucoma side. It secondarily reveals that the "normal" eye of unilateral PCOAG may be equal or only less abnormal in respect to its angle condition.

When four asymmetric bilateral cases of PCOAG were examined, more severe angle changes were found on the side with the higher pressure in each case. It seems appropriate to conclude that variable expression in this disorder is visible in the angle structure and that relatively more anomalous angle changes are likely to be associated with glaucoma in unilateral PCOAG and with more severe glaucoma in bilateral PCOAG.

As with the other abnormalities of PCOAG reported earlier, it is of interest to correlate the angle abnormalities in each of the proposed types of PCOAG—neonatal, infantile, and late recognized (Table XXIII).

TABLE XXIII: PCOAG—COMPARISON OF THE ANGLE APPEARANCE AND RESPONSE TO GONIOTOMY (41 EYES)

PCOAG—Type	Eyes	TM Vis. abn.	Absent SS	CCB Vis. abn.	Response to Goniotomy
Neonatal PCOAG	8	8/8	8/8	8/8	0/8 - 0%
Infantile PCOAG	29	10/29	23/29	18/29	27/29-93%
Late-Recognized PCOAG	4	4/4	4/4	4/4	2/4 -50%

The uniformity of the eyes in the oldest and youngest group of patients may reflect in part the small number of patients seen. The angles of all patients with neonatal PCOAG were, however, severely abnormal with narrow more opacified trabeculums and resembled those "atypical" patients already described by others who have responded less well to

goniotomy.[7,42] A like poor result with goniotomy in my patients with similar abnormal angles assigned to the neonatal PCOAG was found, suggesting that this type of PCOAG may have identity of therapeutic significance (Table XXIII).

The severe angle changes in the late recognized group and the less favorable response of their eyes to goniotomy suggests a similar experience to that of Barkan and others as described earlier.

D. THE LENS IN PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA

Review

There is no evidence to suggest that there exists a primary associated defect of the lens in primary congenital open angle glaucoma. An abnormal inward pull on the ciliary processes and ciliary body by the zonular fibers when the globe is enlarged is suggested by pathologic examination.[48] The lens may be shifted posteriorly behind an already deepened anterior chamber.[49]

Findings

No abnormal lens findings were observed in the 41 eyes with PCOAG that were studied.

E. THE INTRAOCULAR PRESSURE IN PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA

1) THE NORMAL CHILDHOOD INTRAOCULAR PRESSURE UNDER GENERAL ANESTHESIA

Review

The specific pressure lowering effect of general anesthetic agents on normal infants and infants and children with glaucoma has been studied and it is universally accepted that the effect is significant and can be misleading. When 100 unoperated eyes in patients with glaucoma from age three days to one year were examined under general halothane anesthesia, the average pressure determined was 32.6 mm Hg with a range from 17 to 59 mm Hg.[50] When 10 other children of various ages were examined without and with general anesthesia, the intraocular pressure was found to decrease as much as 34 to 43 mm Hg in five patients.[51] Measurement of eye pressure under general anesthesia in 408 normal infants revealed tensions lower than the usual adult values, with an average value of 13.5 mm Hg when halothane was used along with nitrous oxide in the anesthesia of 14 infants.[52]

Grant concludes that the examiner "can never be certain" of the intraocular pressure under general anesthesia and that tonometry is sometimes fairly easy under local anesthesia in an office setting.[53]

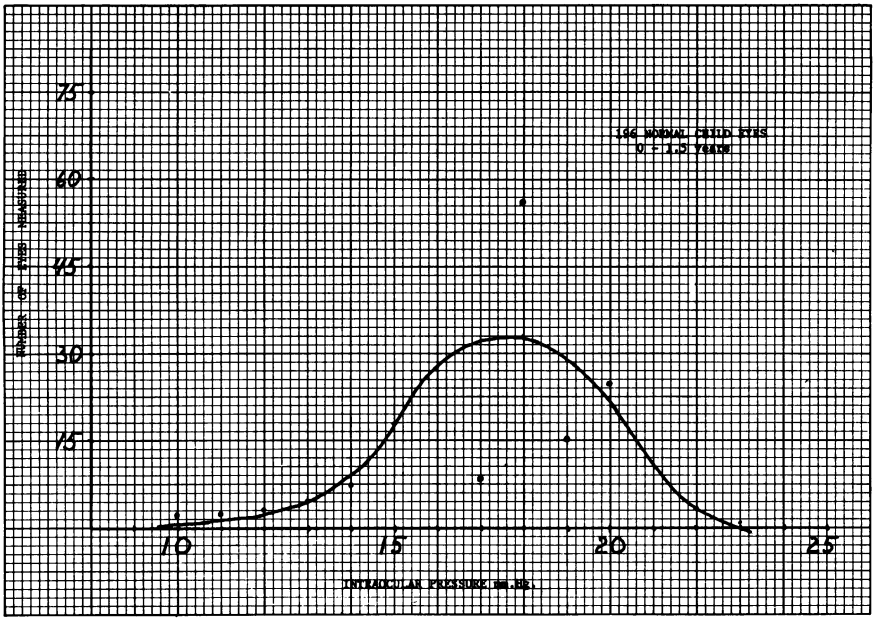
2) THE NORMAL CHILDHOOD INTRAOCULAR PRESSURE WITHOUT GENERAL ANESTHESIA

Review

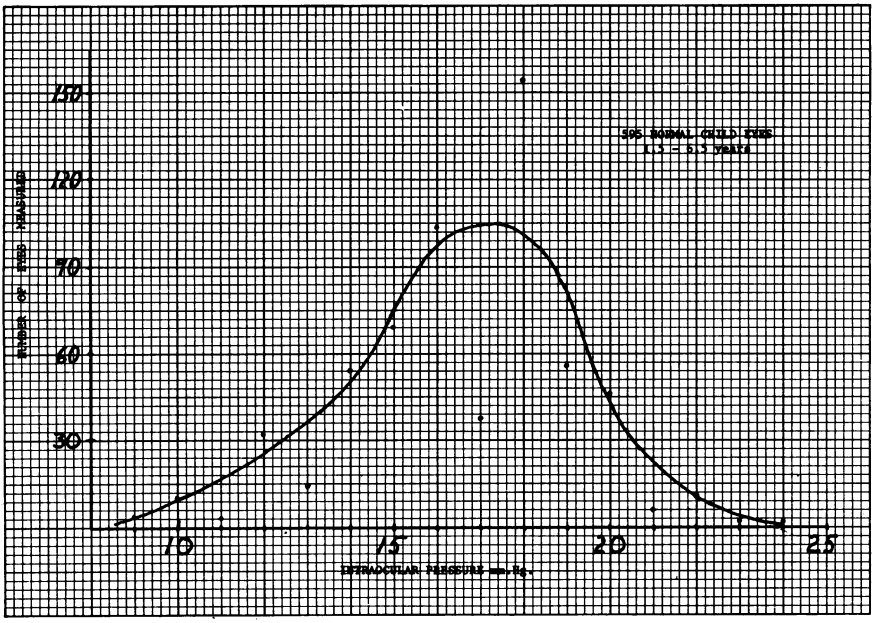
The intraocular pressure measurements of normal children and infants and children with glaucoma awake and without sedation and under general anesthesia have been reported infrequently. When 60 awake normal newborns were examined by applanation tonometry a measured intraocular pressure of 11.4 mm Hg was found with a range of 6 to 17 mm Hg.[54]

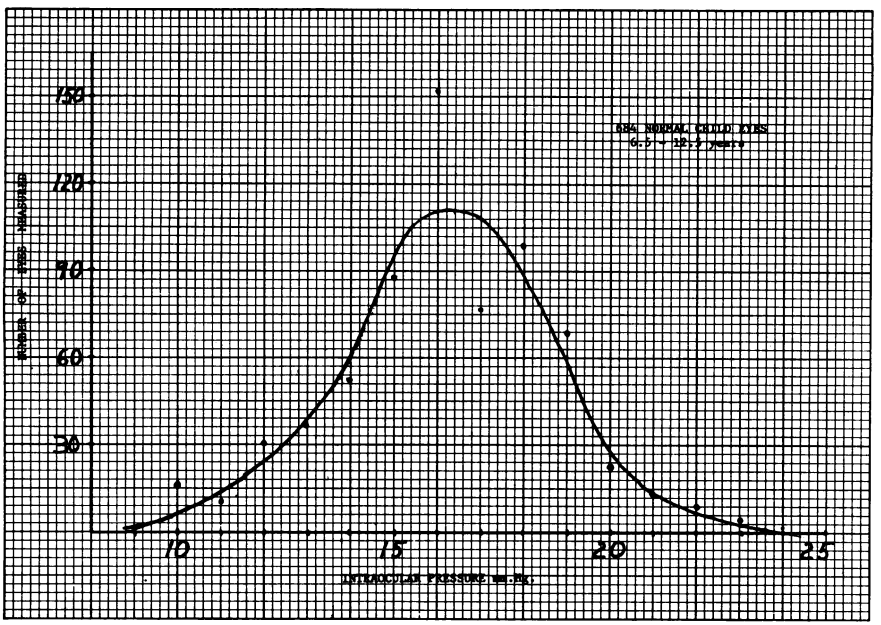
Findings

To provide a basis to which to compare the eye pressure of infants and children with suspected glaucoma a study was carried out on normal children to determine the normal awake applanation intraocular pressure for infants and children. One thousand four hundred seventy-five normal eyes were measured by the author in children from birth to 12 years of age. The results of this pressure survey are shown in graphs, which show the frequency of each pressure measurement for certain age groups up to 12 years of age. It is of value to know that the range of normal pressure for children, awake and unanesthetized, resembles that of adults. A measurement of 18 mm Hg was the most frequent measurement until age six years, (Graphs I, II) and 16 mm Hg the most frequent measurement from 6-12



GRAPH I


595 NORMAL CHILD EYES
1.5 - 5.5 YEARS
NUMBER OF EYES MEASURED
150
120
90
60
30
10
15
20
25
INTRAOCULAR PRESSURE MM. HG.
GRAPH II


684 NORMAL CHILD EYES
6.5 - 12.5 YEARS
NUMBER OF EYES MEASURED
150
120
90
60
30
10
15
20
25
INTRAOCULAR PRESSURE MM. HG.
GRAPH III

years (Graph III). It seems possible that this slight shift to a lower pressure in older children could be explained by less anxiety in response to the test procedure and a willingness of the examiner to extend the measurement period for a longer period of time in older children. I cannot explain the infrequency of recordings at certain odd number pressures except to acknowledge a bias towards even numbers; I doubt that this is of physiologic significance.

3) THE ABNORMAL INTRAOCULAR PRESSURE IN PRIMARY CONGENITAL OPEN ANGLE GLAUCOMA

Review

Barkan (1942) employing ether anesthesia found the intraocular pressure elevated in each of 10 patients at levels most often between 30 to 50 mm Hg (Schiotz), and above a range of normal (20-28 mm Hg) found in normal eyes under similar circumstances.[34,36] He thought that a corneal diameter above 12 mm would give an abnormally low pressure reading.[36] Friedenwald studied the effect of corneal curvature in congenital glaucoma and calibrated scales for various internal corneal radii of curvature; he thought a flatter cornea would indicate an abnormally low pressure reading.[18] Haas recorded the intraocular pressure in 181 eyes under general anesthesia and showed a range of abnormal pressures similar to those of Barkan.[16] Costenbader reviewed 58 cases of PCOAG and found an average intraocular pressure under general anesthesia of slightly over 40 mm Hg and found no correlation between the pressure and the age of diagnosis.[7] It has been the experience of the author to have witnessed the measurement of the intraocular pressures in patients with PCOAG that were found misleadingly low, or at other times elevated, when such children were examined under general anesthesia.[55]

Findings

Because of the early administration of carbonic anhydrase inhibitors to some patients, the intraocular pressure measurements of only 18 of 41 eyes were appropriate for analysis in respect to determining the true eye pressure of PCOAG. The values, reported in Table XXIV, were measured in awake children without sedation using a hand-held Perkins applanation tonometer. It was often helpful to have the infant feeding during this part of the eye examination to obtain good pressure measurements. The average pressure measurement for these 18 eyes was 37 mm Hg.

Children first seen with PCOAG and possessing significant opacification of the cornea often received acetazolamide by mouth for variable periods to achieve clearing of the involved cornea in preparation for an internal

TABLE XXIV: PCOAG—APPLANATION AWAKE INTRAOCULAR PRESSURE MEASUREMENTS BEFORE TREATMENT (18 EYES)

Pressure Range mm Hg	Number of Eyes
20-25	0
26-30	3
31-35	5
36-40	4
41-50	6

goniotomy. The awake applanation pressure of 19 eyes with PCOAG before and after the administration of acetazolamide at a dose of 15 mgm/kg were recorded. Thirteen of these eyes showed a lessening of the eye pressure with an average improvement of 9.6 mm Hg. Three eyes showed no change in pressure. Three other eyes showed a variable small increase in eye pressure when remeasured while on acetazolamide.

The awake applanation eye pressure of 25 children with glaucoma was measured as described above at approximately 12 hours before surgery. Many of these children were on acetazolamide therapy, but none was administered during this twelve hour period. Following the administration of general anesthesia using a fluothane, nitrous oxide, and oxygen mixture and after intubation, the eye pressures were again measured by Schiotz tonometry. When these operative pressures were converted to millimeters of mercury, using the 1948 calibration, and compared with the preoperative values, 18 eyes showed a fall of pressure an average of 8.4 mm Hg (range 0-18 mm Hg). Four eyes showed no change, and two eyes showed an increase of 5 mm Hg.

SUMMARY & CONCLUSIONS

1. The anterior segment defects of 25 children with PCOAG were recorded over a 10 year period and analyzed for this report.

2. A classification for PCOAG was proposed based on the time of diagnosis, supported by the different clinical behavior and ocular findings of children in each group.

3. Corneal abnormalities secondary to glaucoma were found in all patients and showed evidence of progression in older infants. Corneal opacification is an important diagnostic sign. Enlargement of the cornea also was near universal and greater in older infants. The significance of corneal diameter measurements must take into account the patient's age. An enlargement of more than 2.0 mm is characteristic for PCOAG patients. Breaks in Descemet's membrane are frequent and more frequent in older infants and those with more enlarged corneas. Enlargement of the fellow

eye in the absence of glaucoma is present and enigmatic; this fact should be correlated with the occurrence of angle anomalies in the normal fellow eye.

4. The iris in PCOAG is normal but shows anatomic variation at its periphery in relation with the angle deformity.

5. The angles of cases with PCOAG were found to possess variable expressions of certain abnormalities. Increased opacification of the trabeculum, loss of visibility of the scleral spur, and increased translucency of the ciliary body band region were the most frequent abnormalities. Where asymmetry of the angle was present in unilateral and asymmetric cases of PCOAG, more severe expression of the defects were found on the side with greater intraocular pressure. Neonatal and late-recognized PCOAG tended to possess more advanced angle abnormalities and responded less well to goniotomy surgery.

6. The lens was found abnormal only in its position relative to the cornea.

7. The normal-awake childhood intraocular applanation pressure range was documented for the first 12 years of life. A range of normal values was found similar to the adult range, with 18 mm Hg being most frequent measurement for children less than seven years of age.

8. The average awake eye pressure for children with PCOAG before treatment was found to be 37 mm Hg. Acetazolamide was shown to decrease the eye pressure in 13 of 19 eyes, and the administration of general anesthesia was shown again to have a significant pressure lowering effect. The unreliability of pressure measurements in the management of PCOAG when performed under general anesthesia was again documented.

REFERENCES

1. Merin S, Morin D: Heredity of congenital glaucoma. *Br J Opthalmol* 56:414-417, 1972.
2. Rasmussen DH, Ellis PP: Congenital glaucoma in identical twins. *Arch Ophthalmol* 84:827-830, 1970.
3. Leighton DA, Phillips CI: Infantile glaucoma-steroid testing in parents of affected children. *Br J Ophthalmol* 5427-30, 1970.
4. Collins T: Researches into the anatomy and pathology of the eye, London, 1896.
5. Seefelder R: Kleinische und anatomische untersuthugen zur pathologie und therapie des hydrophthalmus congenitus. I Teil Kleinisches II Teil Anatomisches. *v Graefes Arch Ophthalmol* 63:205; 481, 1906.
6. Lamb HD: Hydrophthalmos. *Am J Opthalmol* 8:784-789, 1925.
7. Costenbader FD, Kwitko ML: Congenital glaucoma. *J Pediatr Opthalmol* 2:9, 1967.
8. Haas J: Principles and problems of therapy in congenital glaucoma. *Invest Ophthalmol* 7:140-146, 1968.
9. Salzmann M: Die ophthalmoskopie der kammeibucht. *Z Augenhk* 31:1-19, 1914.
10. Barkan O: Operation for congenital glaucoma. *Am J Ophthalmol* 25:552, 1942.
11. von Mavralt: Uber hydrophthalmus congenitus (Thesis), Zurich, 1869.
12. von Graefe A: *v Graefe Arch Ophthalmol* 15:(3) 108, 228, 1869.

13. Hetherington J: Congenital glaucoma, *Clinical ophthalmology,* Duane TD ed, New York, Harper & Row, 1978, p 1.
14. The Eye in Childhood, Chicago, Year Book Publishers, Inc, 1967, pp 270-271.
15. Morin JD, Marin S, Sheppard RW: Primary congenital glaucoma—a survery. *Can J Ophthalmol* 9:17-28, 1974.
16. Haas J: Principles and problems of therapy in congenital glaucoma. *Invest Ophthalmol* 7:140-146, 1968.
17. Gernet H, Hollwich F: Resultats oculometriques a propos du glaucome infantile. *Bull Soc Franc Ophthalmol* 82:41-47, 1969.
18. Friedenwald, JS: Calibration of tonometers for microphthalmic and buphthalmic eyes. Decennial Report of the Committee on Standardization of Tonometers, American Academy of Ophthalmology and Otolaryngology. Monography Suppl. *Bull Am Acad Ophthalmol Otolaryngol* 1954, p 153.
19. Gernet H: Kompensatorisches verhalten von hornhaulbrechkraft und bulbuslange bei buphthalmus. *Klin Monatsbl Augenheillo* 144:429-431, 1964.
20. Scheie HG: *Congenital glaucoma*—congenital anomalies of the eye. St Louis, CV Mosby Co, 1968, p 345.
21. Haab: Atlas d. Ausseien Erkank d. Auges. 1:222, 1899.
22. Spencer WH, Ferguson WJ, Shaffer RN, Fine M: Late degenerative changes in the cornea following breaks in Descemet's membrane. *Trans Am Acad Ophthalmol Otolaryngol* 70:973-986, 1966.
23. Sheppard LB, Shanklen WM, Ferguson JG: A cytologic aid in the diagnosis of congenital glaucoma. *Trans Am Ophthalmol Soc* 75:382-396, 1977.
24. Christensen RE, Garai MH: Corneal curvature and diameter in developmental glaucoma. *Am J Ophthalmol* 71:490-494, 1971.
25. Maumenee AE: Surgery for congenital glaucoma—symposium on glaucoma. St Louis, CV Mosby Co, 1959, p 212.
26. Barkan O: Surgery of congenital glaucoma. *Am J Ophthalmol* 36:1523-1533, 1953.
27. Lister A: The prognosis in congenital glaucoma. *Trans Ophthalmol Soc UK* 85:5-18, 1966.
28. von der Helm FGM: Hydrophthalmia and its treatment. New York, Hafner Publishing Co Inc, 1963, p 11.
29. Shaffer RN: Pathogenesis of congenital glaucoma gonioscopic and microscopic anatomy. *Trans Am Acad Ophthalmol Otolaryngol* 59:297-308, 1955.
30. Chandler PA, Grant WM: *Lectures on glaucoma.* Philadelphia, Lea & Febiger, 1965, pp 315-316.
31. Kluyskens J: Le Glaucome Congenital. *Bull Soc Belge Ophthalmol* 94:5-248, 1950.
32. Hara K: Basic and clinical studies on glaucoma in childhood Pt V fine structures of the trabecular meshwork in congenital glaucoma. *Acta Soc Ophthalmol Jap* 81:995-1005, 1977.
33. Anderson DR: Pathology of the glaucomas. *Br J Ophthalmol* 56:146, 1972.
34. Barkan O: Operation for congenital glaucoma. *Am J Ophthalmol* 25:552-568, 1942.
35. Barkan O: Goniotomy for the relief of congenital glaucoma. *Br J Ophthalmol* 701-728, 1948.
36. Barkan O: Surgery of congenital glaucoma. *Am J Ophthalmol* 36:1523-1533, 1953.
37. Lister A: The surgery of congenital glaucoma. *Trans Ophthalmol Soc Aust* 11:39-56, 1952.
38. Maumenee AE: Surgery for congenital glaucoma, Symposium on glaucoma. St Louis, CV Mosby Co, 1959, p 211.
39. Scheie HG: Congenital glaucoma in symposium, *Congenital anomalies of the eye.* St Louis, CV Mosby Co, 1968, p 347.
40. Barkan O: Pathogenesis of congenital glaucoma. *Am J Ophthalmol* 1-11, 1955.
41. Shaffer RN: Pathogenesis of congenital glaucoma: gonioscopic & microscopic anatomy. *Trans Am Acad Ophthalmol Otolaryngol* 59:297-308, 1955.
42. Iwata K: On the mechanism of elevation of intraocular pressure of congenital glaucoma. *Acta Soc Ophthalmol Jap* 80:246-250, 1976.

43. Maumenee AE: The pathogenesis of congenital glaucoma (a new therapy). *Trans Am Ophthalmol Soc* 56:507-569, 1958.
44. Lister A: The prognosis in congenital glaucoma. *Trans Ophthalmol Soc UK* 86:5-18, 1966.
45. Portney GL: *Glaucoma Guidebook*. Philadelphia, Lea & Febiger, 1977, p 81.
46. Hoskins HD, Shaffer RN: Evaluation techniques for the congenital glaucomas. *J Pediatr Ophthalmol* 8:31-87, 1971.
47. Hetherington J: Congenital glaucoma—*Clinical ophthalmology*, Duane TD Ed, New York, Harper & Row, 1978, pp 2-3.
48. Maumenee AE: Further observations on the pathogenesis of congenital glaucoma. *Am J Ophthalmol* 55:1163-1176, 1963.
49. Parsons JH: The refraction in buphthalmia. *Br J Ophthalmol* 4:211-216, 1920.
50. Hetherington J, Shaffer RN: Tonometry and tonography in congenital glaucoma. *Invest Ophthalmol* 7:134-137, 1968.
51. Auskinsck B, Munan ES. Levy NS: Intraocular pressure in children with glaucoma during halothane anesthesia. *Ann Ophthalmol* 9:1391-1394, 1977.
52. Dominquez A, Banos MS, Alvarez MG, et al: Intraocular pressure measurements in infants under general anesthesia. *Am J Ophthalmol* 78:110-116, 1974.
53. Chandler PA, Grant WM: *Lectures on glaucoma*, Philadelphia, Lea & Febiger, 1965, pp 298-305.
54. Radtke ND, Cohan BE: Intraocular pressure measurements in the newborn. *Am J Ophthalmol* 78:501-504, 1974.
55. Walton DS: Diagnosis and treatment of glaucoma in childhood. In Chandler PA, Grant WM: *Glaucoma*, 2nd edition. Philadelphia, Lea & Febiger. Part IV, chapt 33-43 (in press).