MAJOR REVIEW

Angle-closure Glaucoma: The Role of the Lens in the Pathogenesis, Prevention, and Treatment

Pamela Tarongoy, MD,1 Ching Lin Ho, FRCSEd,2 and David S. Walton, MD3

1Associated Cebu Eye Specialists (ACES), Cebu City, Philippines; 2Singapore National Eye Centre, Singapore, Republic of Singapore; and 3Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, USA

Abstract. Primary angle-closure glaucoma is a major cause of blindness worldwide. It is a disease of ocular anatomy that is related to pupillary-block and angle-crowding mechanisms of filtration angle closure. Eyes at increased risk for primary angle-closure are small with decreased axial length, anterior chamber depth, and filtration angle width, associated with a proportionately large lens. Angle-closure glaucoma afflicts Asian and Eskimo eyes more frequently than eyes in other races with similar predisposing dimensions. The treatment of primary angle closure addresses its causal mechanisms. Laser peripheral iridotomy equalizes the anterior and posterior pressures and widens the filtration angle by reducing the effect of pupillary block. Argon laser peripheral iridoplasty contracts the iris stroma to reduce angle crowding and is helpful for some affected eyes. Lensectomy dramatically widens the angle and eliminates pupillary block. Clinical reports of lensectomy with posterior chamber intraocular lens implantation in the treatment of acute, chronic, and secondary angle-closure glaucoma describe very favorable results. The appropriate role for lensectomy in the management of primary angle closure, however, remains unproven. Prospective, randomized clinical trials are ongoing to determine the value and comparative risks and efficacy of lensectomy versus medical therapy, laser peripheral iridotomy, laser iridoplasty, and filtration procedures for the treatment of acute and chronic primary angle closure and for the prevention of chronic angle-closure glaucoma, both after and in place of laser peripheral iridotomy. (Surv Ophthalmol 54:211–225, 2009. © 2009 Elsevier Inc. All rights reserved.)

Key words. angle-closure glaucoma • blindness • goniosynechialysis • iridotomy • lensectomy

I. Introduction

Angle closure is a disorder of ocular anatomy characterized by closure of the drainage angle by appositional or synechial approximation of the iris against the trabecular meshwork, blocking its access to aqueous humor. The final common result in related disorders is an elevation of the intraocular pressure (IOP), due to the secondary impairment of aqueous humor outflow from the eye, followed by the development of glaucomatous optic neuropathy. This review will focus on the role of the lens in the pathogenesis and treatment of primary and secondary angle closure.

II. Clinical Types of Angle-closure Glaucoma

Angle-closure disorders can be divided into primary and secondary groups. Primary angle closure includes those that are caused by pupillary

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block, angle crowding (from plateau iris configuration or anterior lens position) or a combination of both. A classification endorsed by the American Academy of Ophthalmology subdivides the primary group into primary angle-closure suspect, primary angle closure without optic neuropathy (PAC), and primary angle-closure glaucoma with neuropathy (PACG). These useful subdivisions may clinically overlap or be potentially related, as patients move from one category to the next depending on the initial stage and progression of their disease. Secondary angle-closure disorders are those that occur in the presence of a second ocular disease such as with iris neovascularization, uveitis, trauma, or lens disease–related conditions.

III. Epidemiology of Primary Angle-closure Glaucoma

It has been estimated that 67 million people worldwide are affected with a primary glaucoma and that one-third have PACG. In European and African populations primary open-angle glaucoma (POAG) occurs approximately five times more frequently than PACG; in Chinese, Mongolians, and Indians, however, the rates of PACG may equal or be greater than POAG. In Eskimos/ Inuit the prevalence of PACG is felt to be higher than any other ethnic group. A prevalence study reported PACG as occurring more frequently in Italy than in the rest of the European population (0.6–0.1%). In China alone an estimated 3.5 million people are afflicted with the disease, and 28 million are estimated to have occludable drainage angles. A Singapore study reported the highest annual rate of acute primary angle closure (APAC) as 12.2 per 100,000 among persons over age 30 years. The incidence of PAC increases with age and is greater in females. The annual rate of APAC in Singapore was highest (68.5/100,000) for elderly Chinese women with a two times higher rate than in males. In reported populations from Japan, Israel, Finland, and Thailand, women show a consistently more frequent occurrence of PACG. Angle closure is a disease of older persons, peaking in incidence between 55 and 70 years of age. The risk of APAC in elderly Singaporeans greater than 60 years of age was nine times greater compared with the 30- to 59-year-old population. Review of a database of 2,864 patients with angle-closure found only 2.3% under 40 years of age, with a plateau iris in 52%, and evidence of papillary block in only 3%

PACG is more visually destructive than POAG, and it is responsible for the majority of the bilateral glaucoma-related blindness in Singapore. The proportion of those with PACG who become blind is over 25%, which is double that of POAG. Angle-closure glaucoma patients, presenting with an acute attack, are felt to represent only a minority of patients potentially visually affected by PACG. The predominant form of PACG is the chronic, asymptomatic type, and because the diagnosis does require gonioscopy, it is likely that a large proportion of those at risk remain undiagnosed and untreated. Even in Singapore, where glaucoma is responsible for 60% of blindness and the incidence of angle closure is high, awareness of the problem is low. The full extent of the problem must also take into account that patients with acute angle closure do best with early treatment, which may not be available or be utilized; and those with chronic (asymptomatic) angle-closure glaucoma (CAGC) require careful gonioscopy for recognition, which is rarely practiced as a screening tool in China where PACG is endemic.

IV. Mechanisms in Angle-closure Glaucoma

Pupillary block is the most frequent and important mechanism responsible for angle closure, but in many cases it is not the only mechanism involved. Iris angle-crowding may co-exist with pupillary block to cause the angle closure. In the plateau iris configuration, the iris is held anteriorly by the ciliary processes, but a pupillary block component may also be present. These pathologic mechanisms exist because of primary anatomic variations in the size, position, and relationship of the anterior segment structures (cornea, iris, ciliary body, lens), or occur secondary to other acquired ocular pathology. For example, the lens may shift anteriorly secondary to trauma or to drugs that result in the formation of fluid in the supraciliary space, or the lens may move anteriorly secondary to expansion of posterior segment structures (vitreous, subretinal space, choroid). Anterior traction on the peripheral iris may pull the iris over the trabecular meshwork with resultant blockage of access to aqueous. This mechanism of trabecular obstruction occurs with contraction of neovascular, inflammatory, or proliferative fibrocellular membranes and is common in clinical ocular conditions including rubeosis irides, chronic anterior uveitis, aniridia, and after cataract surgery in infancy. Because this article will only review the role of the lens in the pathogenesis of the angle closure, these mechanisms related to anterior traction on the iris, which cause angle obstruction independent of the lens, will not be further discussed.
A. PUPILLARY BLOCK MECHANISM

Aqueous humor (AH) is produced into the posterior chamber and normally flows anteriorly between the posterior surface of the iris and the anterior lens capsule, to enter the anterior chamber through the pupil, and exits through the trabecular meshwork (TM). Relative resistance to flow of AH from the posterior chamber (PC) into the anterior chamber (AC) is normal and reflected by an estimated pressure drop of 0.23 mm Hg between the PC and AC. This pressure differential may increase greatly when the dimensions of the iris-lens channel are changed in such a manner that flow of AH is more impeded.113 The incremental greater pressure differential between the PC versus the AC is an important variable that determines the iris contour. As this pressure increment increases, the iris becomes more convex. Clinically significant pupillary-block is present when the increased iris convexity brings the iris into apposition with the TM or appears close enough to do so in the future. Extreme anterior iris-bulging, iris bombe, would be expected with pressure differentials of 10–15 mm Hg.35

The variables that influence the AH flow through the “pinch region” (iris-lens channel) and influence the pressure differential and related iris contour have been studied extensively.35,48,78,105,113 Changing pupillary size within the normal range of 3 to 7 mm was determined to have little effect, however, miosis of 2 mm was predicted to significantly increase the pressure differential especially in the presence of increased channel length (>1 mm) or decreased height (<5 μm).35,113 Increased channel length and decreased height were associated with increased pressure increments and were accompanied by the expected increased iris convexity. Movement of the iris insertion posteriorly or the lens anteriorly also was associated with an expected increase in the pressure differential and iris convexity, which itself lessens the area of iris-lens canal. Other variables exist and interact to determine the iris contour, including eye size, especially the dimensions of the anterior segment,78 lens size and position, iris stroma and iris musculature characteristics,35 ciliary body anatomy, and physiologic parameters including aqueous humor flow rate, facility of outflow, vitreous-aqueous fluid flow, and the effects of accommodation and blinking. These potentially significant dimensional and physiologic parameters vary and may become risk factors of more or less importance in determining iris contour and the development of pupillary-block in eyes which become at risk for angle closure.

It should be clear that the lens plays a pivotal role in the pathogenesis of angle closure secondary to the pupillary block mechanism. If an iridotomy or iridectomy is performed the pressure differential between the AC and PC becomes minimal and iris deformation secondary to pupillary-block is relieved. If the lens is removed and posterior synechiae lysed, the prerequisite anatomical relationship for iris-lenticular (pupillary) block is eliminated, and the anterior chamber angle will widen as the iris leaf becomes flat and rotates to a more posterior position.

B. ANGLE CROWDING

This mechanism for angleclosure may exist alone, but more often co-exists with pupillary-block. Angle crowding can be thought of as the sandwiching of the peripheral iris between the trabecular meshwork and some other structure, compared to the pupillary-block related anterior iris shift secondary to the pressure differential between the anterior and posterior chamber. The clinical primary condition possessing this mechanism is the plateau iris configuration.132 In this condition, anteriorly positioned ciliary processes prop up the iris anteriorly resulting in the peripheral iris being held forward in approximation with the trabecular meshwork.103 Depending on the amount of trabecular obstruction that develops, acute or chronic angle closure can occur. Indentation gonioscopy reveals a characteristic double iris hump, and ultrasound biomicroscopy (UBM) of the ciliary body reveals the anterior position of the ciliary processes filling the ciliary sulcus.88,133 Gonioscopy after an iridotomy (LPI) will reveal persistence of the narrow and occludable peripheral angle. This helps explain why creating a patent LPI to relieve the pupillary block component in the presence of this cause of angle crowding may not prevent progression to ACG.

In plateau iris configuration, removal of the lens with intraocular lens implantation increases ACD but does not change iridociliary apposition. This explains why the elimination of iris support by the lens also does not cause the angle to significantly widen.126 Age-related lens changes and other ocular conditions associated with a forward shift of the anterior lens plane and decreased ACD can also cause significant angle-crowding, as seen clinically in nanophthalmos, microphthalmia, retinopathy of prematurity (ROP), spherophakia, and axial anterior ectopia lentis.

V. Pathogenesis of Angle-closure Glaucoma and the Role of the Lens

Eyes with primary angle closure have significant anatomic differences from normal eyes.13,75 The most significant clinical hallmarks of an eye with angle-closure are the shallow AC and narrow angle.
The mean anterior chamber depth (ACD) in PAC eyes is approximately 1.8 mm, which is 1 mm shorter than in normal eyes. Angle closure becomes a rarity when anterior chamber depth exceeds 2.5 mm. Decreased AC volume, small corneal diameter, and short axial lengths are all characteristic of eyes with PACG. The most satisfactory explanations for the more shallow AC is the age-related increase in lens thickness and more anterior position of the lens. The axial lens thickness is greater than in normal subjects, and the thicker lenses are significantly more anteriorly positioned than in normal eyes. Lowe estimated that increased lens thickness causes 0.35 mm of AC shallowing, and forward lens position causes 0.65 mm of shallowing, accounting for the total of 1 mm difference in AC depth of the smaller eye compared to the normal eye. Growth of the lens, with an increase in the number of lens fibers continuing throughout adult life, results in an increase in lens thickness and anterior curvature. Ocular biometry of Alaskan Eskimos, an ethnic group at high risk for PAC, confirmed the presence of decreased anterior chamber angle width, depth, and axial length associated with increased hyperopia and lens thickness. The age-adjusted angle width and ACD were significantly less than other ethnic groups. When the biometry of contralateral eyes of patients having an APAC were studied and compared to population-based controls, unfavorable dimensions were found consisting of more shallow anterior chambers and narrow angles, and thicker lenses. These differences were considered to explain in part the estimated 50% risk for APAC in these eyes. These observations also explain the tendency of PAC to affect older patients and its relative rarity in young adults. Decreased ACD is accelerated in women between the fourth and fifth decades, which may explain their greater propensity for PAC.

Biometry and clinical examination of PAC patients identifies anatomic risk factors for angle closure and supports the pivotal role of the lens position and size in the active or potential mechanism of closure. These assessments, however, have not conclusively explained its more frequent occurrence in the eyes of certain ethnic groups (Eskimos and Chinese) with dimensions similar to eyes in other populations (whites and blacks) with a less frequent rate of angle closure. Environmental risk factors, including the association of PAC with tropical temperatures and sunspots, and with systemic autonomic dysfunction, has been studied with inconclusive results.

Lens disorders of position and size as seen with lens dislocation and spherophakia can also result in pupillary-block and secondary angle-closure. Unlike PAC, which usually afflicts older patients aged 50 years and above, lens-related secondary angle closure occurs in patients of all ages. Shallowing of the anterior chamber occurs from increased thickness and curvature of the lens and/or forward shifting of the dislocated lens in the pupil to cause crowding of the angle and potential pupillary block. With an intumescent age-related cataract or with lens swelling after a perforating lens injury, the sheer increased thickness and bulk of the lens can push the peripheral iris (angle crowding) against the trabecular meshwork. As with the plateau-iris syndrome, lens-induced angle crowding can lead to acute or chronic angle closure despite a patent LPI. Argon laser peripheral iridoplasty (ALPI) has been used to manage acute phacomorphic angle-closure with favorable results. Extraction of the abnormal lens in these conditions is ultimately the only way to definitively eliminate both the angle-crowding and co-existing pupillary-block.

VI. Current Surgical Treatment Options for Primary Angle-closure Glaucoma

Understanding and caring for patients with APAC requires repetitive careful clinical ocular examinations including evaluation of the filtration angle to determine the mechanism of the angle-closure and the active stage of the disease. The treatment of a patient with acute disease should be followed by care to prevent the development or worsening of chronic angle closure glaucoma. In a patient with established synechial angle closure and advanced glaucomatous optic neuropathy (GON), active management of the IOP is essential. Appropriate surgical decisions for angle closure should be congruous with the patient’s anatomic defects, offending pathophysiology, and the stage of disease. Randomized clinical trials are lacking to support the efficacy of procedures for primary angle closure glaucoma.

A. LASER PERIPHERAL IRIDOTOMY

Laser peripheral iridotomy (LPI) eliminates the pressure differential between the anterior and posterior chambers and is the current standard treatment to correct pupillary block in the initial approach to angle closure. It is also a safe and effective prophylaxis in suspect eyes with occludable angles secondary to pupillary block, including fellow eyes of APAC patients at risk for bilateral angle closure.

Although LPI is an effective treatment for APAC, with resultant widening of the filtration angle and...
reduction of elevated IOP, it is not reliably protective against chronic angle closure. In a study of the benefit of LPI in Asian eyes, 100% had resolution of the acute attack after the LPI, but 58.1% subsequently developed elevated IOP requiring treatment and 32.7% eventually needed trabeculectomy for pressure control. The median time interval for increase in IOP was 5.8 months, and most of these eyes which developed CACG had more than 180 degrees of peripheral anterior synchiae (PAS). The failure of LPI to prevent recurrent elevation of the IOP has been correlated with the amount of PAS present in these eyes. The amount of PAS may or may not progress despite a patent iridotomy; however, the suspected progression of angle closure after successful LPI has not been well-correlated with the development of chronic IOP elevation over time. Design of alternative therapies to both treat angle closure and prevent further progression of the angle defect must be based on understanding of the angle following the treatment of APAC and the mechanisms of the progression to chronic angle closure, with consideration given to all the causes of angle closure, including the potential injurious affects of LPI such as PAS formation, cataract progression, and ciliochoroidal effusion.

B. ARGON LASER PERIPHERAL IRIDOPLASTY

ALPI is a procedure to induce immediate focal iris stromal contraction to pull the iris root away from the angle wall thus widening it. In the long term, it produces thinning and contraction of the peripheral iris, giving it a flatter contour. Histopathology suggests that heat shrinkage of collagen may account for its short-term effect and contraction of the induced fibroblastic membrane may be responsible for its long term effect. Hence, it is used to reduce angle crowding in nanophthalmos, PAC, lens-induced angle closure, and reported to be very effective in the plateau iris configuration by eliminating and reducing the amount of residual appositional angle closure after LPI. In the initial treatment of APAC it can assist to lower the IOP by pulling open the angle, and it can be useful also when initial medical treatment fails. A study of 10 APAC patients treated with ALPI after administration of pilocarpine and timolol showed a remarkable decrease in IOP from 59.5 mm Hg to 21.7 mm Hg at 30 minutes and 16 mm Hg at 1 hour post-ALPI. A follow-up study was done to confirm the effect was predominantly from the ALPI by managing eight APAC patients with ALPI alone and produced similar results. In 2000, a randomized controlled interventional trial comparing ALPI against conventional systemic IOP-lowering medications in the first-line treatment of APAC showed the ALPI-treated group had lower IOP than the medically treated group at 15 minutes, 30 minutes, and 1 hour after the start of treatment. The differences were statistically significant. The differences in IOP became statistically insignificant from 2 hours onwards. In chronic PACG, a study with a follow-up period of 6 months suggested that in eyes which had failed medical therapy, the effect of iridoplasty may not be sustained in some eyes even though at least half the angle was opened at the time of the procedure. In another report on the short-term benefit of iridoplasty after 180 degrees goniosynechialysis in 5 eyes with chronic PAC and total synchial angle closure, satisfactory IOP was achieved in 80% (4 eyes), with a mean follow-up period of 7.6 months. Re-closure of the angle occurred in the remaining eye with IOP elevation. There is a paucity of data on the long-term effect of iridoplasty in PAC. ALPI alters the peripheral configuration permanently and may help prevent subsequent angle closure from peripheral anterior synchiae formation. A long-term study with a mean follow-up period of 33.0 ± 9.3 months showed a 70% (21 eyes) success rate after either 180°/360° argon or 360° diode laser iridoplasty and maintained normal IOP without medications. Nine eyes developed CACG with PAS.

C. ANTERIOR CHAMBER PARACENTESIS

Immediate anterior chamber paracentesis is a maneuver that rapidly lowers IOP in APAC providing instantaneous relief of symptoms and prevention of further optic nerve and trabecular meshwork damage secondary to the acutely elevated IOP. The IOP-lowering benefit of a paracentesis may decrease by 1 hour after the procedure and thus anti-glaucoma medications will become necessary to sustain the IOP control. Paracentesis may not break the pupillary block but can allow the LPI to be performed sooner. Possible complications include excessive shallowing of the anterior chamber, lens trauma, choroidal effusion, and hemorrhage due to the sudden decompression.

D. GONIOSYNECHIALYSIS

When extensive synechial angle-closure has occurred, goniosynechialysis (GSL) is an option for removal of PAS of recent onset; long-standing PAS are likely to be associated with permanent trabecular damage. On its own, the long-term success of GSL for PAC is unlikely because the procedure does not address the underlying cause for the synechial angle closure, be it pupillary-block
or angle-crowding. Hence, goniosynechialysis is often performed with other procedures such as LPI,120 ALPI61,119 or lens extraction62,121 to open the angle in eyes with minimal to moderate neuronal damage. It can also be complicated by hyphema, fibrinous inflammation, and synechial re-closure of the angle.120

E. TRABECULECTOMY

After the onset of permanent trabecular dysfunction, the surgical management of PACG is in principal much like POAG.59 In medically unresponsive APAC, trabeculectomy is associated with high risk of post-operative complications such as shallow anterior chamber and surgical failure.7 Trabeculectomy in chronic PACG is also associated with higher risk of failure, postoperative anterior chamber shallowing, malignant glaucoma, and a significant rate of cataract formation1,7,41,45,127 compared to POAG. Even when the filtration surgery has successfully reduced the IOP, the ailing trabecular meshwork does not regain its function, and so the disease is not cured. The eye must be followed for life to ensure that the aqueous outflow remains adequate and the IOP sufficiently controlled to prevent further progression of the glaucomatous optic neuropathy.

F. LENSECTOMY

Lensectomy in the treatment of PACG has been actively studied and reported in recent years.30,34,39 Cataract surgery in PACG is generally more challenging and complicated than in normal eyes or eyes with POAG because of the shallow AC, large cataractous lens, and a sometimesatomic pupil after an acute angle closure attack. The phacoemulsification procedure offers the advantages of a smaller self-sealing incision, better maintenance of the AC intraoperatively with less risk of iris prolapse, less iris manipulation, better intraocular maneuverability when the pupil is small, faster postoperative visual rehabilitation, and better preservation of the superior conjunctiva for future trabeculectomy if needed.

VII. Lens Extraction in Primary Angle-closure Glaucoma

The role of lensectomy in the management of PACG has not been established. The potential importance of this definitive procedure to correct persistent pupillary-block and angle crowding after LPI in both the treatment and prevention of acute and chronic angle closure glaucoma cannot be overestimated.

A. BIOMETRY FOLLOWING LENSECTOMY

Hayashi has shown that after phacoemulsification and PCIOL implantation, the ACD and angle width in ACG eyes approximates that of POAG eyes and control eyes without glaucoma, even though differences of 1.0 mm of anterior chamber depth and 10 degrees of angle width existed preoperatively.34 They thought that these changes contributed to the significant IOP reduction seen in the postoperative follow-up period of 12 months. Another study,144 done in chronic PACG eyes, also showed a mean increase in AC depth, from 2.04 mm to 3.44 mm, after cataract extraction and IOL implantation followed by control of IOP postoperatively. This increase in ACD and angle width was created by the exchange of the thickened lens (5 mm) for a 1-mm acrylic or polymethylmethacrylate lens.111 Even with the definite deepening of the anterior chamber and widening of the angle after lens removal, a small residual increment has been reported when PACG and POAG eyes were compared, amounting to approximately 0.3 mm of ACD and 2 degrees of angle width.35 A comparison of the UBM findings before and after cataract extraction in plateau iris syndrome eyes after LPI and ALPI found the central anterior depth increased; the iris-ciliary-body approximation, however, remained unchanged.126

B. CLINICAL STUDIES AND IOP CONTROL AFTER LENSECTOMY

In Table 1, 22 clinical studies, reported from 1988 to 2007, are summarized, which describe the results of lensectomy in PAC suspects, PAC, and PACG patients as well as control groups, who were selected in a nonrandom manner. In the early studies2,28–30,138 extracapsular cataract extraction (ECCE) was performed with posterior chamber IOL implant (PCIOL). The cataract extractions were made through a corneal incision, except in Acton’s study,2 where some were performed via a limbal corneoscleral incision after a fornix-based conjunctival incision. The cataract extractions were made through a corneal incision, except in Acton’s study,2 where some were performed via a limbal corneoscleral incision after a fornix-based conjunctival incision. In most of these studies, the patients included had visually significant cataracts in addition to PACG of different severity, chronicity, amount of PAS, and various extents of IOP control with medications, previous filtration surgeries, or laser procedures. A high proportion (>65%) of these patients were considered successes post-cataract extraction with normal IOP without medications, whereas preoperatively glaucoma medications were needed. In the studies by Gunning and Greve,29 Roberts,104 and Jacobi,44 clear lens extractions were performed mainly for glaucoma control. High preoperative IOPs, in these cases of uncontrolled glaucoma, were followed by high rates
<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Lens Procedure</th>
<th>Glaucoma Type (# of eyes)</th>
<th>Preop Gonioscopy</th>
<th>Follow-up (months)</th>
<th>Preop → Postop IOP (mm Hg)</th>
<th>Success % IOP &lt;22</th>
<th>Qualified Success % IOP &lt;22 on Rx</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greve28 (1988)</td>
<td>ECCE+PCIOL</td>
<td>AACG (5)</td>
<td>Near or complete closure</td>
<td>Range 6–42</td>
<td>31 → 16</td>
<td>76%</td>
<td>24%</td>
<td>Early IOP spikes</td>
</tr>
<tr>
<td>Wishart138 (1989)</td>
<td>ECCE+PCIOL</td>
<td>CAGG (14)</td>
<td>PAS (8)</td>
<td>Mean 11.2</td>
<td>19.1 → 15.6</td>
<td>65%</td>
<td>35%</td>
<td>9% IOP spikes</td>
</tr>
<tr>
<td>Gunning30 (1991)</td>
<td>ECCE+PCIOL</td>
<td>CAGG (23)</td>
<td>Open (21)</td>
<td>Mean 14.8</td>
<td>19.4 → 19.6</td>
<td>5%</td>
<td>95%</td>
<td>14% IOP spikes</td>
</tr>
<tr>
<td>Yang144 (1997)</td>
<td>ECCE+PCIOL</td>
<td>CAGG (20)</td>
<td>PAS 77%</td>
<td>Mean 53</td>
<td>28 → 17</td>
<td>Overall success of 68% reported in both groups</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acton2 (1997)</td>
<td>ECCE+PCIOL</td>
<td>CAGG (9)</td>
<td>No data</td>
<td>Mean 53</td>
<td>Controlled 17</td>
<td>0%</td>
<td>100%</td>
<td>IOP spikes; iritis</td>
</tr>
<tr>
<td>Gunning29 (1998)</td>
<td>ECCE+PCIOL vs Trabeculectomy</td>
<td>CAGG (18)</td>
<td>PAC</td>
<td>Mean 53</td>
<td>17 → 15.6</td>
<td>No Data</td>
<td>32% IOP spikes 16% iritis</td>
<td></td>
</tr>
<tr>
<td>Teekhasaenee121 (1999)</td>
<td>ECCE+PCIOL+GSL</td>
<td>CAGG (52)</td>
<td>PAS mean 310° to 60° Postop</td>
<td>Mean 21</td>
<td>30 → 13</td>
<td>90%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Roberts104 (2000)</td>
<td>PHACO+PCIOL</td>
<td>AACG (3)</td>
<td>360° PAS (2)</td>
<td>36, 24 mos, and no data</td>
<td>39 → 17</td>
<td>67% (2 eyes)</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>Ge26 (2000)</td>
<td>PHACO+PCIOL</td>
<td>AACG (18)</td>
<td>Narrow angles</td>
<td>Mean 9</td>
<td>23 → 12</td>
<td>84%</td>
<td>16%</td>
<td>Early IOP spike</td>
</tr>
<tr>
<td>Le22 (2001)</td>
<td>PHACO+PCIOL+GSL+DLPI</td>
<td>CAGG (68)</td>
<td>No data</td>
<td>Mean 25</td>
<td>21 → 15</td>
<td>41%</td>
<td>51%</td>
<td>No data</td>
</tr>
<tr>
<td>Hayashi33 (2001)</td>
<td>PHACO+PCIOL</td>
<td>POAG (68)</td>
<td>Partial closure (7)</td>
<td>Mean 10</td>
<td>41 → 18</td>
<td>72%</td>
<td>16%</td>
<td>9% IOP spikes</td>
</tr>
<tr>
<td>Jacobi44 (2002)</td>
<td>PHACO+PCIOL CSI</td>
<td>AACG (43)</td>
<td>CAGG (32)</td>
<td>Mean 10</td>
<td>40 → 20</td>
<td>35%</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Staso117 (2002)</td>
<td>PHACO+PCIOL</td>
<td>CAGG (12)</td>
<td>Angle width 19°</td>
<td>9</td>
<td>21 → 15</td>
<td>100% both groups, but use of meds not described</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td>Yoon147 (2003)</td>
<td>PHACO+PCIOL</td>
<td>AACG (18)</td>
<td>No data</td>
<td>Mean 6</td>
<td>50 → 12</td>
<td>70%</td>
<td>30%</td>
<td>20% IOP spikes</td>
</tr>
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<th>Qualified Success % IOP &lt;22 on Rx</th>
<th>Complications</th>
</tr>
</thead>
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<tr>
<td>Kubota(^{55}) (2003)</td>
<td>PHACO+PCIOL+GSL (5 eyes)</td>
<td>CACG(13) AACG(5)</td>
<td>PAS &gt;180° (5)</td>
<td>Mean 14</td>
<td>13→14</td>
<td>62%</td>
<td>38%</td>
<td>40% iritis</td>
</tr>
<tr>
<td>Wang(^{134}) (2004)</td>
<td>PHACO+PCIOL</td>
<td>AACG (2)</td>
<td>PAS 90°</td>
<td>No data</td>
<td>19→14</td>
<td>100%</td>
<td>No data</td>
<td>No complications</td>
</tr>
<tr>
<td>Harasymowycz(^{31}) (2005)</td>
<td>PHACO+PCIOL+GSL</td>
<td>AACG (12)</td>
<td>No data</td>
<td>Mean 12</td>
<td>41→15</td>
<td>3.8→1.7</td>
<td>pre-op to post-op meds</td>
<td>No complications</td>
</tr>
<tr>
<td>Nonaka(^{85}) (2005)</td>
<td>PHACO+PCIOL</td>
<td>PAC (13) CACG (21)</td>
<td>2 Q closed by UBM ≤90°→270° closed</td>
<td>3</td>
<td>Mean 21</td>
<td>19→15</td>
<td>66.7%</td>
<td>33%</td>
</tr>
<tr>
<td>Liu(^{74}) (2006)</td>
<td>PHACO+PCIOL</td>
<td>PACG (29) PAC/suspect (28)</td>
<td>PAS 9 clock hours (17%)</td>
<td>3</td>
<td>15→12</td>
<td>41%</td>
<td>59%</td>
<td>21% IOP spike</td>
</tr>
<tr>
<td>Imaizumi(^{40}) (2006)</td>
<td>PHACO+PCIOL</td>
<td>AACG (18) CACG (8) control (27)</td>
<td>No data</td>
<td>6</td>
<td>49→13</td>
<td>100%</td>
<td>No data</td>
<td></td>
</tr>
</tbody>
</table>

AACG = acute angle-closure glaucoma; CACG = chronic angle closure glaucoma; CD = choroidal detachment; CSI = conventional surgical iridectomy; ECCE = extracapsular cataract extraction; GSL = goniosynechialysis; IOP = intraocular pressure; mos = months; # = number; PAC = primary angle closure; PACG = primary angle-closure glaucoma; PAS = peripheral anterior synechia; PCIOL = posterior chamber intraocular lens; PHACO = phacoemulsification; Postop = postoperative; Preop = preoperative; Rx = glaucoma medication; yrs = years.
(67–72%) of IOP control without medications postoperatively, even though the patients in the different studies were variable in terms of the stage of their disease, chronicity, and amount of PAS present preoperatively. The decision to do clear lens extraction for angle closure is even more controversial considering that patients’ vision often improves when the corneal edema and inflammation settle. In one study, more than half of test subjects recovered good vision (6/12 or better) within a few days of an acute angle closure attack.118

The greatest IOP reduction after lens removal occurred in acute PAC eyes with uncontrolled IOP preoperatively.44,104,129 This is expected as this group of patients would have the greatest amount of pupillary block and appositional angle closure, as well as the highest baseline IOP. IOP reduction occurred to an extent that medications were not required postoperatively, even in eyes with extensive PAS preoperatively.28,121,138 Many eyes were found to have less PAS after surgery,2 suggesting that gonioscopic examination preoperatively may overestimate the extent of PAS, when the angle is narrow. Another possible explanation for finding less PAS postoperatively, when no additional maneuver was done during the lens extraction to open the angle, is the positive pressure of viscoelastic material and fluid as it is introduced into the eye during the surgery.58 Although gonioscopic details of those who failed to have IOP control were not described, we suspect that a residual open angle does not guarantee successful IOP control. Acton et al’s failure to achieve IOP control in some subjects occurred even though only eyes with a maximum of two quadrants of PAS were included in the study.1

The residual open trabecular meshwork can be potentially damaged by high IOP, inflammation associated with an acute attack, or by the adverse effect of appositional closure. Phacoemulsification and PCIOL combined with GSL, performed within 6 months of chronic ACG with an acute attack despite LPI and argon laser peripheral iridoplasty, has been found to control IOP without medications in 90.4% of eyes.121 Another study combining phacoemulsification and PCIOL with limited (inferior) GSL and diode laser peripheral iridoplasty in the treatment of seven eyes with cataract and CACG with total synchial angle closure found a short-term success rate of 100% during a mean follow-up period of 8.9 months.82

The study by Gunning and Greve29 compared the results of lens extraction to trabeculectomy without antimetabolites, except for use of postoperative 5-fluorouracil in 6 of 25 eyes following surgery. Long-term IOP control was found to be better in the trabeculectomy group, but there were also more sight-threatening complications such as hypotony and central field loss, poorer visual outcome, and more surgical reintervention in this group. Sixty percent of the trabeculectomy eyes required cataract extraction after a mean postoperative period of 32 months. When phacoemulsification was compared to conventional surgical iridectomy (CSI) in the study by Jacobi, phacoemulsification was found to have more than doubled the success rate in terms of IOP control and much lower rate of surgical reintervention than the CSI group.44

Imaizumi subdivided his study groups into: 1) APAC at first visit without prior treatment, 2) PACG with earlier laser iridotomy (LI), and 3) a control group. His results show that the post-cataract surgery IOPs of group 1 are significantly lower than the preoperative IOP of group 2 even with glaucoma medications.40 This suggests that lens extraction lowers IOP as well as, if not better, than LPI.

Lens extraction in PAC, whether clear or cataractous, not only deepens the AC and opens the angle but also decreases diurnal IOP variation74 and improves facility of outflow.81 Evaluation of patients by tonometry and with tonography demonstrated immediate spiking of pressures following surgery, and persistence of increased facility measurements at 1 year following surgery in those patients with decreased outflow preoperatively.81

This IOP reduction following cataract surgery is not observed to the same extent in POAG eyes. Some studies have found that IOP control in POAG eyes are largely unaffected by cataract surgery,80,138 whereas others found a reduction in IOP in the short term that is smaller104 and less sustained87,104 than that seen in PACG eyes. The mechanism for IOP reduction in POAG eyes is unclear.

C. COMPLICATIONS OF LENSECTOMY

Intraocular surgery in patients with angle closure is more challenging than regular surgery because of the shallow AC, atomic pupil from the acute attack, and residual corneal edema. The reviewed studies (Table 1) of lensectomy for treatment of angle closure glaucoma report lensectomy, by either ECCE or PHACO, to be potentially safe in the hands of a skilled cataract surgeon. The complication causing the most frequent concern was the immediate postoperative pressure spike, which occurred in 9–60% of eyes. Significant postoperative inflammation was seen in 16–40% of eyes reported in at least four studies.2,121,144,147 The addition of GSL may be associated with increased rates of hyphema, fibrinoid anterior chamber reaction, IOP spikes, and cystoid macular edema postoperatively, secondary to the iris manipulation.121 Kubota
described the successful addition of GSL to PHACO and PCIOL, in the presence of PAS of more than two quadrants, and reported no significant complications in 5 eyes. Endothelial cell damage is common after acute angle closure and elevated IOP. One study shows that endothelial cell counts are not significantly diminished following lens surgery compared to preoperatively.

VIII. Lens Extraction for Secondary Angle-closure Glaucomas

The lens plays a significant role in the development of angle closure in other important eye conditions, which occur less frequently than PACG but in patients of all ages. It is of value to appreciate that the same mechanisms of pupillary block and angle crowding, as seen in patients with PACG, also occur in these other conditions. Angle-closure develops in these conditions when the lens is disproportionately large, when the eye is abnormally small, when the lens is thickened, or when the lens becomes subluxated and blocks the flow of AH through the pupil and/or closes the narrowed angle by crowding. Treatment choices should be determined by the underlying pathology and can include lensectomy when irreversible anatomic abnormalities exist that are unresponsive to medical therapy, laser iridoplasty or iridotomy, or surgical iridectomy.

A. NANOPHTHALMOS

Nanophthalmos is a rare, bilateral, sporadic or familial condition characterized by small eyes, with adult axial lengths of less than 20 mm, shallow anterior chambers with narrow angles and convex irides, small corneal diameters, high hyperopia, thick sclera and choroid, high lens/eye volume ratio, high corneal refractive power, absence of other congenital malformations, and the frequent occurrence of angle closure.

The mechanism of the angle-closure in nanophthalmos relates to the angle-crowding secondary to the normal-sized lens in a small eye and anterior segment. This leads to progressive PAS formation as the iris is forced anteriorly against the trabecular meshwork by the worsening pupillary-block and expansion in the posterior segment as the lens enlarges with age. The mechanism explains the rarity of long term success in IOP control with LPI alone, and the beneficial effect of combined LPI and ALPI in some eyes. The thickened sclera is felt to impede venous drainage from the choroid and is responsible for the uveal effusion that can be corrected by therapeutic or prophylactic sclerostomy procedures. The potential role for lensectomy in the management of nanophthalmos is shadowed by an awareness of vision loss and complications after intraocular surgery in the past. The potential goals of lensectomy are for cataract removal, to deepen the AC, and widen the angle to halt and prevent progressive closure. Successful cataract removal with phacoemulsification and PCIOL implantation in nanophthalmos is now reported. If medical therapy, LPI, ALPI, combined with therapeutic sclerostomy procedures for uveal effusions fail to halt progressive angle closure, lensectomy with PCIOL implantation with prophylactic sclerostomy procedures should be considered.

B. RETINOPATHY OF PREMATURITY

Retinopathy of prematurity (ROP) occurs in premature infants with the risk of occurrence inversely related to the birth weight, reaching 90% for infants less than 750 g. Affected eyes may be small depending on the stage of the active disease, possess steep corneas, shallow anterior chamber depths, narrow angles, proportionately large lenses, and exhibit progressive lenticular myopia. Secondary angle closure associated with anterior displacement of the iris-lens diaphragm is common in advanced ROP with onset in infancy. Closure of the angle is secondary to angle crowding, a belief supported by the clinical failure of iridectomy only to open the angle and improve IOP control. The angle-closure may be of acute onset or occur more slowly and cause CACG.

Progressive growth and forward movement of the lens secondary to contraction of posterior retro-lenticular membranes are also felt to contribute to the development of pupillary-block related angle closure. Posterior diversion of AH (ciliary block glaucoma) and neovascular glaucoma also have been seen in ROP glaucoma patients. In the study by Hartnett and coworkers of 26 untreated stage IV or V ROP eyes in 17 children between 4 and 35 months, 65% had open angles, 35% had 90° or more of closure with associated glaucoma in only 3 (12%) eyes.

The treatment of angle closure associated with ROP depends on the clinical indication and stage of the illness. When glaucoma is acquired later in childhood and in adults, active therapy to treat the pupillary block with iridectomy, LPI, lensectomy, and with glaucoma procedures have been successful. PHACO with PCIOL has been performed in adults with ROP resulting in improved vision and IOP control in glaucoma patients.
C. PHACOMORPHIC GLAUCOMA

In phacomorphic glaucoma, angle-closure and secondary glaucoma is caused by the enlargement of the swollen lens as seen after lens trauma and more frequently in the intumescent age-related cataract. The need and benefit of lens removal for improvement of vision and correction of the pupillary block and crowding mechanisms for angle-closure is obvious.

D. CILIOCHOROIDAL EXPANSION SYNDROMES

Ciliochoroidal expansion places even an eye of normal size at risk for angle-closure glaucoma. In the average human eye the vitreous volume is 5,000 μl, the choroidal volume is 480 μl, and the anterior chamber volume is about 150 μl. Hence, it can be appreciated that minimal sustained expansion of the choroid can decrease the AC volume and ACD significantly and create the prerequisite anterior segment configuration for angle closure. Furthermore, in these syndromes, separation and thickening of the ciliary body has been documented by UBM. The related anterior rotation of the ciliary body and relaxation of the zonules would be expected to contribute further to the development of the angle closure.

Ciliochoroidal expansion syndromes occur secondary to inflammation, choroidal venous congestion, choroidal metastases, trauma, drugs, systemic diseases, from aggressive Panretinal Photocoagulation (PRP), or may be idiopathic. Treatment is directed to the underlying illness and to management of the related angle closure. Lensectomy is rarely indicated because often these conditions can be treated medically or can resolve spontaneously.

E. LENS SUBLUXATION GLAUCOMA

Eyes with lens subluxation or dislocation are at increased risk for secondary glaucoma. When the lenticular zonular attachments weaken or detach, the lens thickens and may move from its normal position. If the weakened zonules are confined to less than half of the lens circumference, the thickening of the lens will occur asymmetrically and create refractive astigmatism and the lens will remain approximately in its normal position. This circumstance is seen in young patients with Marfan syndrome whose eyes are rarely complicated by lens-related glaucoma. In older patients with Marfan disease, or in those conditions where circumferential weakening of the zonules occurs, the lens becomes mobile and moves anteriorly with resultant shallowing of the anterior chamber, increased iris convexity, increased pupillary block, and risk for acute or chronic ACG. The subluxated or dislocated lens may enter the anterior chamber or acutely obstruct the pupil and cause an acute attack associated with a flat anterior chamber.

Treatment of glaucoma caused by lens subluxation is best directed to the lens itself. Surgical iridectomy or LPI can help by decreasing the iris convexity and increasing the angle width, and will prevent the occurrence of acute angle closure but can not be relied on to definitively treat or prevent this secondary ACG. These measures can be considered for prophylaxis for selected young patients. Angle-crowding is an important component causing the angle closure and can be marginally benefited by ALPI. The definitive treatment for lens subluxation related glaucoma is lensectomy. The indication for implantation of anterior chamber IOL or PCIOL is controversial. The addition of successful GSL combined with lensectomy for the treatment of this PAC has been reported, and deserves continued clinical study.

IX. Conclusion

PACG is a leading cause of blindness and is potentially preventable. It is projected that 15.7 million will have ACG in 2010 and 3.9 million will be bilaterally blind from it. The lens plays an essential and pivotal role in the pathogenesis of primary and secondary ACG. Clinical studies suggest that lensectomy and PCIOL implantation for ACG patients may offer successful IOP control, and maintenance of improved vision. Lensectomy eliminates pupillary block, widens the angle to lessen angle crowding thus reducing the iridotrabecular proximity, and is the only treatment alternative that reduces if not corrects the responsible anatomic predisposition to angle closure. Medical management and LPI remain the most common modes of treatment of an acute attack but newer approaches including early lens removal are gaining popularity because of their potential long-term success in IOP control. Uncertainty persists as to when after an acute attack lensectomy is most appropriate or whether or not it should be combined with a filtration procedure. Randomized, controlled studies are ongoing in Hong Kong and Singapore and should help clarify this surgical decision. Although lens extraction for angle closure is biologically plausible, as of this time, there is no evidence from good quality randomized trials or non-randomized studies of the effectiveness of lens extraction for CACG. More longitudinal biomorphometrical studies of PACG eyes treated with and without lensectomy are needed to determine its role in the prevention of
progressive angle closure and to determine which patients will benefit from lens extraction.

X. Method of Literature Search

A search of the PubMed database was conducted for the years 1900–2007, using the following key words: angle closure glaucoma, pupillary block, angle crowding, lensectomy, cataract extraction. Additional references were recovered from bibliographies of the references. Pertinent articles available from the medical files of the authors were also reviewed.

References

27. Friedman DS, Vedula SS. Lens extraction for chronic angle-closure glaucoma (review). Cochrane Database of Systematic Reviews; Issue 3, art. no. CD005555, 2006.


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Reprint address: David S. Walton, MD, 2 Longfellow Place, Suite 201, Boston, MA 02114, USA.

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