ANGLE CLOSURE GLAUCOMA

edited by
Chul Hong and
Tetsuya Yamamoto

Kugler Publications, Amsterdam, The Netherlands

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Associate editors

Ki Ho Park and Yong Yeon Kim

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Preface

It is a great pleasure and honor to announce that members of the Asian Angle-Closure Glaucoma Club (AACGC) have finally launched the publication of the Angle-Closure Glaucoma textbook. We, the editors of the AACGC, would like to convey our deepest appreciation to the members of the AACGC who dedicated their time and efforts to developing the book, and celebrate this landmark publication in angle-closure glaucoma with all of the members of the AACGC.

On October 18, 2001, the AACGC was founded by Chul Hong, Yong Yeon Kim, Ki Ho Park (Korea), Tetsuya Yamamoto (Japan), Prin Rojanapongpun (Thailand), and Kwou-Yeoung Wu (Taiwan), with the aim of playing a leading role in the resolution of prevailing issues related to angle-closure glaucoma in Asian countries. The incidence of angle-closure glaucoma is common throughout Asia, and numerous people have lost their sight as a result. Before the AACGC was established, there had been no sufficient coordination among glaucoma specialists in Asian countries with regard to terminology, classification, and pathophysiology as part of a scholarly effort among glaucoma specialists. On October 18, 2001, a few forward-thinking, young Asian glaucoma specialists took initiatives to set up the AACGC as an Asian-wide scholarly club with the intent of playing a key role in resolving issues related to angle-closure glaucoma. The Organization Committee was soon formed, and it was decided that the first meeting of the AACGC would be held in Seoul, Korea. The Organizing Committee included Advisory Committee members (Dong Ho Youn (Korea), Yoshiaki Kitazawa (Japan), Por-Tying Hung (Taiwan)); Committee members; (President Chul Hong (Korea), Vice-president Tetsuya Yamamoto (Japan), General Secretary Yong Yeon Kim (Korea)); and Scientific Committee members (Ki Ho Park (Korea), Ningli Wang (China), Paul Chew (Singapore), Prin Rojanapongpun (Thailand), Kwou-Yeung Wu (Taiwan), Goji Tomita (Japan), and Tsing-Hong Wang (Taiwan)).

The first official meeting of the AACGC was held in Seoul, Korea on November 7-8, 2002, with about 110 Koreans and 27 foreigners attending the meeting to address the characteristics, terminologies, diagnosis, and treatment of angle-closure glaucoma through 33 presentations and subsequent discussions. Professor Chul Hong chaired the meeting. Research papers presented in this first meeting were published under the title "Angle-Closure Glaucoma Update 2002" in November 2003, serving as the start of the written history of AACGC.

The second meeting was held in Bangkok, Thailand on November 28, 2003 with about thirty attendees, in conjunction with the 19th Asia-Pacific Academy of Ophthalmology. This meeting was chaired by Professor Prin RojanaPongpun.

The third meeting was held as a pre-meeting event in Wuhan, China, on September 7-8, 2004 in conjunction with the Annual Meeting of Chinese Ophthalmological Society, with about thirty attendees to address the latest in research activities. Professor Ningli Wang chaired the meeting.

The fourth meeting was held in Taipei on October 29-30, 2005. This meeting was chaired by Professors Kwou-Yeung Wu and Tsing-Hong Wang. About fifty attendees held two special symposiums on ACG, and 32 topics were presented and discussed.

The fifth of these meetings is to be held in Gifu, Japan on September 15-16, 2007 in conjunction with the Annual Meeting of the Japan Glaucoma Society, and Professor Tetsuya Yamamoto will chair the meeting. A total of 34 topics, including special lectures, will be presented.

Since its founding in October 2001, the AACGC has held four meetings and has actively undertaken activities to promote its missions. The consistent attention and support of the members has been a key in the success that the AACGC has achieved through its annual meetings.

Although the AACGC has grown into an important scholarly club over a short period of time, members still need to forge an alliance through information exchange and cooperation, and must pursue future-oriented collaborative studies, keeping in mind the dreams and visions for the future of the AACGC. As a way of forging cooperation among members, the publication of the ACG textbook was suggested in the board meeting, held in October 2005, and executive board members agreed to pursue the project.

Chul Hong and Tetsuya Yamamoto were appointed as editors, and Ki Ho Park (scientific committee member) and Yong Yeon Kim (general secretary) were appointed as associate editors. The executive board members as well as scientific committee members from each country were appointed as regional editors.

The book was intended to provide information on the basic and essential concepts and mechanisms of angle-closure glaucoma, and the latest developments in diagnosis and treatment. The AACGC was committed to developing a book that is easy to read and understand through sufficient illustrations, figures, and tables, and more importantly, is clinically useful, effective, and necessary. The AACGC intends to make it the 'angle-closure glaucoma bible' for clinicians and students across the world.

Each chapter of the book was assigned to glaucoma specialists specializing in the respective area of research, and all members in Asian countries were encouraged to contribute. The topic of each chapter was fixed, and authors were invited through the regional editors by referring to research findings presented in meetings. The publication of the book was scheduled to occur prior to the Gifu meeting in September 2007. Completed manuscripts were submitted to the office in Seoul in February 2007 and reviewed by editors over a three-day period.

In the AAO meeting held on November 12, 2006, Ki Ho Park (associate editor) met Mr. Peter Bakker, the CEO of Kugler Publications, and discussed issues that needed to be addressed prior to the publication of the book. Despite time constraints, Kugler expedited its process for the AACGC, and published the book as scheduled. The published book will make the forthcoming Gifu meeting a festival environment for all members of the AACGC.

Dear fellow members, we have finally developed a book of ourselves, by ourselves, and for ourselves. After a great deal of hard work and dedication by the members of the AACGC, our dreams of publishing this book have finally become reality. This book will remain a precious asset of the AACGC. It was a time of joy and excitement for us to edit the manuscripts that had been eagerly prepared by authors, and it has been a tremendous honor to write the preface of the book.

We attribute the successful publication of the book to all of the members who have been dedicated to the activities of the AACGC since the foundation of the club, and to those who have written manuscripts for the book. We would like to thank them for their dedication and excellent work. We would also like to thank AACGC regional editors for their service in inviting authors and contacting authors for the submission of manuscripts; and Professor Ki Ho Park and Professor Yong Yeon Kim for their significant contributions to the editing process.

We should also add that the book would not have become available as scheduled without the kind assistance of Mr. Peter Bakker and his son, Mr. Simon Bakker, of Kugler Publications. We offer our sincere thanks for their valuable assistance in the making of final decisions and for publishing the book.

August 8, 2007

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President of the AACGC

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History

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Introduction

Duke-Elder described, in his chapter on glaucoma and hypotony in system of ophthalmology, an episode of acute angle closure attack, a topic that drew attention as early as the 10th century in Arabian writings from At-Tabari, and was considered to be a chronic inflammatory condition.[1] In the early days of glaucoma classification, inflammatory glaucoma, otherwise known as acute congestive glaucoma, was the term used instead of today's acute angle-closure glaucoma. Chronic congestive glaucoma has been used to refer to the end stage of angle-closure glaucoma, while noncongestive glaucoma or simple glaucoma referred to open angle glaucoma and chronic angle-closure glaucoma.[2]

Duke-Elder[1] introduced Otto Barkan as a representative of the great ophthalmologists for the classification of primary glaucoma into open and closed angles.[3] Barkan was of Hungarian descent, studied in Oxford, London, Vienna, and Munich, and then returned to America in 1920.

Duke-Elder[1] also pointed out that glaucoma is not a single disease entity, but different mechanisms of ocular disorders that have common features such as the elevation of ocular pressure with the same end results of optic nerve damage and functional impairment. He emphasized the concept of ocular hypertension and low tension glaucoma, the latter of which is called normal tension glaucoma today.

In *A history of primary angle-closure glaucoma (PACG)*, written by Lowe in 1995,[4] the early stages of observations and theories of angle-closure begin to include chamber angle study, which leads to the early stage of study for the classification of angle-closure glaucoma. These studies also reflect the modern history of ophthalmology, which originated in Europe and subsequently traveled across the world. In addition, Lowe[4] introduced Curran's investigations because his surgical success in iridectomy was an important milestone for PACG in the 20th century at a point where our knowledge of glaucoma treatment was only limited to 'glaucoma', without the idea of closed or open angle. Lowe[4] described in detail many follow-up studies of iridectomy, such as those of Gifford of the USA, Banziger of Switzerland,

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Elschnig and Raeder of Germany, and Rosengren of Sweden. Among their works, there was agreement, disagreement, and suggestions of anterior chamber depth as an indicator for iridectomy. After having performed more than 500 iridectomies, Curran recommended iridectomy only on an eye with the iris bulging forward and a shallow anterior chamber. At this turning point of surgical success, a new era for primary angle-closure glaucoma began.

With the introduction of the gonioscope by Salzmann and the introduction of glaucoma classification by Barkan in 1954,[3] studies of the incidence or prevalence of angle-closure glaucoma began from the concept of open to closed angles. However, during this period, even though with the introduction of gonioscopy, the exact incidence was quite difficult to ascertain, as modern epidemiology was still budding.

Classifications and epidemiology

To be acceptable for investigating the prevalence of glaucoma, studies should be based on the examination of all eligible subjects or a truly representative sample of a population of known composition. Detection of glaucoma should be appropriately sensitive, and should use a standardized method and criteria for structural evaluation of angle and optic nerve, and functional defects of visual field must be detectable and repeatable.

In surveys of glaucoma, especially for angle-closure in Asian subjects, we have to deal with the basic difficulties of gonioscopic examination in addition to primary open angle glaucoma (POAG) survey standards, to formulate and conduct a sound population-based survey. In the past decade, a number of investigators have demonstrated the general characteristics of PACG incidence and prevalence.[6-8]

Through long-term studies to characterize the optic nerve in glaucoma,[9-11] the introduction of glaucoma as an optic neuropathy was widely accepted, along with the advanced methodology of epidemiological study on glaucoma based on disc examination. Therefore, POAG study has come to the forefront in a new model, through investigations such as the early Bedford glaucoma study in 1968[14] and the Framingham eye study in 1988[13] to the Barbados eye study by Leske in 1994[6] and the Baltimore eye study by Tielsch and Sommer.[15]

In contrast to all of those well-established glaucoma surveys, most of them emphasized the POAG aspect, and few of them seriously considered the importance of PACG or set a well-designed approach for a PACG survey, except in the reports such as the Bedford by Bankens[12] or the most recent report of the Enga-Neumarkt study by Bonomi[16] (Table 1).

In 2002, Foster described[20] the idea of the ISGEO (International Society of Geography and Epidemiology of Ophthalmology) scheme for classification of a glaucoma population study based on the definition of glaucoma as optic neuropathy and his experience in conducting a prevalence survey (Table 2). To overcome the difficulties of a practical survey for angle-closure, such as visual-field examination, slight modifications followed.

The history of classification of glaucoma reflects the advances and understanding of our knowledge of glaucoma. In 1996, in *The glaucomas, clinical science*, Shields proposed and discussed the traditional classification of 'primary' as artificial, and with the recent expansion of knowledge, such classification of 'primary' is arbi-

Table 1. Criteria for PACG in major glaucoma surveys

Authors	Criteria
Bedford glaucoma survey[12] Bankens, London 1968	History of halo, gonioscope for capable angle-closure, & iris root closure IOP above 21 mmHg
Framingham eye study[13] Kini, Boston 1978	Gonioscope, for narrow or closed angle, but no results of PACG mentioned
Japan national survey[17] Shiose, Japan 1991	Slit lamp (Van Herick)
Beaver Dam eye study[18] Klein, Wisconsin 1992	History only
Baltimore glaucoma screening[15] Tielsch, 1991	Routine POAG study only
Rotterdam study[19] Dielemans, Netherlands 1994	Slit lamp, disc by mydriatics
Barbados eye study[14] Leske, 1989, 1994	POAG routine examination
The Enga-Neumarkt study[16] Bonomi 1988	• Gonioscope grading and closed or PAS • Disc & visual field • Objective evidence slit lamp
The Tajimi Report 2[7] Yamamoto 2005	ISGE scheme

Table 2. Summary of the International Society of Geography and Epidemiology of Ophthalmology (ISGEO) Scheme for classification of angle-closure in prevalence surveys

1. The word glaucoma should be used to indicate glaucomatous optic neuropathy
   The symptomatic classification such as acute or chronic angle-closure should associate with glaucomatous disc damage.
2. Primary angle-closure suspect (PACS)
   (1) Occludable angle without evidence of PAS
   (2) Normal IOP, disc and field
3. Primary angle-closure (PAC)
   (1) Occludable angle with either elevated IOP and/or PAS of non-secondary
   (2) Disc and visual field are normal
4. Primary angle-closure glaucoma (PACG)
   (1) Primary angle-closure
   (2) Glaucomatous optic disc damage and field defect

trary.[21] Therefore, he classified glaucoma based on five stages of processes. The five-stage classification can be summarized as follows: Evidence of an event may lead to optic nerve damage as stage 1; structural changes such as tissue changes that may lead to functional changes as stage 2; physiological changes may lead to functional changes as stage 3; optic nerve damage such as ganglion cells or axons as stage 4; and eventual progression from the above stage to visual loss as stage 5. Allingham emphasized the stage classification again after ten years.[22] We are currently able to analyze and predict some of the primary open angle glaucomas for their onset, clinical course, or even the response to medication by the study of genetic loci.[23] Different loci represent specific phenotypic characteristics. Such genetic progress may challenge the use of 'primary' classifications in the future.

POAG-based studies can also be used in the formulation of a genetic study model for PACG. As a matter of fact, the five stages of classification clarified some important clinical observations such as the intraocular pressure-independent pathway of normal tension POAG, or, in the acute form of PACG, optic neuropathy or visual field defects that cannot be detected, although initial symptoms and signs of acute evidence or events can lead to visual field loss. Such classification may be used to determine the advantages of these characteristics in the future. As for angle-closure glaucoma, such stage classifications may be practical from a clinical point of view.

The method of classification in *The Glaucoma* by Ritch and Lowe in 1996,[24] which was based on mechanisms of outflow obstruction, is easy to understand and probably provides another method for PACG classification. This classification also shows the modern advances in the understanding of PACG on pulling or pushing mechanisms, including the pupillary block and plateau iris, and emphasized the iris-lens diaphragm factor.

Study from open angle to angle-closure

With the introduction of new technologies, the epidemiological study of POAG has been well-established in the past few decades, while the PACG study lags behind in this regard, beginning only during the last decade of the 20th century.

As early as 1976, Alsbirk[25] called attention to the importance of early detection of PACG due to the huge number of global sufferers. In 1996, Quigley[26] estimated that PACG subjects would account for half of all glaucomas worldwide, and would number greater than thirty-three million in 2000. Therefore, the epidemiological study of PACG began to draw attention in the last decade, and the number of PACG surveys in Asia has increased considerably. A recent report by Quigley on glaucoma also ranked it as the second leading cause of blindness in the world.[27]

The majority of PACG subjects have a characteristic structure with a smaller-than-average eye. It was well-demonstrated in numerous biometric studies, and was established by Lowe in the 1970s,[28] namely: (1) shallow anterior chamber depth; (2) a thicker and more anteriorly-positioned lens; and (3) shorter axial length. Those data are also important for the current surveys of PACG using A-scan ultrasonography.

Another characteristic difference is the chamber angle. The dynamic change of width showed by gonioscopic examination is well-accepted, but the most important golden concept was pointed out by Kronfeld in 1948.[29] He emphasized that a parallelism can be observed between partial and total closure of entrance and elevations of intraocular pressure (IOP). Since then, many investigators have established gonioscopic findings using various direct or indirect gonioscope techniques, and through recent advances of ultrasounbiomicroscopy (UBM) or optical coherence tomography (OCT). In the future, the OCT dynamic gonioscope could add to the procedure for more accurate diagnosis, and could confirm the accuracy of PACG.

However, the pitfalls in the PACG study still require considerable effort, including: (1) Acceptable and practical definitions for PACG; (2) The symptomless picture of the chronic form and plateau iris group. An understanding of the subtypes of PACG is essential; (3) Gonioscopic techniques and standardization.

Risk factors of racial differences and Asian PACG

Among the demographic risk factors for angle-closure glaucoma, such as age and sex, race is probably the most prominent risk factor from the viewpoint of epidemiology. In general, PACG is more common in Asians, excluding the Japanese, than in Caucasians or Africans. Prevalence of PACG among Eskimos of Northwest Alaska[30] and Greenland Eskimos[31] demonstrated a high rate of 2.65%, from 0.9% in males and 2.1% in females, up to 2% in males and 10% in females. In 1996, Foster estimated the prevalence of PACG to be 9.7% in a study of Mongolian subjects.[6]

In 2001, Foster also reported a population survey on East Greenland Inuits; an applanation tonometer was utilized in this investigation.[32] A lower IOP was confirmed among Inuit and Mongolians. Two subjects had definite PACG (2.5%) among 79 subjects. Sino-Mongoloids are considered to be racially related to Eskimos. Thus, in 2001, Foster[33] estimated that 9.1 million people in Chinese have significant angle-closure with raised IOP and peripheral anterior synechia. Foster also conducted a population based-study in Guangzhou,[34] in the southern part of China, according to the classification scheme of ISGEO in 2006. The result indicated that POAG was 2.1% and PACG was 1.5%, respectively, showing that POAG is more common than PACG. Another study in rural and urban parts of Beijing[35] also demonstrated lower rates of PACG than were previously expected. In subjects above 40 years of age, the average rate of PACG was 1.2%, with a significant difference observed between rural and urban residents.

Japan has been the location of the most long-term PACG prevalence studies. The earlier report by Suda[36] showed that "the overall rate of glaucoma was 2.28% in subjects above 30" in 1960. Suda[37] also reported that acute glaucoma accounted for 54% of all glaucoma in 1962. However, a subsequent study on PACG by Shiose[17] indicated a prevalence of 0.34% in contrast to the POAG rates of 0.58%, while normal tension glaucoma showed a significant rate of 2.04% in 1991. The most recent report by Yamamoto,[26] conducted in 2005, indicated a PACG prevalence rate of 0.6% in the Tajimi study, which utilized the ISGEO scheme.

Asian studies of glaucoma prevalence have increased significantly in the past few years. These include a Japanese national survey conducted by Shiose in 1991[17], a rural Taiwanese study by Congdon in 1996,[38] a Mongolian study by Foster in 1996,[6] a Chinese-Singaporean survey by Foster in 2000,[8] urban Indian studies by Jacob in 1998 and[39] Dandona in 2000,[40] a Chinese study by Wang in 2002,[41] a Beijing study by Zhao in 2002,[42] a long-term Indian study by Thomas in 2003,[43] a Bangkok study by Bourne in 2003,[44] a Bangladesh survey by Rahmam in 2004,[45] and another Beijing study by Xu in 2004.[35] These surveys had different standards, designs, plans, and included different ethnic groups, and the end results of those studies could be expected to be quite variable.[46]

Nevertheless, most of the surveys indicated that PACG was more frequent in older females than in males, with a ratio of approximately 3:2, and it is more frequently seen older subjects, but the onset is seen at a rather young age compared with POAG. Chronic PACG is usually asymptomatic, and constitutes the majority of PACG subjects.

Interestingly, in the Egna-Neumarkt glaucoma study in Italy, Bonomi[6] reported that an occludable chamber angle was seen more frequently than that reported from previous studies in the Caucasian population, which suggested that the prevalence of PACG is not as low as usually thought.

The genetic study indicated that advanced molecular biology might also provide another tool for classification or epidemiological studies in the future, while family history should also be emphasized for reference in diagnostic study. However, as pointed out by Lowe,[47] PACG is related to a multifactorial hereditary disorder that it seems important, yet complicated. Wang focused a study on the ocular coat of the cornea and the sclera, which are responsible for ocular growth and overall size. An initial study of extracellular matrix-related MMP9 by Wang showed significant results (presented in the 4th Meeting of the Asian Angle-closure Glaucoma Club, Oct. 29-30, 2005, Taipei, Taiwan), which can be applied for the study of PACG in the future.

Evolution of eye-changing prevalence of PACG and the ratio between PACG and POAG

Serial epidemiological studies can be used to understand the general characteristics and natural course of a specific disease. It can also reflect the environmental factors involved and genetic factors affecting the disorder, such as in myopia. In serial PACG epidemiological studies, some of the facts uncovered by the studies are particularly important and interesting, namely: (1) The early study of PACG among Caucasians[5] as compared with the recent survey;[14,15] (2) The 1962 Japanese study by Suda[37] and the 2004 Tajimi study;[7] (3) The Chinese descendents in Singapore and Guangzhou Chinese surveys, both by Foster.[8,34]

In 1954, the glaucoma survey by Barkan[2] indicated that the ratio of simple glaucoma POAG to angle-closure glaucoma was 1.22:1. In another word, the rate of POAG is about the same as that of PACG, or is higher than that of PACG in North America at that time. Today, surveys of glaucoma in North America demonstrate that more than 80% of glaucoma subjects show POAG, while PACG is seen in less than 5% of all glaucoma subjects in the survey.

In 1962, Suda[25] reported the incidence of adult glaucoma in 4808 outpatients at 49 eye clinics from university and Red Cross hospitals in Japan. The report disclosed that the incidence of simple glaucoma was 54.4%, while at the same time, that of acute glaucoma was 45.6%. In 1991, the rate of POAG in the survey by Shiose [8] was 2.62% including normal tension glaucoma as POAG, and only 0.34% for PACG.

In recent Japanese national surveys by Iwase in 2004[48] and Yamamoto in 2005,[7] respectively, the prevalence of PACG was 0.6%, and that of POAG, including normal tension glaucoma, was 3.9% among 3870 eligible subjects.

The studies of Guangzhou Chinese[34] and Chinese Singaporeans,[8] both conducted by the Foster group, were interesting in that the rates of both studies indicated that POAG was more common than PACG in Southern Chinese urban areas. Considering that PACG was found to be more common among Chinese in the past, this is an important implication of changes in prevalence.

However, the glaucoma prevalence rates in surveys of Caucasians were quite variable, and the methodologies for early stages of surveys were not well-standardized to a degree at which 'eye evolution' could be determined. This topic requires further investigation.

Conclusions

1. Glaucoma has become a major cause of blindness worldwide, overtaking ocular infections during the last decade of the past century.
2. Glaucoma shows prominent racial differences. POAG is more frequent in Caucasians, while most subjects of Asian, Eskimo, and Sino-Mongolian descent have higher rates of PACG.
3. Further clarification of the characteristics of PACG and studies of its natural course are necessary.
4. Some epidemiological studies in the last century suggested a changing prevalence of PACG and a change in the ratio between PACG and POAG.
5. Genetic study and gonioscopic images will continue to play important roles in the coming years.

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Epidemiology of angle closure glaucoma

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Introduction

In this chapter we will discuss the prevalence and demographic/biometric features of primary angle closure glaucoma (PACG) and its associated conditions. The definition of PACG has changed somewhat, recently: PACG is presently defined as cases with primary angle closure associated with glaucomatous optic neuropathy (GON), and differentiated from primary angle closure without GON. The description of PACG in this chapter, however, follows that of the original article.

A. Prevalence of PACG among different ethnic groups

The prevalence of angle closure glaucoma with relative pupillary block differs among different ethnic groups. Table 1 shows the prevalence of occludable angle and PACG in several ethnic groups.[1-13] Inuit have been reported to have the highest prevalence of occludable angles. Asians tend to have a higher prevalence of occludable angles and PACG as compared with Caucasians and Africans. There are also differences in prevalence among Asians, with the highest prevalence of PACG encountered in Mongolians.

1. East Asia

A large population-based prevalence survey of glaucoma among residents aged 40 years or older was performed in Tajimi City, Japan in 2000-2001. This survey revealed that the prevalence of PACG was 0.6% in the Japanese population.[6] An epidemiologic survey of glaucoma was performed in Beijing, China, and revealed the prevalence of angle closure glaucoma to be 0.41%.[14] Another epidemiological survey conducted recently in Guangzhou, China found a prevalence of primary angle closure glaucoma to be 1.5%.[4] Foster[5] *et al.* examined 942 individuals aged 40 years and older in Mongolia to estimate the prevalence of glaucoma, and found the prevalence of PACG to be 1.4%.

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Table 1. Prevalence of occludable angle and PACG

Ethnicity	Prevalence (%)	Type	Country
Asian	2.21[1)]	occludable angle	India
	1.08[1)]	PACG	India
	0.5[2)]	PACG	India
	1.0[3)]	PACG	China
	1.5[4)]	PACG	China
	6.4[5)]	occludable angle	Mongolia
	1.4[5)]	PACG	Mongolia
	0.6[6)]	PACG	Japan
Caucasian	0.8[7)]	occludable angle	USA
	0.1[8)]	PACG	Australia
	0.6[9)]	PACG	Italy
	0.1[10)]	PACG	Hispanic
African	0.6	occludable angle	USA
	0.1	PACG	South Africa
	0.59	PACG	Tanzania
Inuit	17.0	occludable angle	USA (Alaska)

2. South & Southeast Asia

Nguyen *et al*[15] retrospectively reviewed the angle status in 482 Vietnamese subjects to assess the prevalence of occludable angles in a Vietnamese population. Angles were graded according to the Shaffer classification, and 47.8% of participants aged 55 years or older had grade 0 to 2 angles. Vietnamese patients had a greater risk of angle closure glaucoma than white patients. Foster *et al*[3] examined 1,232 Chinese Singaporeans, aged 40 to 79 years, to estimate the prevalence of glaucoma: the prevalence of PACG was found to be 1.13%.

Two papers have been published on the prevalence of glaucoma in India: subjects in a rural population and those in an urban population. In the urban population, the prevalence of PACG was 1.08% in participants 40 years of age or older.[1] In the rural population, a total of 5,150 subjects aged 40 years and older were examined, and the prevalence of PACG was 0.5%.[2]

3. Caucasians

Among Caucasian populations in the United States and Europe, the majority of glaucoma, *i.e*., 75-90% of glaucoma, is primary open-angle glaucoma. The prevalence of PACG is very low within this population: 0.09% of subjects over age 40 in Wales,[16] 0.17% over age 40 in Bedford (volunteer population),[9] and 0.1% over age 55 in Dalby, Sweden.[17] Wensor *et al*.[8] performed a population-based study to determine the prevalence of glaucoma in Melbourne, Australia. The overall prevalence of definite primary open-angle glaucoma cases in persons older than 40 years of age was 1.7%, whereas the prevalence of PACG in Melbourne was very low, accounting for only 0.1% of the population. A cross-sectional epidemiological study

was performed in a rural, northern Italian community to assess the prevalence of various types of glaucoma. PACG was defined as follows: at least two of the following criteria observed at the second or third examination: IOP ≥ 22 mmHg; glaucomatous optic disc abnormalities; glaucomatous visual field abnormalities; chamber angle partly or totally closed, or goniosynechiae extending to at least one-third of the circumference, or with a very clear, narrow angle prone to occlusion; objective evidence (*e.g.*, atrophy of the iris, irregular pupil, nonreactive mydriasis) and/or anamnestic evidence of episodes of angle closure; and no signs of secondary angle closure (*e.g.*, uveitis, intumescent or dislocated lens, microspherophakia). These investigators examined 1,882 men and 2,415 women from a total of 5,816 subjects, with an overall participation of 73.9%. Twenty-six people were diagnosed with PACG, and the prevalence was 0.6%.[9]

4. Inuit

It is well known that the prevalence of PACG in the Inuit population is very high. Many studies have reported on the prevalence of PACG in Inuits. A population-based general ophthalmic prevalence survey among the Inuit of northwestern Alaska was performed to determine the prevalence of glaucoma. Among 1,686 Inuit subjects, ten cases of angle closure glaucoma and one case of open-angle glaucoma were found. The prevalence of narrow angle glaucoma was 2.65% in Inuits older than 40 years of age. Women were affected almost four times as often as men, and the sex difference persisted across all age groups. They also found that the prevalence of occludable angles in Inuits older than 50 years was 17%.[13] Van Rens *et al.*[18] examined the prevalence of PACG among 1,673 Inuit subjects in Alaska. The prevalences in men and women above the age of 40 years were 2.1% and 5.5%, respectively. Angle closure glaucoma was found in 11.8% of women above the age of 60 years. A shallow anterior chamber was found twice as frequently in women as in men. In a population of 541 Greenland Inuits, Alsbirk[15] performed a survey to detect PACG in an early stage. In persons over 40 years of age, the prevalences of PACG in men and women were 2% and 10%, respectively. Among Inuits, West Greenlanders with a predominantly Inuit physiognomy showed smaller anterior chambers than unmixed East Greenland Inuits and Eskimo-Caucasian hybrids.[20] Alsbirk[21] also performed a survey to evaluate the stability of the anterior chamber depth distribution and its inherent morbidity risk in a different environment, immigrant Greenland Eskimo women in Copenhagen, aged 40 years or older, who had lived in Denmark for at least 25 years. The prevalence of PACG in this population was 3.0%. The anterior chamber depth level of immigrants was significantly higher than that of their background population. One hypothesis to explain this phenomenon is that the small anterior chamber observed in Inuits is a result of genetic adaptation to an arctic environment.[22]

5. Africans

Buhrmann *et al.*[23] made a survey to estimate the prevalence of glaucoma among Africans aged 40 years or older and found that the prevalence of PACG was 0.59%. The prevalence of PACG in a rural district in South Africa was 0.50%.[11] Clemmsen *et al.*[24] compared a group of Africans without any ocular diseases, a group of Africans with angle closure glaucoma, and a normal Danish population in terms of anterior

chamber depth, lens thickness, vitreous body length, and axial length of the globe. It was found that the normal African population showed significantly thinner lenses than those of the African population with angle closure glaucoma and the normal Danish population. The latter two groups showed similar lens thicknesses.

B. Factors that influence the development of PACG

1. Refraction

Primary angle closure glaucoma typically occurs in hyperopic eyes. The volume and depth of the anterior chamber are smaller in hyperopic eyes than in normal eyes.[25] Lee *et al.*[26] perfomed a photogrammetrical study in 273 patients with clinical diagnosis of narrow angles and acute, subacute, or chronic angle closure glaucoma. They found that the anterior chamber depths, volumes, and diameters of the eyes of all of these patients were significantly smaller than age-, sex-, and refractive error-matched normal controls. Furthermore, in cases of acute angle closure glaucoma, the refractive error in the eye with the attack very often is lower than that in the fellow eye, reflecting cataract progression or a slight, forward shift in the position of the lens.[27] In addition, the corneal curvature correlates with the incidence of angle closure glaucoma, and the average radius of the corneal curvature was significantly shorter than that of age-matched controls.[28]

Marchini *et al.*[29] performed ultrasound biomicroscopy (UBM) and standardized A-scan ultrasonography to determine the biometric dimensions of ocular structures in primary angle closure glaucoma. They found that the patients with PACG have a shorter axial length, a shallower anterior chamber depth, a thicker lens, and a more anteriorly located lens compared to normal subjects.

Barkana *et al.*[30] studied 17,938 patients from their glaucoma database to evaluate the clinical characteristics of all patients with angle closure and high myopia, and they found 20 appropriate patients. One patient showed a miotic-induced angle closure, and others showed secondary conditions of various etiologies: keratoconus, retinopathy of prematurity, plateau iris configuration, and plateau iris syndrome. The biometric parameters in patients with angle closure and normal controls have been published in a couple of papers.[9,31,32] The typical eye with relative pupillary block has a hyperopic refractive error, shorter axial length, thicker lens and a shallower anterior chamber than the average eye (Table 2).

2. Sex

The prevalence of acute angle closure glaucoma in women is three to four times higher than that in men of races. There might be some reasons for this difference. One possible reason stems from the fact that the anterior chamber of the female eye is significantly narrower than that of men in normal subjects.[33] The Tajimi study shows the age-specific prevalence of primary angle closure glaucoma in Japan.[6] Overall prevalences of PACG and suspected PACG were 0.6% and 0.2%, respectively. The prevalence significantly increased with age but was not significantly different between women and men. A significant difference was observed in the prevalence of primary angle closure (PAC), including PACG and suspected PACG between women and men. Okabe *et al.*[34] studied 1,169 eyes of participants in a glaucoma

Table 2. Published biometric parameters in patients with angle closure and, when available, comparison with normal controls. (From: reference 30)

	Axial Length (mm)		Anterior Chamber Depth (mm)		Lens Thickness (mm)	
	ACG	Normal	ACG	Normal	ACG	Normal
PACG[9]	22.01±1.06	23.10±0.82	1.80±0.25	2.80±0.36	5.09±0.63	4.50±0.34
Acute/intermittent ACG[31]	23.10±0.82	22.38±1.23	2.41±0.25	3.33±0.31	5.10±0.33	4.60±0.53
Chronic ACG[31]	22.27±0.94	23.38±1.23	2.77±0.31	3.33±0.31	4.92±0.27	4.60±0.53
Acute ACG[32]	21.856	23.188	1.687	2.585	5.224	4.763

Table 3. Width of angle, biometrical parameters and sexual distinction. (From: reference 35)

	Men	Women	P-value
Width of angle (Shaffer grade)	3.10±0.31	3.00±0.36	0.01
Anterior chamber depth (mm)	2.78±0.31	2.60±0.33	0.01
Lens thickness (mm)	4.49±0.38	4.45±0.40	NS
Axial length (mm)	23.19±1.10	22.55±0.89	0.01
Diameter of cornea (mm)	11.31±0.40	11.16±0.38	0.01
Corneal refractive power (D)	44.11±1.58	44.61±1.42	0.01
Refractive error (D)	-0.25±1.85	0.08±1.64	0.01
Lens thickness/axial length	0.194±0.019	0.198±0.021	0.01
Relative lens position	0.238±0.01	0.236±0.012	0.05

(Mean ± SD)

survey to clarify the relationship among angle width, age, and sex. Angle width was found to be reduced with age in both women and men. In all age groups, the angle width of women was significantly narrower than that of men. Investigators also reported on the correlation of sex and some biometric parameters of the eyes (Table 3). Significant differences were observed between women and men, except in the thickness of the lens.[35] In an urban population in southern India, Dandona *et al.*[1] revealed that the odds of manifest PACG or occludable angles without PACG were higher in females, though this difference was not statistically significant.

3. Age

The depth and volume of the anterior chamber decrease with age. Accordingly, the prevalence of angle closure glaucoma increases with age. In normal eyes, the angle narrows with age. In contrast, the angle was not found to narrow with age in subjects showing angle closure glaucoma. The depth and volume of the anterior chamber significantly decreased with age; the depth of the anterior chamber decreased by 0.21mm per 10 years and the volume decreased by 19 μl in 10 years. In angle closure glaucoma, no significant correlation was found among the depth and volume of the anterior chamber and age.[28] Sakai *et al.*[28] proposed a hypothesis

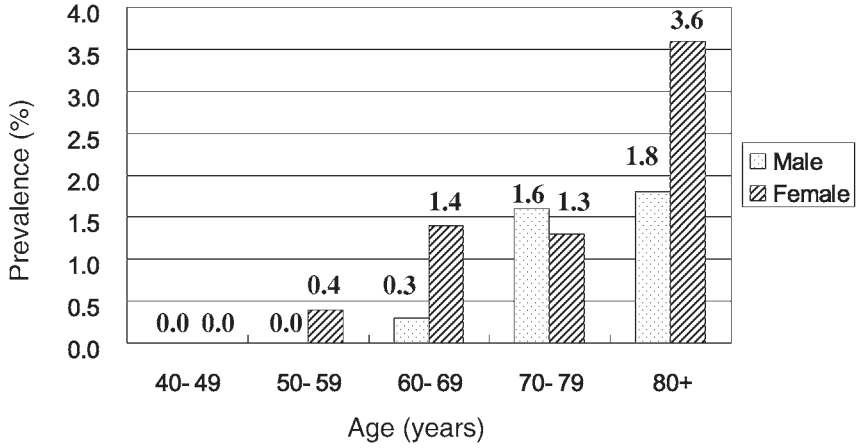

Fig. 1. Prevalence of primary angle closure glaucoma in Japan (Tajimi Study). (From: reference 6)

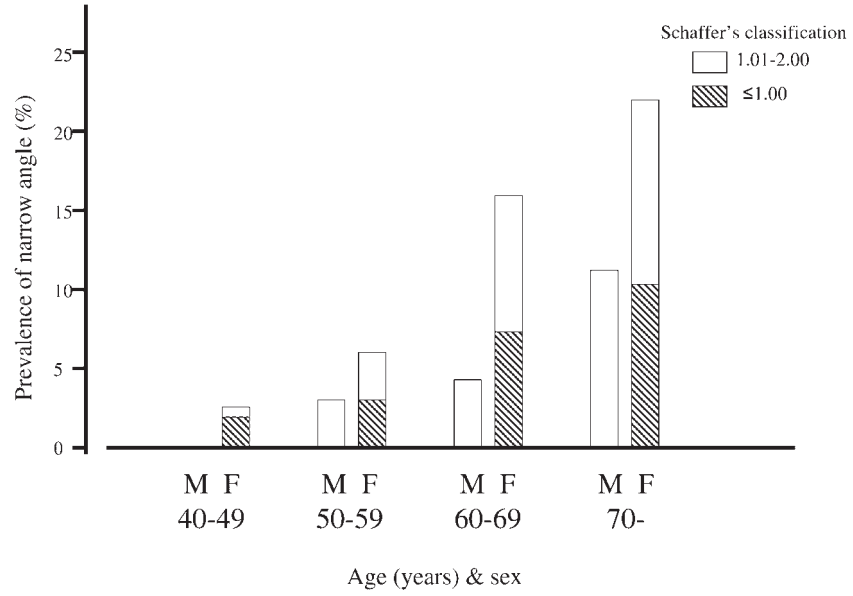

Fig 2. Age-specific prevalence of narrow angle. (From: reference 34)

that angle closure occurs in the presence of an anterior chamber of a certain depth regardless of age. In the Tajimi Study, the prevalence of PACG was found to increase significantly with age, as shown in Figure 1.[6] In another Japanese study, the prevalence of narrow angle (Shaffer grade < 2) increased with age[34] (Fig. 2). The prevalence of pupillary block angle closure glaucoma also increased with age, and

reached a maximum at 55 to 70 years of age. The incidence of acute angle closure glaucoma increased to its maximum at between 55 and 60 years old.[27] In contrast, angle closure has been reported less commonly in younger populations.[36,37] Ritch *et al*.[38] evaluated findings for patients aged 40 or younger with angle closure in their database, and found 67 patients (49 females, 18 males). The majority of these cases were caused by plateau iris syndrome. Hence, when we encounter a young angle closure patient, the contribution of a plateau iris mechanism must be ruled out.

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Anatomy and biometry

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Introduction

Ocular biometry is the study analyzing the measurements of the living eyes.

More than one century ago, Smith revealed that human lens increased in size throughout life,[1] and glaucomatous eyes have smaller corneas than normal.[2] He found a large lens and crowded anterior segment in 'congestive glaucoma', and initiated the concept of ocular biometry. In 1923, Raeder proposed a new glaucoma classification according to the anterior chamber depth.[3] Some years later, Curran recognized peripheral iridotomy solved the problems only in eyes with shallow anterior chambers, but not in eyes with normal depth.[4] However, it was not until the 1970s before Delmarcelle[3] and Lowe started to evaluate the ocular biometry quantitatively in eyes with angle-closure glaucoma.

Compared to normal eyes, primary angle closure eyes show the following biometric characteristics: (a) a smaller corneal diameter[3, 6] and smaller radius of the corneal curvature[3,5-8] (Table 1); (b) a shallower anterior chamber depth[3,5-7,9-15] (Table 2) and a smaller anterior chamber volume;[11,12] (c) a thicker lens[3,5-7,9,10,13-15] with a steeper curvature of the anterior lens surface;[16] (d) a more anterior lens position;[9,10,14-18] (e) a greater lens thickness/axial length factor;[13,14,17-19] and (f) a shorter axial length.[5-7,9,10,13-15,17,19] Recently, choroidal expansion with anterior movement of the lens was discussed as a possible mechanism for acute primary angle closure.[20,21]

Talking about the ocular biometry, we have to remember that many biometric studies of eyes with angle closure were performed thirty years ago. They remain valid, but a few points should be raised.[22] First, a sharp rise in the frequency of performance of iridotomy took place in the early 1980s, and made acute angle closure less common than it was before. Second, cataract is operated on much earlier, and decreases the proportion of patients with thick lenses in the population. Third, earlier investigations were performed on whites, in whom angle closure is regarded less common. Last but not least is the evolving classification of angle closure glaucoma.[23] It is likely that the classification of angle closure will be further revised in

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the coming few years, and put less emphasis on symptomatology.

Table 1. Corneal parameters of eyes with primary angle closure glaucoma (ACG) compared with normal.

Parameters	Normal	ACG	Authors
Corneal diameter	11.6	11.15 ± 0.54	Smith,
	11.63 ± 0.40		Grieten and Weekers
	11.76 ± 0.42	10.85 ± 0.37	Delmarcelle *et al.*
	11.05	10.72	Tomlinson and Leighton
Corneal radius anterior	7.78	7.53 ± 0.02	Tornquist
	7.84 ± 0.29	7.64 ± 0.29	Grieten and Weekers
	7.67 ± 0.24	7.61 ± 0.29	Lowe
	7.92 ± 0.29	7.64 ± 0.25	Delmarcelle *et al.*
	7.65	6.55	Tomlinson and Leighton
Posterior	6.46 ± 0.26	6.23 ± 0.34	Lowe and Clark

Expressed as (mean ± standard deviation) in mm.
(This table is a modification from reference 3.)

Table 2. Axial length (AL), anterior chamber depth (ACD) with or without central corneal thickness (CCT), and lens thickness (LT) of eyes with primary angle closure glaucoma (ACG), and primary angle closure (PAC) suspect compared with normal (in mm)

Parameters	Normal	Acute ACG	Chronic ACG	PAC suspect	References
ACD + CCT	3.15 ± 0.01		2.38 ± 0.09		Rosengren [3]
ACD + CCT	3.03 ± 0.37		2.38 ± 0.22		Grieten [3]
AL	23.26 ± 0.76	22.25 ± 0.77			Lin [17]
ACD + CCT	3.11 ± 0.25	2.28 ± 0.23			
LT	4.48 ± 0.3	4.94 ± 0.28			
AL	23.38 ± 1.23	22.31 ± 0.83	22.27 ± 0.94		Marchini [32]
ACD + CCT	3.33 ± 0.31	2.41 ± 0.25	2.77 ± 0.31		
LT	4.60 ± 0.53	5.10 ± 0.33	4.92 ± 0.27		
AL	22.5 ± 0.8			22.2 ± 0.7	Thomas [61]
ACD + CCT	3.2 ± 0.4			2.7 ± 0.3	
LT	4.2 ± 0.5			4.7 ± 0.5	
AL	22.76 ± 0.78		21.92 ± 0.70	22.07 ± 0.69	George [62]
ACD + CCT	3.00 ± 0.30		2.63 ± 0.39	2.53 ± 0.26	
LT	4.31 ± 0.31		4.23 ± 0.69	4.40 ± 0.53	
AL	23.10 ± 0.82		22.01 ± 1.06		Lowe [3]
ACD	2.80 ± 0.36		1.80 ± 0.25		
LT	4.50 ± 0.34		5.09 ± 0.34		
ACD	2.91± 0.40		1.72 ± 0.22		Delmarcelle [3]
ACD (UBM)	2.86 ± 0.32	1.89 ± 0.22	2.30 ± 0.34		Marchini [32]

Methods of measurement

Central anterior chamber depth may be measured with the Haag-Streit slit lamp biomicroscope and A-scan ultrasonography.[22,24-26] Newer technologies, such as optical coherent tomography (OCT), ultrasound biomicroscopy (UBM), and Scheimpflug photography show great promise not only in the measurement of anterior chamber depth, but also other anterior chamber angle parameters and the volume after three-dimensional reconstruction. Another instrument is scanning peripheral anterior chamber depth analyzer. It is a slit lamp type system to be used for the evaluation of peripheral anterior chamber depth non-invasively.[27]

Optical pachymetry

The Haag-Streit pachymeter (Haag-Streit, Bern, Switzerland) is the most commonly used instrument for optical pachymetry. There are two measuring devices: one measures widths up to 1.2 mm and is used for measuring corneal thickness, and the other one measures widths up to 6.0 mm and is used for anterior chamber depth (ACD) measurements with or without inclusion of corneal thickness. Haag-Streit recommends that for the most accurate ACD results, the corneal thickness, as determined with the first attachment, should be deducted from a measurement from corneal epithelium to the anterior lens surface, made with the second attachment. However, many ophthalmologists only use the measurement made from the corneal endothelium to the anterior lens surface by using only the second attachment. This is certainly more rapid in that it uses only one pachymeter device. Bourne found these two methods will give different results and recommended that one should standardize ACD measurements when using the Haag-Streit optical pachymeter.[26]

Optical coherence tomography

Although gonioscopy has been the clinical standard for characterizing the anterior chamber (AC) angle, it is a subjective procedure and requires the expertise of a specialized physician. Optical coherence tomography (OCT) is a light-based imaging modality that has several advantages over the other techniques used for objective assessment of the AC angle. It has a high image resolution, and is a totally noncontact procedure with minimal expertise. The noncontact nature of OCT not only enhances patient comfort and safety but also makes it especially suitable for ocular biometry and AC angle assessment since there is no mechanical distortion of the tissue being imaged.[28,29]

Unlike OCT using 0.8-μm as the light source, which is best suited for retinal imaging, 1.3-μm OCT provides excellent visualization of both the cornea and the AC angle. This is due to the lower scattering loss at 1.3 μm.[28-30] The 1.3-μm wavelength of light is also strongly absorbed by water in the ocular media and, therefore, only 10% of the light incident on the cornea reaches the retina.[28,29,31] This improves retinal protection and allows for the use of higher-power illumination that enables high-speed imaging. However, the visualization of the ciliary body with OCT is not as complete as with UBM, and the angle recess may not be well defined in some eyes.

Compared to UBM, OCT tended to give larger measurements. There are several explanations for this difference, including patient position during imaging, and the effect of the UBM eyecup.[28,29]

Ultrasound biomicroscopy

High-frequency ultrasound biomicroscopy (UBM) is an ultrasonographic diagnostic procedure and provides high-resolution images (50-μm lateral resolution in the commercially available system) of the AC angle region. It has a depth of penetration of 5 mm in tissue, and is able to image through opaque media. The UBM allows the visualization of retroirideal region and ciliary body, which was impossible *in vivo* before. It offers a better understanding of the mechanisms of angle closure and the measurement of new parameters capable of defining the characteristics of normal and glaucomatous eyes.

By using UBM and A-scan ultrasonography, Marchini[32] studied ocular biometry in angle closure glaucoma (ACG) and normal subjects. In patients with ACG, the anterior segment is more crowded because of the presence of a thicker, more anteriorly located lens. The UBM confirms this crowding of the anterior segment, showing the forward rotation of the ciliary processes. A gradual progressive shift in anatomic characteristics is discernible on passing from normal to chronic ACG and then to acute/intermittent ACG eyes.

The central depth of the anterior chamber measured without the corneal thickness on the UBM images of the acute/ intermittent ACG, chronic ACG, and normal eyes showed the same pattern observed at conventional biometric A-scan (Table 2). The differences between the mean A-scan and mean UBM measurements in each of the three groups ranged from 0.47 to 0.52 mm, a value that is very close to that of the normal thickness of the central cornea. This result testifies to the accuracy of the conventional A-scan measurements.[32]

However, the UBM requires an immersion bath and a highly skilled operator to obtain high-quality images. It is more time-consuming, and has the risk of infection or corneal abrasion due to the contact nature of the examination. Its inadvertent pressure on the eyecup used while scanning can influence the angle configuration as demonstrated by Ishikawa.[33]

Scheimpflug photography

Scheimpflug photography is another technique that has been used for quantitative evaluation of the AC angle.[34] However, the actual AC angle recess is not visualized by this technique and important structural information in this region is likely to be missed.

Biometric features of eyes with angle closure glaucoma

Anterior chamber depth (ACD)

Central ACD is primarily determined by the position of the anterior lens surface, which depends on the lens position and lens thickness. The mean depth of eyes

with angle closure is about 1.0 mm shallower than that of normal eyes (Table 2). Increased lens thickness accounts for 0.35 mm of this and a more forward lens position for 0.65 mm.[35]

Diurnal variations

There are diurnal and day-to day variations in ACD. Mapstone found that the peripheral anterior chamber is significantly shallower in the evening than in the morning,[36] correlating with the other observation that acute glaucoma is also most common in the evening.[37] Other investigators found day-to-day fluctuations of up to 0.2 mm in the depth of the anterior chamber.[38] One investigation found an inverse correlation between the intraocular pressure and the ACD in eyes with poorly controlled pressures.[39]

The fellow eyes

The fellow eyes of patients who have suffered unilateral acute glaucoma, have the same range of ACD as the primarily affected eyes.[40] Significant asymmetry of ACDs between the two eyes is unusual, but slightly different is common.[22] The ACD and volume are less in hyperopic eyes than emmetropic eyes, which, in turn, have shallower and smaller chambers than myopic eyes.[41,42] Angle closure can occur in eyes with high myopia. Causes of angle closure other than relative pupillary block are more common in these patients. Careful gonioscopy accompanied by biometry measurement and ultrasound biomicroscopy can lead to the correct diagnosis and individualized management in these highly myopic eyes,[43] or eyes with unusual asymmetric biometry.

The relatives of patients

The ocular dimensions of patients with angle closure glaucoma resemble those of their siblings and offspring with regard to corneal diameter, anterior chamber depth, corneal height[44] and lens thickness. A relatively forward position of the lens is found in angle closure glaucoma patients, but not in their siblings or offspring. The axial length is less than normal in angle closure glaucoma patients and, perhaps, in their siblings, but not in their offspring.[44]

The effect of aging

The anterior chamber becomes gradually shallower throughout life.[41,42] Different methods of investigation give more or less parallel curves, but the absolute values differ: the ACD decreases by 0.4-0.9 mm between the ages of 25 and 65 years and is rarely less than 2.5 mm before the age of 55 years.

Senile shallowing of the anterior chamber is only partially accounted for by increased lens thickness and it appears that the lens moves forward with advancing age and/or that lens growth is mainly on its anterior surface.[45] The effect of cataract on the depth of the anterior chamber is unpredictable,[44] unless the lens is intumescent.

Ethnic difference

Racial differences in the prevalence of primary angle closure glaucoma (ACG) have long been recognized, although the mechanisms underlying these differences are not fully understood. Congdon[46] has not found shallower ACDs or narrower angle measurements among Chinese, a population with high rates of ACG (Table 3). It may be that Chinese ACG prevalence is higher for some other reason.

Wojciechowski[47] suggested a more rapid shallowing of the anterior chamber over life among Chinese and Eskimos. It is postulated that younger individuals in these two populations exposed to greater opportunities for near work become more myopic, presumably with deeper ACD and wider angles. A similar finding was also reported for a Chinese population in Singapore.[48] It was interpreted by the authors of that study as evidence of a cohort effect related to increased myopia prevalence among younger patients.

The rapid narrowing of the anterior segment found in Eskimo and Chinese eyes could also be explained by the development of creeping angle closure, or more rapid progression of lens opacity, because of factors such as diet, increased exposure to ultraviolet B light near the equator (among Singapore Chinese) or reflected from snow (among Alaskan Eskimos).[47]

The fall of ACD and increase in lens thickness throughout life have been reported by many other investigators, based on cross-sectional[49] and longitudinal[50] data. The reversal of both of these tendencies in the seventh decade was observed in Chinese,[17,46] blacks and whites,[46] Eskimos,[47] and Mongolians.[51] The declining prevalence of ACG seen in the seventh decade in several groups may be associated with this reduced tendency toward shallow ACD late in life.[47] A possible explanation for apparent deepening of the anterior chamber in the 70s and above could be atrophy and posterior rotation of the ciliary body with aging, as suggested by studies with ultrasound biomicroscopy[32] and magnetic resonance imaging.[52]

Table 3. Axial length, anterior chamber depth, and lens thickness in different races

Races	AL	ACD	LT	References
White	23.40 ± 0.10	3.05 ± 0.03	4.45 ± 0.04	Congdon[46]
Black	23.00 ± 0.10	3.01 ± 0.03	4.35 ± 0.04	Congdon[46]
Chinese	23.30 ± 0.06	3.00 ± 0.02	4.55 ± 0.02	Congdon[46]
Eskimo	23.70 ± 0.15	2.96 ± 0.04	4.74 ± 0.05	Wojciechowski[46]
South India	22.76 ± 0.78	3.00 ± 0.30	4.31 ± 0.31	George[62]

Risk for glaucoma

A shallow ACD has been identified as a risk factor for ACG.[7,11,35] There is a dose-response relationship between shallower anterior chamber and higher rate of peripheral anterior synechiae (PAS) noted in Mongolia and Singapore.[53] However, the relationship appears to differ between these two populations. In Singaporeans, it showed a consistent, incremental increase in PAS across the entire range of ACD examined. In Mongolia, there was a clear threshold for ACD around 2.4 mm, above which PAS was very uncommon. With ACD less than 2.4 mm, the rate of PAS rose rapidly to overtake that seen in Singaporeans. This reinforces the importance

of gonioscopy in the assessment of all glaucoma suspects and gonioscopy should be part of the routine eye examination.

A pronounced increase in angle width occurs in Mongolian people with narrow angles after laser iridotomy, indicating that pupil block is the predominant mechanism responsible for angle closure.[54] A review suggested that only 40% of angle closure in Chinese people was attributable to pure pupil block, 8% resulted from non–pupil block (including plateau iris), and 55% was due to a combination of the two factors.[55] It does hint that ACD may be less promising as a screening tool among Chinese people than was shown in the Mongolian population.[56]

Lens

It is believed that the relative size and position of the crystalline lens play a major role in the pathogenesis of angle closure[7,22,57] (Table 4). With age, there is an increase in lens thickness, and a relatively more anterior lens position. In eyes that are hyperopic with small anterior segments, the result is angle crowding and a greater predisposition to pupillary block due to iridolenticular apposition.

Table 4. The relative lens position and size in angle closure patients and normals

Parameters	Acute	PACG	PAC suspect	Normal	References
RLP		2.0.2 ± 0.1		2.2 ± 0.2	Lowe[3]
RLP		2.24		2.4	Tomlinson[3]
LAF			2.24 ± 0.15	1.93 ± 0.15	Lin[17]
RLP	2.22 ± 0.12	2.34 ± 0.16		2.41 ± 0.15	Marchini[32]
LAF	2.28 ± 0.12	2.20 ± 0.11		1.97 ± 0.12	
LAF		1.91 ± 0.30	1.99 ± 0.20	1.92 ± 0.10	George[32]

RLP: Relative lens position adding the anterior chamber depth to half the lens thickness and then dividing the sum by the axial length The RLP was multiplied by 10.
LAF : Lens/axial length factor: the lens thickness to axial length ratio multiplied by 10.

Lim et al[57] did not find significant differences in lens thickness or greater degree of lens opacity in acute primary angle closure (APAC) -affected eyes compared with fellow eyes. They found that the degree of cortical opacity was greater in fellow eyes than APAC eyes. This may be due to poorer dilatation of the pupil in APAC-affected eyes and lead to an underestimation of cortical opacity. Other lens factors that were not studied may also be implicated in APAC, such as the volume of the lens, the lens curvature, the laxity of the lens zonules, and mobility of the lens–iris diaphragm.

Thicker lenses tend to be situated more anteriorly.[22,58] Anterior movement of the lens also occurs with age.[22,45] The aging results in about 0.75 to 1.1 mm increase in thickness and 0.4 to 0.6 mm forward movement of the anterior lens surface.[22,59] The ratio of lens thickness and ocular axial length also increases with age and is greater in angle closure patients.[19,22]

The lens surface steepens and the radius of curvature of the lens surface decreases as the lens thickness increases.[16,60] In eyes with shallow anterior chamber, the lens is situated more anteriorly,[17,60] and pushes the iris forward and increases the resistance to aqueous flow between the posterior and anterior chamber.

Choroid

Smaller ocular biometry is a risk factor for ACG. However, there could be other physiological factors which are equally important. One mechanism proposed for APAC in anatomically predisposed eyes has been choroidal expansion causing a forward movement of the lens and greater iris convexity.[20] Yang *et al.* compared the biometric parameters, anterior chamber depth, lens thickness, and lens position within 24 hours of presentation and again after two weeks in eyes with APAC. They found, however, there was no change observed in these parameters in both APAC-affected and fellow eyes. These findings do not support the hypothesis of lens movement due to choroidal expansion in APAC.[21]

Conclusion

Ocular biometric measurement is important in the screening, diagnosis and management of angle closure patients. However, the ocular biometry is dynamic and influenced by many factors that are still not fully understood. There are many new instruments available nowadays, and they provide better images and understanding of the mechanism of angle closure. However, there is no parameter that is reliable for identifying eyes at risk of developing acute angle closure attack. The large parts of the eye, such as lens zonules, vitreous, and choroid, are still lack of sensitive instruments that can clarify the roles that they may play in the formation of angle closure. We may need a more open-angle of view and consider the eye as a whole rather than constrain ourselves only at the anterior quarter of the eye in the research of the angle closure in the future.

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Pathophysiology of angle-closure glaucoma

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Introduction

Angle closure begins at the level of the trabecular meshwork as a result of its contact with the iris, which causes obstruction of outflow. Traditionally, the pupillary block-angle closure-peripheral iridotomy principle has been the core concept in the pathophysiology of primary angle-closure glaucoma. However, several mechanisms including pupillary block, plateau iris, lens-related block, and others alone or in combination, can cause contact between the iris and trabecular meshwork.

Mechanism of angle closure

Pupillary block

The concept of pupillary block is centered on the pressure gradient created between the anterior and posterior chambers. This pressure gradient is created owing to the sequestration of aqueous in the posterior chamber, because of no or restricted passage through the pupil. This situation eventually results in a convexity of the iris, and it is this convexity that causes iris and trabecular contact, especially when the chamber angle is narrow (Fig. 1). Iris convexity resolves after iridectomy, as was observed by slit-lamp photography and ultrasound biomicroscopy.[1-3]

Mapstone hypothesized using a mathematical model, that a mid-dilated pupil and an anteriorly placed lens are related to increased pupillary block.[4] Tiedeman hypothesized that a mid-dilated pupil and forward lens movement increase pupillary block. On the other hand, the author also mentioned that an extremely miotic pupil is subjected to the increase of pupillary block.[5] Silver and Quigley suggested that pressure difference between the anterior and posterior chambers increases when (1) aqueous flow increases; (2) the channel length between the iris and lens surface is greater; and when (3) the gap between the iris and lens surface is nar-

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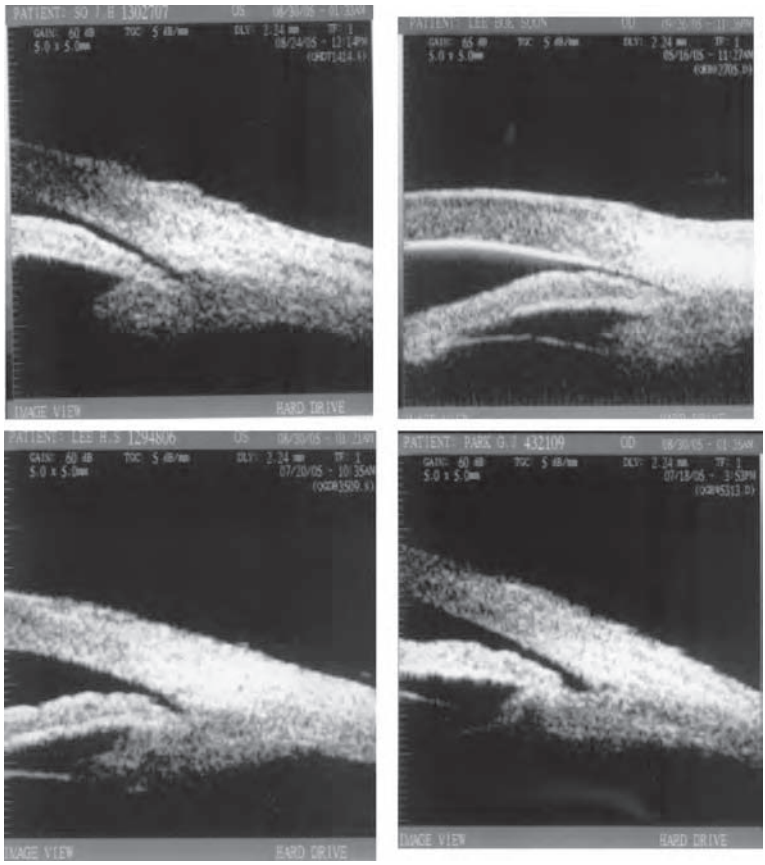

Fig. 1. Pre-laser ultrasound biomicroscopic findings of pupillary block (upper figures) showing iris bowing and plateau iris configuration (lower figures) and a sharp drop and backward angulation at the peripheral iris.

rower.[6] Wyatt and Ghosh also mentioned that if an eye has a thicker iris, posterior to anterior pressure difference increases.[7]

A high proportion of eyes with primary angle-closure glaucoma develop an increase in intraocular pressure on long-term follow-up despite patent laser iridotomy.[8-10] Peripheral anterior synechiae progressed in about 1/3 of angle closure eyes following iridotomy.[11,12] Other mechanisms than pupillary block are related, at least in part, to these continued dysfunctions following laser iridotomy. There are many angle closure conditions with elevated IOP that may follow iridotomy, including: (1) elevated IOP related to iris characteristics, such as plateau iris configuration, iris crowding or prominent last iris roll; (2) phacomorphic glaucoma or lens-induced glaucoma; (3) aqueous misdirection; (4) incomplete iridotomy; (5) extensive synechial closure causing the residual angle closure; (6) ciliary body abnormalities such as ciliary body cyst (Fig. 2); and (7) open-angle glaucoma with a narrow angle.

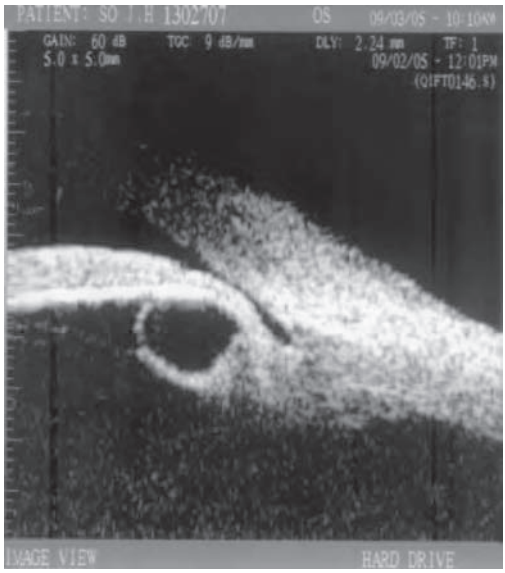

Fig. 2. Ultrasound biomicroscopy revealing a ciliary body cyst and a plateau-like configuration in an angle-closure patient.

Not all angle closure eyes have pupillary block. However, in the majority of angle closure eyes pupillary block is either the sole mechanism or is present in combination with other mechanisms. Wang *et al*. mentioned that 38% of angle closures in Chinese people were attributable solely to pupillary block, 54% resulted from a combination of the mechanisms, and the remaining 8 % were caused by a non-pupillary block.[13]

Peripheral iris configuration and angle narrowing

Traditionally plateau iris refers to eye characteristics that do not have a very shallow anterior chamber but a critically narrow angle.[14-16] Plateau iris configuration can be differentiated from plateau iris syndrome. According to Wand *et al*.,[14] plateau iris configuration refers to the preoperative (pre-iridotomy) findings of a normal depth anterior chamber with a flat iris plane by direct slit-lamp examination, but an extremely narrow or closed angle by gonioscopic examination. Plateau iris syndrome refers to the clinical picture of pupillary dilation induced angle closure despite patent iridectomy in the eye with plateau iris configuration. Chandler and Grant thought that plateau iris might be due to the ciliary process being abnormally rotated forward, causing the iris periphery to be held in a forward position.[17] Later, Pavlin *et al*. observed anteriorly positioned ciliary processes in patients with plateau iris syndrome by ultrasound biomicroscopy.[18] Moreover, a sine-wave sign on indentation gonioscopy is believed to result from resistance to the backward movement of the peripheral iris due to an anteriorly positioned ciliary process (Fig. 3).[19]

Trabecular ciliary process distance (the distance between the trabecular meshwork and the ciliary process at 500 μm anterior to the scleral spur, measured by

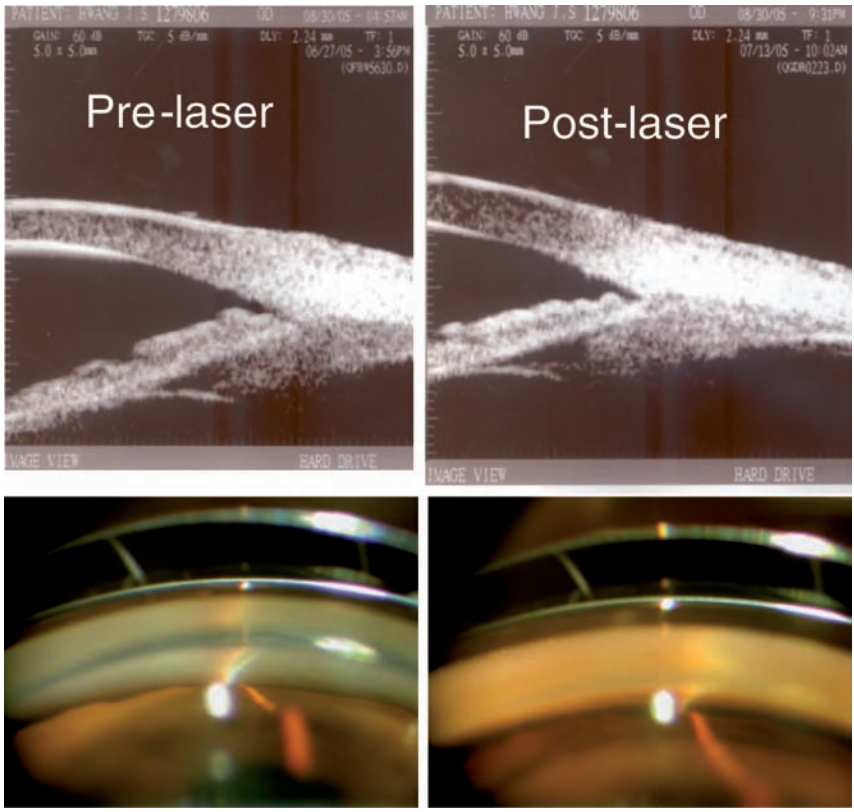

Fig. 3. Ultrasound biomicroscopic findings (upper left, pre-laser iridotomy; upper right, post-laser iridotomy) and related pre-laser gonioscopic findings in a patient with plateau iris configuration. Without indentation (lower left) focal lines show a gap between the iris and cornea. With indentation, the angle base is clearly visible and the iris contour shows the characteristic sine-wave sign. The ciliary process is placed anteriorly and there is no space between the iris and ciliary process.

ultrasound biomicroscopy) in primary open-angle glaucoma and normal eyes was found to be greater than in eyes with primary angle-closure glaucoma.[20,21] On the other hand, in some angle closure eyes ciliary processes were positioned anteriorly with open angles after laser iridotomy (pupillary block), and ciliary processes were placed posteriorly in the presence of occludable angles after laser iridotomy (plateau iris). The authors suggested that the presence of an anteriorly placed ciliary process alone does not cause plateau iris (Fig. 4, left).[22] In addition, Wang *et al*. found that approximately 1/2 of the eyes, which were referred to plateau iris by the Western perspective, had a relatively normal-sized and normal-positioned ciliary body. Ciliary processes in those eyes were away from the peripheral iris.[13] Wang *et al*. observed that the peripheral iris was thick and fleshy, and that the iris root was short and angulated posteriorly in this type, and named this *iris crowding*.[13] He *et al*.[23] described a specific peripheral iris configuration and coined the term *prominent last iris roll*. Eyes with this condition have a thick iris, which is peripher-

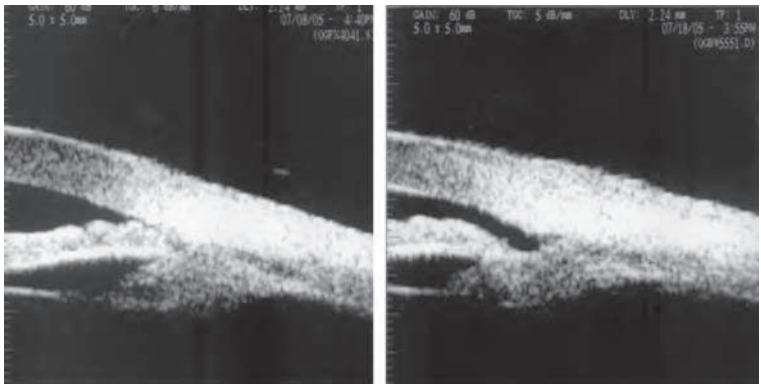

Fig. 4. Ultrasound biomicroscopic findings in plateau iris configuration with a gap at the angle base (right) and without a gap (left). Left photograph shows a normally positioned (not anteriorly located) ciliary process, and it is away from the posterior iris.

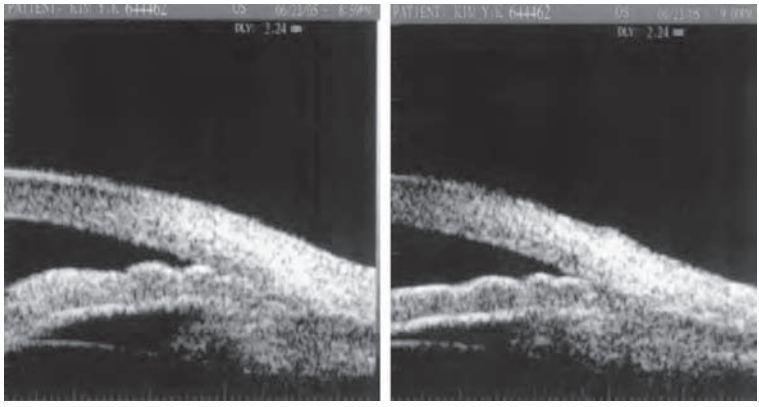

Fig. 5. Ultrasound biomicroscopic findings of an eye with a presumed prominent last iris roll. The folded iris contacted the trabecular meshwork both pre-laser (left) and post-laser (right) iridotomy.

ally thrown into prominent circumferential folds occupying a large proportion of the angle. When the pupil dilates, the folded iris may contact with the trabecular meshwork (Fig. 5).

Central anterior chamber depth in plateau iris is believed to be greater than in pupillary block glaucoma. However, when measured by ultrasound biomicroscopy, central anterior chamber depth in plateau iris syndrome was smaller than in pupillary block,[24] or showed no significant difference.[22] Therefore, to avoid confusion, the author defines the term plateau iris configuration as the specific iris configuration of a sharp drop and backward angulation at the peripheral iris (Fig. 1). The term plateau iris configuration is applicable to both pre- and post-laser iridotomy status.

To distinguish pupillary block from plateau iris configuration before laser iri-

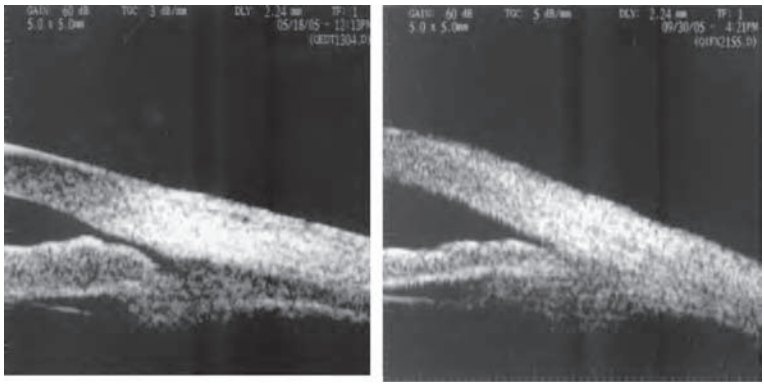

Fig. 6. Post-laser ultrasound biomicroscopic findngs in plateau iris configuration. The height of the plateau iris is high (left) or low (right).

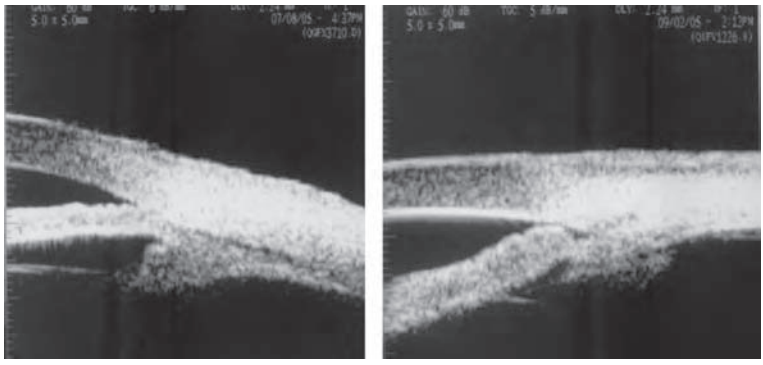

Fig. 7. Ultrasound biomicroscopic findings in plateau iris configuration. When there is no gap at the angle base and the height of the plateau iris is low, then apposition starts from the bottom of the base (left). On the other hand, when there is a gap at the angle base, apposition does not start from the bottom of the base, and leaves a space at the angle base (right).

dotomy is sometimes difficult, and the two conditions frequently coexist, thus plateau iris configuration sometimes cannot be seen before the pupillary block component is eliminated by laser iridotomy.[25] The height of plateau iris configuration varies between eyes, and may be low or high (Fig. 6). There is a gap at the angle base in some plateau iris configurations (Figure 4), and if present, when pupillary block develops, an apposition may start at Schwalbe's line, leaving the angle base open. On the other hand, if there is no gap at the base and the height of the plateau iris is low, then apposition may start from the bottom of the base resulting in *creeping angle closure* (Fig. 7).[26]

In conclusion, certain peripheral iris configurations including plateau iris configuration, iris crowding, or prominent last iris roll can cause angle narrowing and is related to the development of angle closure. Each specific category has specific iris characteristics and may or may not be related to ciliary process position. Moreover, because of the presence of a continuum from normal to specific angle

configurations, it is sometimes impossible to categorize them into specific, single categories. A type exists alone, whereas other types co-exist.

Lens-related

Hung and Chou[27] observed that nearly 60% of the eyes showed positive results when the prone position test was performed in a dark room among the iridectomized eyes. They suggested that this finding supports the theory of direct lens block, that is, block due to forward movement of the lens. Lens-related mechanism was also suggested by the findings that acute and chronic angle closures could be relieved by cataract extraction alone.[28-31] Lens-related mechanism can also act in concert with other mechanisms. Changes in the lens antero-posterior thickness and forward lens positioning are also related to increased pupillary block.

A lens may be susceptible to anterior movement due to zonular instability. Pseudoexfoliation is known to cause zonular weakness, and occludable angles and angle-closure glaucoma were found more frequently in patients with pseudoexfoliation.[32] A smaller corneal diameter, in the presence of a normal-sized lens, would decrease the ciliorenticular distance, and this phenomenon can lead to zonules slackness. Sihota *et al*. reported that corneal diameters were found to be smallest, with thickest and most anteriorly placed lens in eyes with acute angle-closure glaucoma, when compared with other types of angle-closure glaucoma and control eyes.[33] In addition, zonular instability in cases of acute angle-closure glaucoma may be due to intraocular pressure-related damage. The zonules are virtually inelastic and thus they may relax passively following changes in the ciliary body. In acute attack of angle-closure glaucoma, ischemia results in necrosis of iris stroma and ciliary processes due to a sudden rise in intraocular pressure.[34] Such ishemic changes can further distabilize the ciliary complex, and lead to zonular instablilty and forward displacement of the lens.

It is difficult to prove forward lens movement during an acute angle-closure attack using optical and conventional ultrasound techniques, because of difficulty in defining the posterior corneal surface and difficulty avoiding the pupillary margin if the pupil is not dilated.[24] In a report, no change was found in mean central anterior chamber depth, lens thickness, or lens position at the time of an acute attack versus two weeks later.[35] However, anterior lens movement during an acute angle-closure attack can be seen with ultrasound biomicroscopy (Fig. 8).

Choroidal expansion

Expansion of choroidal volume leading to increased vitreous fluid conductivity, and causing a forward movement of the lens and greater iris convexity can also cause the development of angle-closure glaucoma.[36] Normally an increase in volume posteriorly in the choroid would be accommodated by fluid exit from the anterior chamber without any shift in iris or lens position. However, when trans-vitreous flow is insufficient to equalize the pressure differential, the result is anterior movement of the compressed vitreous humor, iris, and lens. Although Yang *et al*. did not support the choroidal expansion theory,[35] Sakai *et al*. found that uveal effusion was observed not only in affected acute angle-closure glaucoma eyes but also in unaffected fellow eyes or chronic angle-closure glaucoma, supporting this theory.[37]

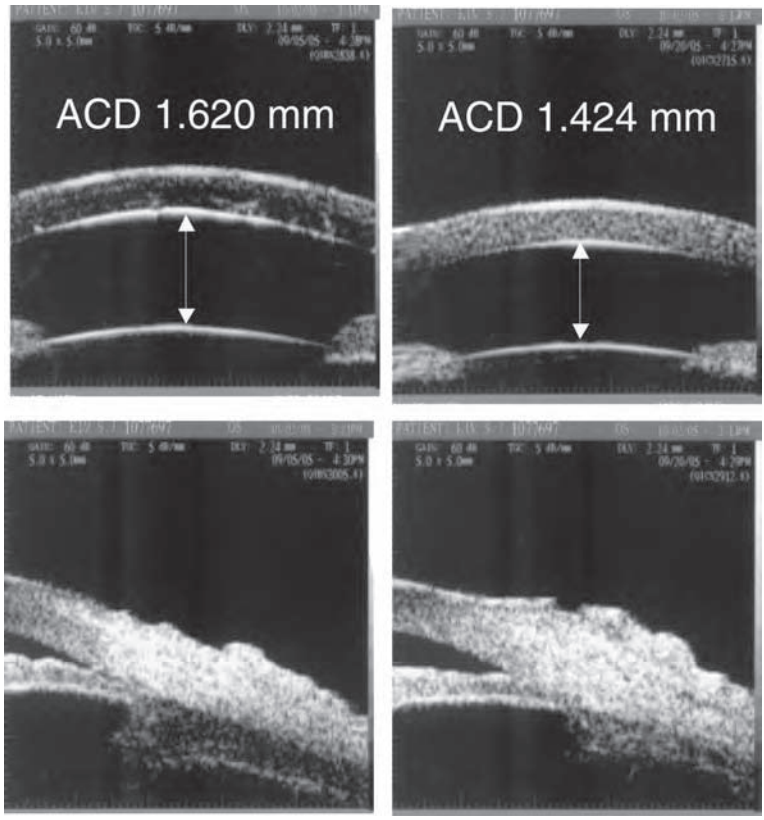

Fig. 8. Ultrasound biomicroscopic findings of a patient that experienced a second attack despite patent iridotomy. Left photographs were taken after resolution of the first angle-closure attack by laser iridotomy, whereas right photographs were taken during the second attack when the IOP was 34 mmHg two weeks after laser iridotomy. During this second attack, anterior chamber depth was reduced and newly formed peripheral anterior synechiae were found in the angle (lower right).

Multi-mechanism

Ritch *et al*.[38] suggested a multi-mechanism for angle-closure glaucoma. In China, approximately half of the chronic PACG cases might be attributable to multiple mechanisms.[13] Theoretically, all mechanisms including pupillary block, lens-block, and plateau iris configuration can be viewed as causes of angle-closure glaucoma in an eye. Wang *et al* classified multi-mechanism angle closure-glaucoma into three subtypes as described in the next chapter by Wang *et al*.[13] They believed that of several mechanisms, the pupillary block mechanism appears to be responsible for the majority of angle-closure glaucoma eyes, either as a sole mechanism or as a contributory factor.

Final pathway of angle closure at the level of the trabecular meshwork

According to the mechanisms described above, contact between iris and trabecular wall causes outflow obstruction. Two types of contact may occur between iris and trabecular meshwork, *i.e.*, appositional and synechial closure.[39] Moreover, two different manners of apposition were observed by ultrasound biomicroscopy: (1) contact beginning at Schwalbe's line; and (2) contact beginning from the angle base (Fig. 7).[40] In addition, two theoretical patterns have been suggested concerning the mode of development of peripheral anterior synechiae (PAS): (1) the peripheral iris first sticks to Schwalbe's line and then the PAS extends out toward the angle recess; and (2) the peripheral part of the iris first attaches to the angle recess and then the PAS extends toward Schwalbe's line (creeping angle closure).[41]

Recently, the mechanisms and characteristics of angle closure (sagittally at a point) have been studied extensively with the aid of ultrasound biomicroscopy. However, a real-time circumferential view of angle closure has not been obtained. In terms of the circumferential aspect of angle closure, the *proportional concept* proposed first by Chandler and Grand and forwarded by Wilensky and Campbell deserves attention.[39] Theoretically, the degree of IOP elevation is proportional to the degree of closure. According to the Goldmann equation (IOP = F/C + EVP, where F is aqueous formation; C the facility of outflow; R outflow resistance (which is the inverse of C); F/C perfusion pressure; and EVP episcleral venous pressure), perfusion pressure is directly proportional to flow resistance when aqueous production remains constant. That is, if resistance increases, then IOP increases proportionally given that aqueous production remains constant. "For example, if the initial IOP is 16 mmHg (within the normal range), then the initial perfusion pressure is 7 mmHg (normal IOP 16 mmHg – normal EVP 9 mmHg). If 1/2 of the circumferential angle is occluded, then the perfusion pressure would be 14 mmHg, and the IOP would be 23 mmHg (14 + 9 = 23 mmHg). If, however, half of the remaining angle is closed further (to 270 degrees of angle closure) the perfusion pressure would double to 28 mmHg and the IOP would be 37 mmHg (28 + 9)."[39] That is, in a healthy eye, an occlusion of the 3/4 of the angle circumference would result in significant IOP elevation.

Peripheral anterior synechiae

PAS refer to a condition in which the iris adheres to the angle. Peripheral anterior synechiae may be complete (synechial closure up to posterior trabecular meshwork) or incomplete; and patch or broad (Fig. 9). The extent of PAS is related to the severity of angle-closure glaucoma. Visual field damage and cup-to-disc ratio were found to be correlated with PAS extent.[42,43] However, the level of severity may vary and depend on the extent of angle closed and on the efficiency of the remaining open angle. The status of uveoscleral outflow and of aqueous production capacity by the ciliary body may also be important variables.

Several studies have evaluated the topographic distribution of PAS. PAS tends to occur first superiorly in the angle, and is found most commonly in the superior sector.[44,45] Broad PAS exceeding 30 degrees is most frequent in the superior sector, although narrower PAS shows no pattern of location.[46] Mok *et al*. suggested that the superior and temporal portions of angle might be the earliest sites of angle occlusion in chronic angle-closure glaucoma, because the incidence of synechial angle

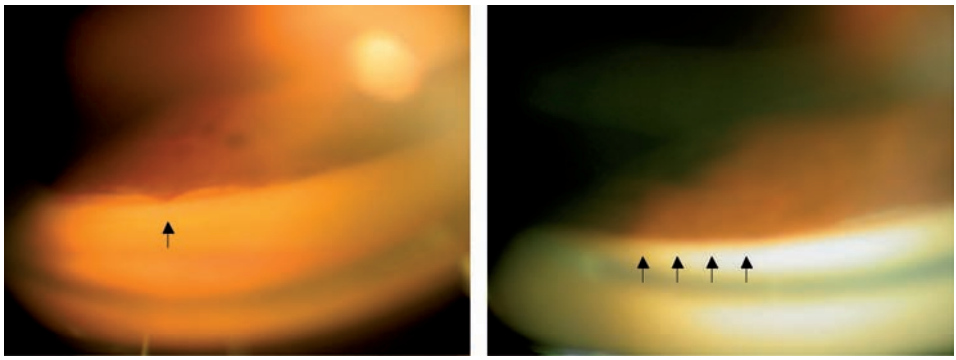

Fig. 9. Gonioscopic findings of patch (left) and broad (right) peripheral anterior synechiae. Arrows indicate the extents of the synechiae.

closure was higher in the superior quadrant than elsewhere.[47] This phenomenon has been interpreted in several ways. It may be due to the weight of the column of aqueous in the anterior chamber;[44] to decentralization of the lens superiorly to the corneal center; or to upper eyelid pressure causing peripheral corneal flattening in the superior part.[48]

The concept of creeping angle-closure,[26] in which PAS slowly advances forward circumferentially, making the iris insertion appear to become more and more anterior, contributes to our understanding of chronic angle-closure glaucoma. The exact cause of the development of creeping angle closure needs to be determined. However, some indirect evidence suggests that creeping angle closure is caused by multi-mechanism.[13]

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Classification

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Introduction

The most appropriate method of classification of angle-closure glaucoma has been a matter of considerable debate. Ideally, classification of this condition should fully identify the causes of the disease and provide evidence-based guidance not only of treatment, but also the prevention of the disease. Thus, the ideal system of classification should be based on etiology. Accordingly, this classification will guide appropriate and effective treatment. To date, such an 'ideal' system of classification has been lacking. Epidemiological and clinical research has improved our understanding of the etiology of PACG, although our understanding of the factors which influence onset and progression of disease is still far from complete. Several different approaches to classification have been proposed. Though none is ideal, they are helpful in describing the mechanism and planning appropriate treatment of angle-closure glaucoma. In this chapter, some approaches to classification of angle-closure will be discussed and their relative merits and limitations discussed.

History of classification

The word 'Glaucoma' is derived from the Greek word glaukos, which signifies a bluish-green or bluish grey color and was probably used to describe the appearance of the pupil in an eye with a mature cataract, or the appearance of an edematous cornea resulting from elevated intraocular pressure. Gradually, the causes of these two types of blindness became more clearly understood. The most important distinction was that cataract could be treated by couching, and that eyes with glaucoma did not benefit. As the understanding of glaucoma as a separate disease accumulated, it was recognized that some patients presented with eyes that were painful, showed vascular congestion, and were hard to the touch, while others lacked these signs and symptoms.[1] Consequently, glaucoma was divided into two categories – congestive and non-congestive glaucoma. This approach to classification

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remained in common usage until the invention of the gonioscope. The widespread usage of gonioscopy, eventually resulted in the abandonment of these terms as it was recognized that they neither describe the pathophysiology of the condition, nor indicate the correct treatment. Furthermore, congestion and corneal edema are not unique to angle-closure glaucoma, occurring in a host of other inflammatory conditions as well as many secondary glaucomas.

Vascular congestion is a better indication of the rapidity with which the pressure rises, rather than the cause.

In the first three decades of the twentieth century, detailed gonioscopic observations were made by Trantas, Koeppe, Salzmann and Troncoso[2] and in 1938, Barkan proposed that primary glaucoma be divided into those with a deep chamber, and a shallow chamber (narrow angle) type.[3] In 1941, Barkan changed the terms for the two forms of glaucoma to 'wide angle glaucoma' and 'narrow angle glaucoma.' Subsequently, primary glaucoma has been classified as angle-closure glaucoma and open-angle glaucoma. Today, the most widespread classification system used to describe angle closure describes the presence of symptoms and disease course, dividing angle-closure glaucoma into three types: acute, sub-acute and chronic. The advantage of this classification is its familiarity to doctors and the ease with which patients who have a symptomatic episode can understand the description. However, there is often overlap in the clinical presentation, which limits the usefulness of this classification.

Another classification system was proposed by Ritch in 1996.[4] This identified four sub-types, based on the mechanisms of angle-closure: pupil-block (block at the level of iris), plateau iris (block at the level of the ciliary body), lens-induced (block at the level of the lens) and causes behind the lens (block posterior to the lens). This four-point classification covers almost all possible mechanisms that may cause angle-closure, and in doing so, is helpful in guiding the appropriate choice of management. However, the mechanism causing some cases remains obscure and controversial, requiring more conclusive evidence to finalize the debate.

Following the advent of ultrasound biomicroscopy (UBM), a combination of UBM and gonioscopy was advocated by Wang as an approach to classification of primary angle-closure glaucoma, based on research into the mechanisms of angle-closure in Chinese people.[5] This system describes three types of cases: pure pupillary block, non-pupillary block and those resulting from multiple mechanisms. In addition, this classification also gives guidance on the appropriate choice of treatment in PACG.

In 2002, Foster proposed a system for classification of glaucoma for use in prevalence surveys, which included primary angle-closure glaucoma. The authors proposed that the term 'glaucoma' be reserved for cases with evidence of structural and functional evidence of optic nerve damage. In this approach to classification, three conceptual stages in the natural history of angle-closure were identified, beginning with cases with anatomically narrow angles, which then may progress to anterior segment signs of disease (raised IOP and/or peripheral anterior synechiae (PAS)), finally culminating in glaucomatous optic neuropathy.[6] The three categories were respectively called primary angle-closure suspect (PACS), primary angle-closure (PAC) and primary angle-closure glaucoma (PACG).

These four main approaches to classification of PACG currently in use around the world are described in greater detail below.

Classification based on symptoms

The presence or absence of symptoms in angle-closure glaucoma has been used to identify three stages of disease: acute, sub-acute, and chronic and latent angle-closure glaucoma suspect.

Acute angle-closure glaucoma

When the chamber angle closes suddenly and completely, the intraocular pressure rises rapidly to very high levels, causing symptoms and damage to the optic nerve at a fairly rapid pace. This has been called acute angle-closure glaucoma.

The typical patient that suffers such an acute attack will have a sudden onset of pain or aching in the affected eye. The pain may be mild to severe and usually accompanied by blurred vision, colored haloes around lights, redness, and sometimes nausea, vomiting, and sweating. Sometimes systemic symptoms such as abdominal or chest pain are predominant and make the diagnosis difficult. The elevated IOP may lead to ischemic damage to the iris musculature causing a mid-dilated, non-reactive pupil. The optic nerve head may be hyperaemic and edematous. The classical description of the resulting visual field defect is that of generalized constriction. Gonioscopy in the acute stage reveals complete iridotrabecular apposition, possibly with some areas of established synechial closure. Such acute attacks of primary angle-closure glaucoma may be self limiting, although this is unusual. Most often, cases that remain untreated, or present to hospital late will progress to chronic angle-closure glaucoma.[7-9]

Sub-acute angle-closure glaucoma

Sub-acute or intermittent angle-closure glaucoma is a milder form of the acute form in which symptoms are less dramatic and are self limiting. Patients may recall such intermittent episodes preceding the onset of an acute crisis occurs. These attacks may last a few hours, during which time the patient notices hazy vision with rainbow-colored halos around lights and aching in or above one eye. These symptoms occur more often at night or in dim illumination, and are relieved by sleep or exposure to light. The angle is closed while symptoms are present and partially open after they have resolved. Between the episodes of subacute angle-closure, IOP and outflow facility are generally normal.[10]

Chronic angle-closure glaucoma

Chronic angle-closure glaucoma is defined by a partially closed angle and raised intraocular pressure. Symptoms are mild or absent until very late in the disease. In this sense, chronic angle-closure glaucoma closely resembles primary open-angle glaucoma in that patients are asymptomatic and have quiet eyes, glaucomatous cupping of the optic discs, and visual field defects. Intraocular pressure (IOP) is moderately or substantially elevated. Gonioscopy is the essential diagnostic test in identifying chronic angle-closure glaucoma. Cases will almost invariably have a very narrow angle with appositional contact between the iris and the trabecular meshwork. Peripheral anterior synechiae are usually present, although they may

be far less extensive than the area of appositional closure. The height of the IOP is directly related to the extent of angle-closure. Creeping angle-closure is a subcategory of chronic angle-closure glaucoma in which peripheral anterior synechiae (PAS) extend inexorably from posterior to anterior and circumferentially.

Latent angle-closure glaucoma

Eyes with a shallow anterior chamber and correspondingly narrow drainage angles may be at a risk of subsequent angle-closure glaucoma.[11,12] The patient may be free of symptoms and will have no signs of glaucomatous optic neuropathy.[13] At particular risk are the contralateral fellow eyes of those which have suffered acute angle-closure. Because of the high risk of progression to PACG, these patients require prophylactic treatment. Eyes in which there is provocative test results in a significant pressure rise, or which have peripheral anterior synechiae (PAS) in an eye that has an open, but narrow angle are all deemed to have latent angle-closure glaucoma.

Conclusion

In this system of classification, acute, sub-acute and chronic angle-closure glaucoma are identified by the presence or absence of symptoms. The advantage of this approach to classification is that it is familiar to doctors and easy for patients to understand. It is the 'traditional' method of classification of PACG, but has specific drawbacks in that it does not describe the degree of angle obstruction or the presence or absence optic neuropathy. Furthermore, there often is overlap in the clinical presentation, limiting the usefulness of this classification. For example, after the acute stage, chronic glaucoma may develop. Conversely, patients with chronic angle-closure glaucoma may experience rapidly rising IOP and develop acute angle-closure glaucoma. The group with latent angle-closure glaucoma, remain more difficult to define. More predictive accuracy is needed in provocative tests to identify who will eventually develop PACG. Ultimately, any classification system based on symptoms cannot identify the etiology of angle-closure glaucoma and provides little guidance in the management of cases.

Classification based on mechanism

Descriptions of the mechanism of angle-closure glaucoma usually identifies four different sites of obstruction to the physiological flow of aqueous, each one lying progressively more posterior. The four mechanisms are usually termed pupillary block, plateau iris, lens-related or cilio-lenticular block and causes behind the lens.[4]

Pupillary block

Pathological pupillary-block is an exacerbation of a physiological phenomenon in which there exists a pressure gradient between the anterior and posterior chambers. When the plane of the pupil lies significantly anterior to the plane of the iris root, the effect of co-contraction of iris sphincter and dilator muscles is to generate a

force at the pupil margin which is directed towards the lens surface. This restricts aqueous flow and produces a pressure gradient between posterior and anterior chambers. This situation may reach equilibrium when pressure gradient across the iris is maintained by a balance between aqueous production and the posteriorly directed force vector of the iris muscles – a phenomenon called *relative* pupil-block. The resulting pressure gradient causes the iris to bow forward, and may bring it into contact with the trabecular meshwork.[14] If the trabecular meshwork is substantially occluded, the normal outflow of aqueous can be impeded and IOP increases. The amount by which IOP increases is related to extent of iridotrabecular contact. It is believed that the pupil-blocking force is maximal when the pupil is in the mid-dilated position. In this situation the pupil may grip the anterior lens surface causing total pupillary block, and a rapid increase in posterior chamber pressure. If further bowing of the iris causes total trabecular occlusion, a rapid, dramatic rise in IOP occurs.

Increased pupillary block and angle-closure glaucoma typically occur in eyes with small anterior segments. These eyes typically have the following features: (a) short axial length of the globe; (b) small corneal diameter; (c) steeper posterior curvature of the cornea; (d) a shallow anterior chamber; (e) a small anterior chamber volume; (f) a relatively anterior position lens; (g) steeper curvature of anterior lens surface; (h) a relatively thicker lens; (i) more anterior insertion of the iris into the ciliary body.

Pupillary block is the commonest mechanism causing primary angle-closure glaucoma. Iridectomy or iridotomy are therefore the key methods of managing most cases.

Plateau iris

Plateau iris configuration is the description given to the gonioscopic appearance of a flat iris plane from the pupillary margin to the mid-periphery, which makes a sharp turn posteriorly before inserting into the ciliary body. The angulation in the peripheral iris creates a narrow angle recess and increases the potential for angle-closure. Ultrasound biomicroscopy often reveals anteriorly positioned ciliary processes that push the peripheral iris forward, or at least prevent it from falling back after iridectomy. In some cases, the peripheral iris has prominent circumferential folds or is very thick. If the pupil dilates in response to pharmacologic agents or exposure to a dark environment, the iris may crowd the angle and cover the trabecular meshwork, leading to an increase in IOP.

Wand and co-workers suggested that plateau iris comprised two entities: plateau iris configuration and plateau iris syndrome.[15] Plateau iris *syndrome* denotes the combination of plateau iris configuration, together with angle-closure and high IOP occuring despite the presence of a patent iridectomy. An element of pupillary block can also exist in eyes with plateau iris configuration. Consequently, angle-closure due to plateau iris cannot be diagnosed until the pupillary-block component has been relieved by iridotomy. Plateau iris syndrome has been further divided into complete and incomplete forms, depending on the presence or absence of an associated rise in IOP on occlusion of the angle.[16] In the complete form, IOP rises when the angle closes with pupillary dilation and some patients may develop acute angle-closure glaucoma. In the far more common incomplete syndrome, IOP does not change.

Lens-induced angle-closure

Levene proposed the possibility of a lens-block mechanism in the development of some cases of angle-closure glaucoma. A swollen, cataractous lens can push the iris forward, causing angle-closure.[17,18] Similarly, forward movement of lens as a consequence of weak or loose zonules or can also cause angle-crowding and block the trabecular meshwork.

Hung and Chou observed that, among the iridectomized eyes, nearly 60% showed positive results when a dark/prone provocative test was performed. These findings support the theory of lens block which the aqueous humor is blocked by the forward movement of the lens.[19,20]

Greve reported that after extra-capsular cataract extraction and posterior chamber IOL in patients with narrow angles, there was a 3.5 mmHg decrease in IOP in cases in which a peripheral iridotomy had been performed. After the pupil block is relieved by peripheral iridotomy, the IOP lowering of 3.5 mmHg is due to widening of a crowded angle caused by lens block, allowing better access of the aqueous.[18]

Retro-lenticular mechanisms (causes behind the lens)

An increase in retro-lenticular pressure, can push the lens-iris diaphragm forwards and block the angle. This type of angle-closure glaucoma is often referred to as malignant glaucoma or ciliary-block glaucoma. It is characterized by a shallow anterior chamber and raised IOP, often in the presence of a patent iridotomy.[21] The condition usually follows intraocular surgery such as filtering surgery, cataract surgery, laser iridotomy,[22-26] and may occur spontaneously or after trauma, inflammation, the use of miotics and in exfoliation syndrome.[27]

Aqueous misdirection has been thought to be a principal mechanism in malignant glaucoma. Shaffer proposed misdirection of aqueous either into or around the vitreous.[28] Aqueous is secreted into or sequestered in the vitreous cavity, pushing the lens, hyaloid face, and iris forward, thus collapsing the anterior chamber and blocking the trabecular outflow system. Weinreb postulated that the ciliary musculature may be hypertrophied in some patients.[29,30] After surgery or some other insult to the eye, the ciliary processes rotate forward, and make a seal with the posterior zonules or lens, causinging aqueous to be secreted into the vitreous. The aqueous is then sequestered in vitreous pockets and in space posterior to the detached vitreous. The rise in pressure pushes the lens forward and leads to the peripheral iris blocking the trabecular meshwork.

Another less-well-described mechanism that may contribute to angle-closure is choroidal expansion. Quigley proposed that expansion of the choroid may aggravate both pupil-block and angle-crowding.[31,32] Many clinical syndromes which cause expansion of choroidal volume lead to shallowing of the anterior chamber, including suprachoroidal hemorrhage and retinal vein occlusions. If the choroidal volume increases, pressure within the corneoscleral shell will rise, and cause the lens to move forward.[33] In eyes with high iris–lens channel resistance and forward convexity of the iris, such forward lens movement would exacerbate the existing anatomic disadvantages of the small eyes. Consequently, it was suggested that primary angle-closure could be the result of expansion of the choroid occurring in a small eye.

Conclusion

Classification based on mechanism of angle closure is easy to understand and helps the choice of treatment. However, the distinction between pupillary block and lens block is not clear, and the mechanisms of retro-lenticular block remain controversial and and lacking in hard evidence. The pupillary-block mechanism is responsible for most of PACG, either as the sole mechanism or in combination with other mechanisms.[34,35] The lens block mechanism has been recognized for a long time, however a large, anteriorly-positioned lens is the major anatomical characteristic causing a shallow anterior chamber in pupillary block.[36,37] Distinguishing between these two mechanisms is still problematic. An anteriorly-positioned ciliary body plays an important role in the mechanism of plateau iris, but the precise cause of this anatomical configuration remains unknown. Retro-lenticular mechanisms are relatively uncommon causes of angle-closure. Many believe that lenticular and retro-lenticular mechanisms are not causes of primary disease, but are actually secondary forms of angle-closure glaucoma.

Classification based on angle-closure configuration

In this system, PACG is classified into three types: angle-closure glaucoma due to pure pupillary block, cases due to non-pupillary block, and angle closure due to multiple mechanisms. Sub-classification of angle-closure glaucoma due to non-pupillary block includes two types: anteriorly-positioned ciliary body and iris crowding. Angle-closure glaucoma due to multiple mechanisms can be divided into three subtypes: pupillary block and iris crowding coexisting (BI); pupillary block and anteriorly-positioned ciliary body coexisting (BC); and all three factors coexisting (BIC).[5]

Considering the configuration of the chamber angle, three factors play an important role in the mechanism of angle-closure: iris bombe, iris crowding and anterior position of the ciliary body. Iris bombe is caused by pupillary block which causes the iris to be pushed toward the trabecular meshwork. Iris crowding is caused by a thick peripheral iris which crowds the angle and blocks the trabecular meshwork when pupil is dilated by pharmacological agents, or in exposure to dark conditions. Anteriorly positioned ciliary processes decrease the distance between iris and trabecular meshwork.

Angle-closure due to pure pupillary block

These patients usually have a shallow anterior chamber, a more anterior lens position, and stronger pupillary-block tendency. According to Mapstone's pupillary block force (PBF) calculation formulae, PBF = (D+E) cos a + S cos b can be measured and calculated. [PBF = pupillary-block force, S = sphincter-contracting force, D = pupil-dilating force, E = iris-stretching force, 'a' is the angle between the vector (D+E) and the line from the iridolenticular apposition to the center of the radius of the lens surface curvature; 'b' is the angle between the vector S and the line from the iridolenticular apposition to the center of the radius of the lens surface curvature.][38] When pupillary-block force increases beyond the posterior chamber

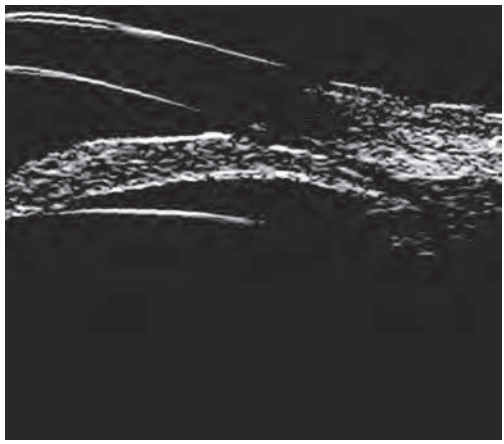

Fig. 1. Pure pupillary block (iris bombe).

pressure, blocking the flow of aqueous from the posterior to anterior chamber, the iris assumes a bombe configuration (anterior convexity), creating a narrow angle or angle closure. The term 'pure pupillary block' is to emphasize that the other two factors (iris crowding and anterior positioned ciliary body) do not contribute to angle closure in these cases (Fig. 1). After iridotomy, the pressures in anterior and posterior chambers are equal allowing the iris to assume a more planar configuration, and causing the angle to widen.[39]

Angle closure due to non-pupillary block

These patients usually have a relative deeper central anterior chamber and a posterior lens position than cases of pupillary block. The plane of the pupil and the

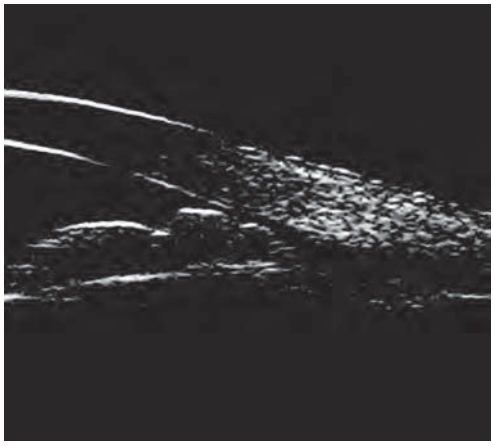

Fig. 2. Iris crowding.

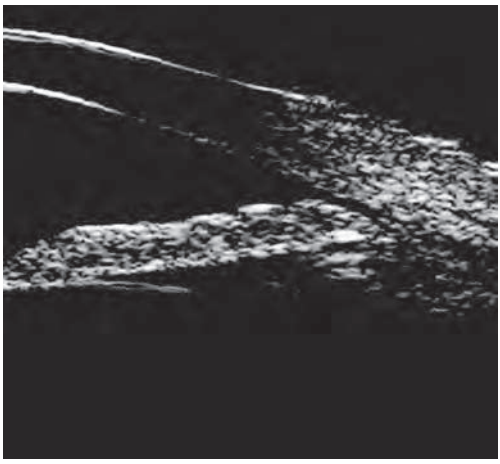

Fig. 3. Anterior positioned ciliary body.

plane of the iris root do not differ greatly. In this situation, according Mapstone's pupillary blocking force formula, the pupillary blocking force should be near zero. Imagines acquired from such patients by UBM, show the anterior chamber to be relatively deep and the iris surface to be flat even though the angle is narrow. Eyes with this angle configuration can be categorized into two subtypes: peripheral iris crowding (Fig. 2) and anteriorly-positioned ciliary body (Fig. 3). Iris crowding is caused by a thicker peripheral iris. In the other group, narrow angle or angle-closure glaucoma is caused by anterior positioned ciliary process.

The other groups are characterized by an abrupt peripheral angulation in the peripheral third of the iris,[40] which is usually a consequence of anteriorly positioned ciliary processes. This sub-type is also referred to 'plateau iris'. The anteriorly positioned ciliary body pushes the peripheral iris forward, resulting in angle closure in some cases. Iridotomy does not increase the angle width in either of these two subtypes.

Angle-closure due to multiple mechanisms

This group of cases have features of both papillary block and non-pupillary block forms of angle-closure. They often have a shallow anterior chamber, an anterior positioned lens and a bombé iris configuration, together with a more anterior insertion of the iris root, a thicker iris and/or anteriorly positioned ciliary processes. Because a pupillary-block is present to some degree in all these multi-mechanism cases, it is difficult to distinguish these from the pure pupillary block cases prior to laser iridotomy.

This category can be divided into three sub-types: one in which pupillary block and iris crowding coexist (BI) (Fig. 4); those in whom pupillary block and anteriorly positioned ciliary processes coexist (BC) (Fig. 5); and those in which all three factors coexist (BIC) (Fig. 6).

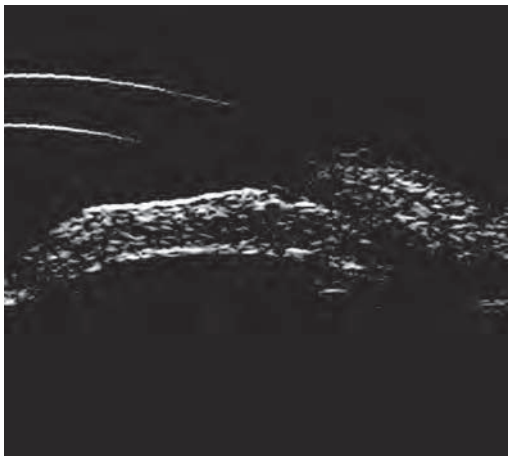

Fig. 4. Pupillary block + iris crowding.

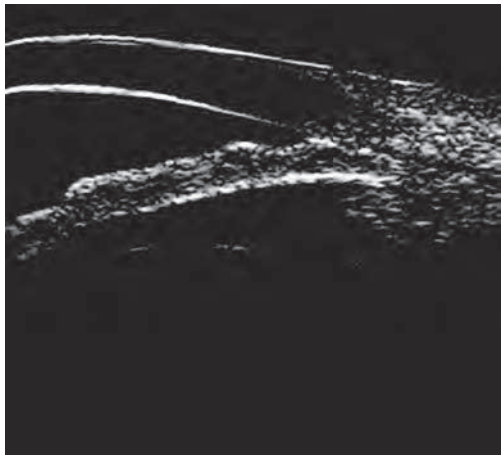

Fig. 5. Pupillary block + anterior positioned ciliary body.

How to distinguish and manage the different types PACG based on angle-closure configuration

UBM may be used to identify the presence of iris bombe, anterior positioned ciliary processes or comparative thick peripheral irises causing angle crowding under dark conditions. Without UBM, the following methods of diagnosis and treatment can be used.

First, depending on the configuration of the iris and the depth of the anterior chamber, PACG can be divided into two categories: plateau iris (non-pupillary block) and iris bombé (pupillary block). For early stage PACG with iris bombe, iridectomy or laser iridotomy are performed. After surgery, the configuration should

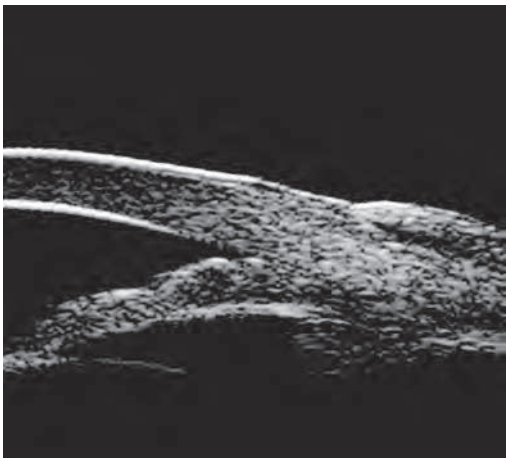

Fig. 6. Pupillary block + iris crowding + anterior positioned ciliary body.

be re-asessed. If the angle has widened dramatically, a diagnosis of pupillary block form can be established. If the angle remains appositional closed on gonioscopic examination, or a positive response to dark room provocative test occurs, a multi-mechanism disease can be diagnosed.

In non-pupillary block angle-closure and multi-mechanism cases, topical pilocarpine or iridoplasty can be used after iridotomy to reduce the thickness of the peripheral iris. If areas appositional closure are opened, the underlying mechanism is iris crowding due to a thick iris. If the angle remains apposition closed after iridoplasty or miotic treatment, the underlying mechanism is anterior placement of the ciliary body.[41,42] In cases of anterior positioned ciliary body, if iridotomy and iridoplasty fail to widen the chamber angle, trabeculectomy should be considered.

Conclusion

The classification of PACG is largely based on clinical observations in Europeans, among whom the condition is scarce. In Asian populations, primary angle-closure glaucoma is a more common disease.[43] This classification system is based upon observations of the mechanism of angle-closure in Chinese people. This scheme is easy to understand and in addition to a classification system it also provides guidance for the management of PACG. However, this classification system is limited to primary angle-closure glaucoma. Lens-block and causes behind the lens are excluded. Neither does this system consider the degree of angle obstruction nor the presence of glaucomatous optic neuropathy.

Classification of angle-closure in epidemiological research

This classification was developed for use in studies of the epidemiology of glaucoma by the International Society of Ophthalmic Epidemiology, and published by Foster

and colleagues. In this classification system, the term 'glaucoma' is used to signify glaucomatous damage to the optic nerve, defined by the combination of visual field defects and enlargement of the cup/disc ratio outside statistical limits for the population studied. The classification of primary angle-closure identifies three conceptual stages in the natural history of the disease from anatomically narrow angles, through anterior segment signs of disease (raised IOP and/or PAS) finally culminating in glaucomatous optic neuropathy.[6]

PACS, PAC, PACG

Primary angle-closure suspect (PACS): An eye in which appositional contact between the peripheral iris and posterior trabecular meshwork is considered possible. In epidemiological research this has most often been defined as an angle in which $> 270°$ of the posterior trabecular meshwork (the part which is often pigmented) cannot be seen.

Primary angle-closure (PAC)*:* An eye with an occludable drainage angle and features indicating that trabecular obstruction by the peripheral iris has occurred, such as peripheral anterior synechiae, elevated intraocular pressure, iris whorling (distortion of the radially orientated iris fibres), 'glaucomafleken' lens opacities, or excessive pigment deposition on the trabecular surface. The optic disc does not have glaucomatous damage.

Primary angle-closure glaucoma (PACG): Primary angle-closure plus evidence of glaucomatous damage to optic disc and visual field.

Glaucomatous optic neuropathy

The feature that differentiates glaucoma from other causes of visual morbidity is a characteristic pattern of damage to the optic nerve head. The vertical cup: disc ratio (VCDR) was adopted as a relatively robust index of glaucomatous loss of the neuroretinal rim. Statistical convention that a probability of $< 5\%$ representing a significant deviation from normal was used to specify the division between 'normal' and 'abnormal'. The 97.5th percentile value for CDR and CDR asymmetry were used as the criteria for defining structural abnormality of the optic nerve consistent with glaucoma.

Glaucomatous optic neuropathy was also been defined in the scheme using three levels of evidence. Category 1 stipulates structural and functional abnormalities consistent with glaucoma. Category 2 stipulates that in the case of advanced loss of vision where field testing cannot be performed using automated perimetry, that glaucoma can be diagnosed on the basis of advanced structural damage to the optic disc. Category 3 applies to cases where the disc cannot be seen. Glaucoma is diagnosed on the basis of visual acuity $< 3/60$ and either IOP > 24 mmHg or signs of previous filtering surgery. It has been proposed that this category be expanded to include those with iris ischemic sequelae and either an afferent pupil defect or no light perception.[6,49]

Conclusion

Epidemiologic studies have used different diagnostic criteria for the definition of angle closure, as well as what constitutes an occludable or narrow drainage angle. This classification of PACG provides a more uniform definition of the disease and is in line with the classification used in primary open-angle glaucoma.[6,48] The focus of this classification is the presence of glaucomatous damage to the optic nerve. This approach differentiates those with a true disease as opposed to suspects who are at increased risk of disease. This scheme provides a framework for classifying cases of glaucoma in cross-sectional, population-based research.

This classification system is more specific, but is perhaps too stringent. It places the emphasis of the diagnosis on glaucomatous optic neuropathy with a reproducible visual field defect, but it also includes criteria for some eyes in which visual field testing or disc evaluation are normal. A patient with PAS or glaucoma optic neuropathy, whose chamber angle opens more than 90 degrees, will be excluded by this scheme. This system provides a framework for classifying cases of glaucoma for use in prevalence surveys; however, it does not specifically guide the management of PACG.

The best current classification in the author's opinion

These four systems classify angle-closure glaucoma in four different ways: symptoms, mechanism, angle configuration and epidemiology. We can choose different classifications for different purposes. For screening and prevention of angle-closure glaucoma, the classification based on epidemiology should be the first choice; however, in clinical practice, the classification system based on angle configuration should be used to guide treatment.

Early detection and prevention is of great importance in the control of PACG, because once the glaucomatous optic neuropathy has occurred, the damage can never be reversed. Research should be conducted to identify factors at baseline that predict who, with narrow angles, is at greatest risk of developing either acute or chronic angle closure glaucoma and, ultimately, significant loss of visual field and central vision. Once such factors are identified, more appropriate screening and treatment recommendations can be made. The classification based on epidemiology proposed by Foster[6] is very helpful for the screening of PACG. As to the treatment of PACG, classification based on angle-closure configuration proposed by Wang[5] is more practical and could guide the treatment of PACG.

When managing cases of angle-closure, the anatomic configuration of the chamber angle should be evaluated by gonioscopy and UBM, followed by miotic and laser therapy. After treatment, the peripheral chamber angle should be re-evaluated. Finally, treatments such as iridoplasty or trabeculectomy should be considered. In summary, the best current classification, in the author's opinion, is a combination of classification based on epidemiology and on the angle configuration.

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Screening for angle-closure glaucoma

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Blindness from angle-closure glaucoma worldwide

It has been calculated that 6.7 million people worldwide have been irreversibly blinded as a consequence of glaucoma.[1] Among the 67 million people suffering from primary glaucoma globally, half are estimated to have primary angle closure glaucoma (PACG). Thus, screening people at risk (people with occludable angles) and prevention of the occurrence of PACG is of considerable importance in terms of public health worldwide.

Tests for screening PACG

Eyes with primary angle closure tend to share certain biometric characteristics. These include a shallow central anterior chamber depth (ACD), thick lens, a relatively anteriorly positioned lens, small corneal diameter, short axial length, and small radius of curvature.[2-4] Among these, shallow ACD is regarded as the cardinal risk factor in most racial groups and several instruments that aim to detect a shallow ACD have been tested as candidates for screening for PACG.

Oblique flashlight test

The oblique flashlight test uses a penlight held parallel to the plane of the iris on the temporal aspect of the eye, and the shadow cast on the nasal iris is estimated. The chief advantages of this technique are that it is low in cost and is said to be easy to use by non-ophthalmologists in population screening. In a study performed in China, where the eyes were measured by the oblique flashlight test and graded according to the standard photos, a sensitivity of 91.7% and a specificity of 91.5% was shown to detect the occludable angle.[5] However, these promising results have

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proven difficult to replicate; the test did not give the same combination of high sensitivity and specificity for detection of angle-closure in a rural population in Taiwan.[6]

Axial anterior chamber depth (ACD) measurement

Measurement of the axial anterior chamber depth (ACD) can be performed in a noninvasive manner, and is relatively quick and easy to perform on a large number of subjects, compared with gonioscopy. It has therefore been proposed as a suitable screening test for angle-closure. In a study performed in Mongolia,[7] axial ACD measurement using optical pachymetry gave a sensitivity of 85% and a specificity of 84% at a screening cutoff of less than 2.22 mm for detecting occludable angles. Similar results have been reported by other investigators. In a community setting in Greenland,[8] optical ACD measurement resulted in a sensitivity of 86% and a specificity of 88%. In rural Taiwan, ultrasonographic ACD measurement in combination with refractive status provided a sensitivity of 84% and a specificity of 83%.

However, in the Chinese population in Singapore,[9] axial ACD measurement yielded sensitivity and specificity of 75.6% and 73.7%, respectively. In this study, the definitions of disease, the age-and sex-standardized prevalence of occludable angles and angle closure were identical with those of the study conducted in Mogolian population, which gave higher sensitivity and specificity figures.[7] It has been suggested that this discrepancy is attributable to the difference in relationship between axial ACD and rate of peripheral anterior synechia (PAS) in different populations. In Mongolian people, PAS were very uncommon in eyes with an ACD > 2.5 mm. Below this level, the proportion of eyes with PAS increased steeply. In contrast, there is a gradual, incremental increase in the rate of PAS across the entire range of ACD in Singaporeans, thereby, in subjects with deeper ACD, the rate of PAS exceeded that seen in Mongolians.[10] This difference, together with the discrepancy in the performance of axial ACD measurement between the two studies supports the suggestions that non-pupillary block mechanisms may play a significant role in the pathogenesis of angle-closure in some groups of East Asian people.[11,12]

Limbal chamber depth (LCD) measurement

The limbal chamber depth (LCD) is usually assessed using the van Herick technique.[13] In this method, a thin slit-beam is focused on the cornea and anterior chamber perpendicular to the temporal limbus. An optical section viewed from the nasal aspect at an angle of 60-degrees. A grading of the peripheral ACD is expressed as a proportion of corneal thickness. A grade-I angle corresponds approximately to a peripheral chamber depth (PCD) < 1/4 corneal thickness (CT), a grade II-angle to PCD of 1/4 CT, a grade III-angle to PCD of ¼ to ½ CT, and a grade IV-angle to PCD ≥ one CT.

Recently, a modification of this grading was developed[14] and has been tested for mass screening.[9,14] This method employed the same technique, in which the slit lamp is used to examine the peripheral ACD, and describe this as a proportion of peripheral corneal thickness. The modification differs by having seven grades (0%, 5%, 15%, 25%, 40%, 75%, and ≥ 100%) instead of the traditional four grades for the van Herick test.

In a recent population-based study of Chinese residents of Singapore,[9] the modified LCD measurement performed well in the detection of occludable angles. A a screening threshold of LCD ≤ 15% (equivalent to the traditional 'grade 1 [PCD <1/4 corneal thickness]') gave a sensitivity and specificity of 83% and 88% respectively, with a positive predictive value of 45.3% in the 50-year old and older population, which means that approximately one in two of those who were abnormal on screening would have an occludable angle. In this study, axial ACD was also measured using ultrasound. The performance of ACD as a screening tool was not as good as that of LCD estimation. The modified LCD grading scheme showed similar results in a previous study performed in a Mongolian population,[14] yielding a sensitivity of 84% and specificity of 86% for detection of occludable angles.

Slit-lamp grading of the mid-peripheral angle

More recently, a new method of assessing the anterior chamber angle was developed by Hong *et al*.[15] This method assesses the mid-peripheral angle. Using a slit-lamp, a very narrow, vertical beam of light, is projected to create a line connecting the limbus at 6 o'clock to the pupil margin. The beam is off-set at an angle of 30 degrees from the sagittal plane. On the inferior surface of the iris, the point at which the thickness of the cornea (CT) is equal to the depth of the anterior chamber (ACD) is identified. The distance from the corneal limbus is described in terms of the corneal thickness (CT). For example, Grade 2 indicates the distance from point at which ACD = CT to the corneal limbus equals twice the corneal thickness. The greatest advantage of Hong's grading method is that it can actually measure the chamber 'angle' (not 'depth') using the concept of arctangent. The second advantage is that the system is not affected by the corneal thickness, in contrast to Van Herick's grading, which is directly affected by the corneal thickness. Another advantage is that Hong's method can be used to measure the anterior chamber angles in all quadrants.

It has been found that Hong's grading score is significantly correlated with the Van Herick limbal chamber depth grades and Scheie gonioscopic grading. Furthermore, this method showed a better, or at least equal, efficacy to differentiate between people with positive or negative dark-room prone-position test (DRPT) compared to Van Herick or gonioscopic grading methods.[15]

So far, the efficacy of this test for screening PAC has not been tested in a population-based study. However, the simplicity and its ability to differentiate DRPT (+) and DRPT (-) patients implicates the usefulness of this test as a screening tool for PAC.

Postscreening management

Once angle closure has been detected, laser iridotomy should be performed, as a safe and effective prophylactic treatment to prevent progression to ACG. Laser iridotomy was shown to be effective in widening the drainage angle and reducing elevated IOP in Mongolian people.[16]

Prospect

The high prevalence of primary ACG in Greenland Inuit has been well documented. In this population, the proportion of blindness due to ACG was reduced from 64% in 1962 to 9% over 37 years following a systemic program of ACD measurement as well as Van Herick testing in older Inuit, followed up by gonioscopy, and if necessary, prophylactic iridectomy or laser iridostomy. These data strongly suggest that early detection of occludable angles and prophylactic laser iridotomy are probably effective methods in the prevention of ACG, at least in some populations.

However, this view may not be directly applicable to other populations, particularly in China or South-East Asia. In southern China, a non-pupil-block mechanism may account for a considerable proportion of angle-closure. Wang *et al*.[12] stated that 55% of all angle-closure in China is caused by combined pupil-block and non-pupil-block mechanisms, with only 38% being attributable to pupil block alone. More recently, researchers in Guangzhou reported considerable variation in the thickness of the iris, its level and angle of insertion, and the position of the iris insertion with respect to the ciliary body as assessed by ultrasound biomicroscopy.[17] Some types of plateau iris are associated with forward rotation of the ciliary body, but in Chinese eyes, some are more related to the innate structure of the iris. Another peculiarly Asian characteristic is that of a very thick iris thrown into prominent circumferential folds. Considering these situations, it becomes clear that conventional YAG laser iridotomy is unlikely to prevent progression of angle-closure. For some of these structural variations, other preventive treatments will need to be devised such as broad surgical iridectomies or laser iridoplasty.

Detection may present similar obstacles as treatment. Measurement of axial ACD by itself will not be an adequate screening test for angle-closure. UBM technology, Scheimpflug photography,and optical coherence tomography (OCT) are increasingly being used examine the living architecture of the anterior chamber. It may be possible to adapt these high-tech imaging devices to become screening tools for large numbers.

In Mongolia, YAG peripheral iridotomy was effective in preventing progression of PAC.[16] Almost half of those with established PACG required no further treatment to control the intraocular pressure. On the basis of this previous work, a randomized controlled trial of screening for angle closure was started several years ago by Nolan and Mongolian colleagues.[18] A total of 4725 people aged 50 years and above were randomized to an intervention or a control arm. Existing glaucoma was detected and all optic discs were photographed before the two arms continued. In the intervention arm, 685 subjects who were screened out by measurement of ACD then progressed to a full ophthalmic examination with gonioscopy. Of these, 156 were treated with laser iridotomy. The follow-up has been completed. The result of this trial will determine if ACG can be prevented and whether a nationwide screening program of the older population for angle-closure should be recommended for Mongolia.

Available evidence suggests that ACG is preventable. Early detection of primary angle-closure appears to be a realistic objective in future prevention of blindness programs in Asia. However, there are considerable variations in the pathogenesis of ACG in different populations. Hence, mechanisms causing angle-closure, potential screening tools, and effectiveness of prophylactic iridotomy will need to be determined for each population at risk.

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Gonioscopy

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Introduction

Gonioscopy is one of the most important standard clinical examinations to diagnose the types of glaucoma, especially in case of elevated intraocular pressure (IOP).[1-5] Although many supportive instruments, such as ultrasound biomicroscopy (UBM), have been introduced, gonioscopy offers the most information about the aqueous outflow system in the anterior chamber angle of both angle-closure and open-angle glaucomas. A correct diagnosis is essential for the decision of a therapeutic strategy, because the treatment for a certain type of glaucoma is not always effective or sometimes even a contra-indication for other types of glaucoma. In this chapter, the methods and principle of gonioscopy, findings and assessment of iridocorneal angle structures in normal and affected eyes are discussed.

Methods and principle of gonioscopy

There are two types of contact lenses for gonioscopy: (a) goniolenses for direct gonioscopy; and (b) gonioprisms for indirect gonioscopy. The original diagnostic goniolens is known as the Koeppe lens,[6] and several lenses are improved for use in infantile eyes, such as the Richardson-Shaffer lens and the Layden lens. The goniolens allows direct visualization of the chamber angle and is useful for glaucoma surgery including goniotomy, goniosynechialysis and trabeculotomy. Widespread goniolenses are the Swan-Jacob lens and the Thorpe lens; both are domed goniolenses with a handle, to be used on patients in a supine position. On the other hand, indirect gonioscopy is conveniently performed with the slit-lamp biomicroscope and permits rapid gonioscopy as a routine clinical examination. To master the use of gonioprism is also needed for the laser treatments of open-angle glaucoma patients. The Goldmann three-mirror lens[7] is one of the most common gonioprisms, with one mirror for gonioscopy, and two other mirrors for retinal

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examination. Ritch's trabeculoplasty four-mirror lens was developed to magnify the view for laser treatment, and contains convex lenses over two mirrors. Zeiss[8] and Posner four-mirror lenses are inclined at 62 degrees and 64 degrees, respectively, allowing visualization of the entire circumference of the anterior chamber angle without rotation. Several gonioprisms with a small contact lens diameter, such as the Zeiss lens[8], the Sussmann lens[9] and the Iwata lens,[10] can be used for indentation gonioscopy, which is an essential technique to detect peripheral anterior synechia in eyes with an extremely narrow angle.[11] The methods and principle of viewing the anterior chamber angle are shown below.

Direct gonioscopy

Direct gonioscopy is performed with a 50-diopter concave goniolens placed on the cornea of a patient in the supine position. The space between the inner surface of the lens and the cornea is filled with a solution, such as saline or methylcellulose. To view the fine structure of the anterior chamber angle, the optical problem 'critical angle' should be solved. When the light ray coming from the chamber angle approaches the cornea-air interface, the total light ray shall be reflected back into the anterior chamber, if the oblique angle exceeds the critical angle, about 46 degrees, for the cornea-air interface. The solution to this problem is to use a contact lens with similar refraction index, to neutralize the corneal refractive power, and eliminate the optical effect of the front corneal surface. The anterior curve of goniolenses is designed such that the critical angle is not reached, so the light ray is refracted at the contact lens-air interface, instead of being internally reflected (Fig. 1). The examiner usually holds the gonioscope in one hand, and a portable slit-lamp in the other. In the case of ocular surgery, an assistant may be needed to move the goniolens to the desired position, but coordination of the direction of the patient's gaze, the lens position and the surgeon's vantage point requires considerable practice.

Indirect gonioscopy

Indirect gonioscopy is performed at the slit-lamp microscope using a mirrored contact lens. The lens of gonioprism neutralizes the corneal refractive power, and the mirror allows indirect visualization of angle structures. A contact lens with a similar refraction index can eliminate the cornea optically, and allow the light ray from the chamber angle to pass through the cornea-contact lens as well as contact lens-air interfaces, in the same manner as described for direct gonioscopy (Fig. 1). A mirror positioned within the gonioprisms may reflect these light rays at nearly a right angle to the contact lens-air interface and allows a straight-ahead vantage point for viewing the angle structures with the slit-lamp biomicroscope. With indirect gonioscopy, the anterior chamber angle appears inverted as it is reflected by the gonioprism mirror. The examiner's view is a reflection of structures 180 degrees away, *i.e.*, a gonioprism mirror positioned superiorly views the inferior angle, a gonioprism mirror positioned temporally views the nasal angle, and so on. Two different types of gonioprisms, the Goldmann[7] and the Zeiss,[8] are generally used in indirect gonioscopy. Goldmann-type gonioprisms are easier to use, because they keep the globe stationary and afford better control during examination. This

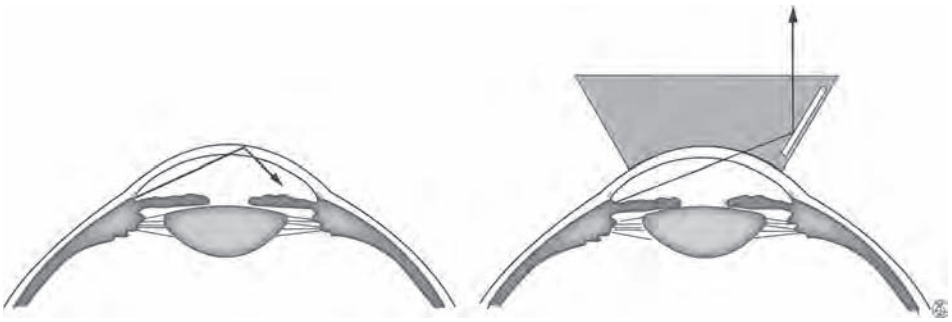

Fig. 1. Principle of indirect gonioscopy. A: Diagram of light ray which originates from the anterior chamber angle, exceeds the critical angle at the cornea-air interface, and is totally internally reflected. B: Diagram of light ray which originates from the anterior chamber angle, passes through the cornea-goniolens interface, and is reflected by a goniomirror. (From: *see* Reference 3)

is an advantage over the Zeiss lens, which does not create a suction effect and therefore requires continued effort to correct for drift. However, the suction effect is not altogether beneficial, since it also distorts the anatomic relationships of the iridocorneal angle and can open a closed angle, causing the examiner to miss the diagnosis of angle-closure glaucoma. Occasionally, the view of the iridocorneal angle is obscured by the convexity of iris root. In such cases, one can see 'over the hill' to angle structures with patient's help to gaze toward the direction of mirror.

One of the major advantages of Zeiss[8] and Iwata[10] gonioprisms is that they can be used for indentation gonioscopy,[11] by oppressing the central cornea and artificially widen the narrow anterior chamber angle. A smaller diameter of these lenses enables direct contact with the anterior corneal surface, depression of the central part of the cornea, and displacement of aqueous humor peripherally and therefore the iris root posteriorly. When the iridocorneal angle is optically closed, this maneuver enables differentiation of reversible appositional closure from irreversible peripheral anterior synechia (PAS). Folds in Descemet's membrane may be often present during indentation and may distort, but not obscure, the observation of iridocorneal angle structure. In these cases, the intensity of indentation may be too much, or the gonioprisms may be positioned too close toward the corneal limbus along the ocular surface. One should not press the cornea too much, and by asking the patient to gaze toward the direction of mirror, one can observe the iridocorneal angle with less indentation.

Normal gonioscopic anatomy

In order to identify the gonioscopic findings responsible for glaucoma, one should understand the anatomy of anterior segments corresponding to the gonioscopic view (Fig. 2), and normal structural variations. Starting from the iris root and progressing anteriorly toward the cornea, the following structures can be identified by gonioscopy in a normal anterior chamber angle.

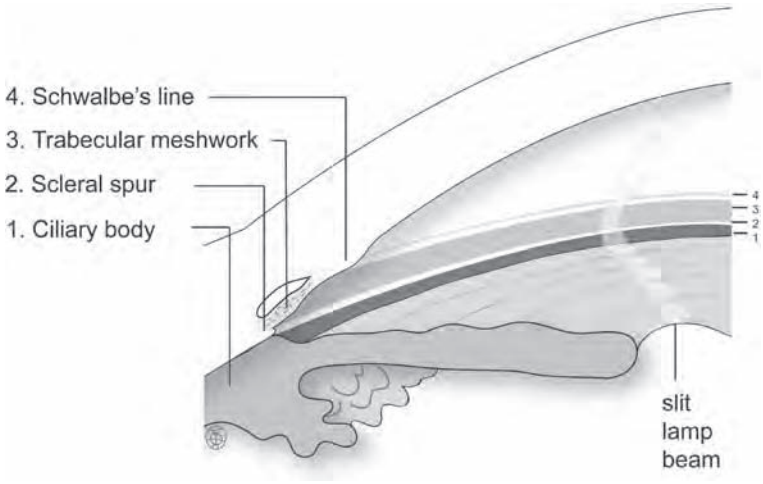

Fig. 2. Normal adult anterior chamber angle showing gonioscopic appearance (right), and cross section of corresponding structures (left). 1. Ciliary body band; 2. Scleral spur; 3. Functional trabecular meshwork (degree of pigmentation varies); 4. Schwalbe's line. (From: *see* Reference 4)

Ciliary body band

This structure is the part of the ciliary body that is visible in the anterior chamber as a result of the iris insertion into the ciliary body. The width of the band depends on the level of iris insertion, and tends to be wider in myopia and narrower in hyperopia. The color of the band is usually gray or dark brown. Occasionally, strands or lacy cords of uveal tissues are extending from the iris root towards trabecular meshwork, and are called iris processes. They appear predominantly in the nasal part, and mostly attach to the level not exceeding Schlemm's canal. If the processes are highly inserted, and dendritic or membranous appearance, one should consider developmental disorder of iridocorneal angle.

Scleral spur

This is the posterior lip of the scleral sulcus, which is attached to the ciliary body posteriorly and the corneoscleral meshwork anteriorly. It is usually seen as a prominent white line between the ciliary body band and functional trabecular meshwork, unless it is obscured by dense uveal meshwork or excessive pigment deposition. Variable numbers of iris processes may frequently be seen crossing the scleral spur from the iris to the functional meshwork. The full width of the scleral spur can be identified, except when a highly inserted iris root covers this structure in developmental glaucoma.

Functional trabecular meshwork

This is seen as a pigmented band just anterior to the scleral spur. Although the trabecular meshwork actually extends from the iris root to Schwalbe's line, it may

be considered in two portions: (a) the anterior part, between Schwalbe's line and the anterior edge of Schlemm's canal, which is involved to a lesser degree in aqueous outflow; and (b) the posterior (or functional) part, which is the remainder of the meshwork and is the primary site of aqueous outflow, especially the part immediately adjacent to Schlemm's canal. The appearance of the functional meshwork varies considerably depending on the amount and distribution of pigment deposition. It has no pigment at birth, but color develops with age from faint tan to dark brown, depending on the degree of pigment dispersion in the anterior chamber. The distribution of pigment may be homogenous for 360 degrees in some eyes and irregular in others. In the functional part of the meshwork, especially when lightly pigmented, blood reflux in Schlemm's canal may sometimes be seen as a red band.

Schwalbe's line

This is the junction between the anterior chamber angle structures and the cornea, and is located where Descemet's membrane ends in a circumferential ring of collagenous fibers. It is a fine ridge just anterior to the meshwork and is often identified by a small accumulation of pigment, especially inferiorly. If there is no pigmentation, the transition between the transparent cornea and translucent trabeculum can be better appreciated when viewed gonioscopically with a thin slit-beam projected into the iridocorneal angle at an oblique angle. The slit of light penetrates the transparent corneal tissues, appearing above Schwalbe's line as a three-dimensional parallelepiped of light. At Schwalbe's line, the figure of light collapses to a two-dimensional stripe of light on the trabecular surface.

Grading anterior chamber depth

Shaffer's classification

Shaffer's classification[12] is based on an estimate of the geometric angle formed by the iris and the corneoscleral wall at the approach to the trabecular meshwork. The iridocorneal angle is graded on a scale of 0 (closed), I (about 10 degrees), II (20 degrees), III (30 degrees) and IV (40 degrees or more) (Fig. 3). It has been found that Shaffer grade-I angles are at considerable risk of closure, either spontaneously or with provocative testing. Smudges of iris pigment on or above the trabeculum or small tentorial PAS provide strong evidence that intermittent appositional closure has taken place. Grade-II angles need cautious follow-up, because they may become shallower in the future, and grade III and IV angles are probably not at risk of angle closure.

Scheie's classification

Grading in Scheie's classification system[13] is opposite to that of Shaffer's system,[12] so special care is required to document the numeric grading of angular width. This system is based on the extent of iridocorneal angle structures visualized by the examiner. A grade-I angle is widely open, a grade-II angle allows one to see just

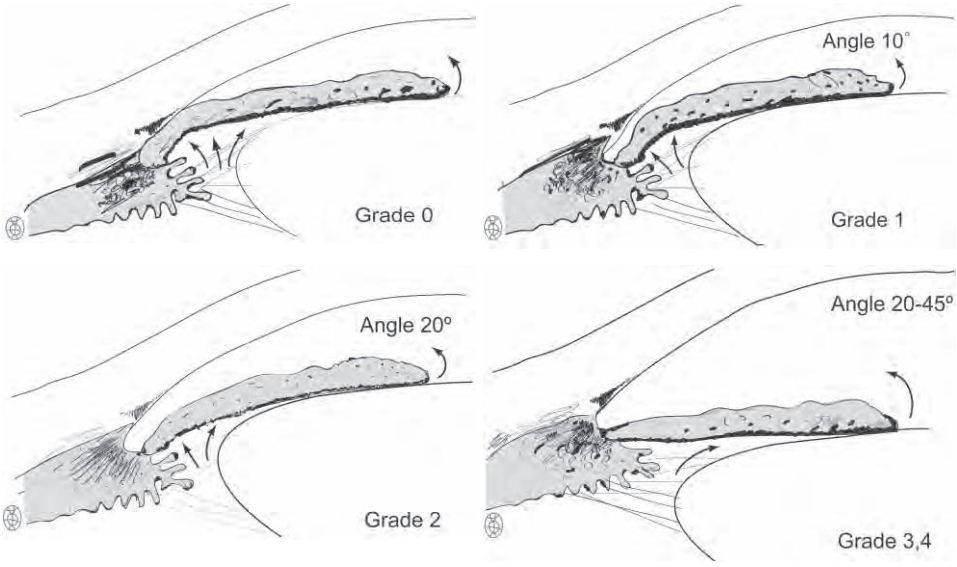

Fig. 3. Shaffer's classification system for grading anterior chamber angle depth. (From: *see* Reference 12)

to the scleral spur but not to the ciliary body. A grade-III angle allows one to see only to the anterior part of trabecular meshwork, and a grade-IV angle is closed. Interpretation of angular width is difficult in those eyes in which the iris root is narrow but open due to plateau iris configuration, and in those eyes in which the iris insertion is abnormally located at or even anterior to the scleral spur.

Spaeth's classification

Spaeth has developed a classification system that expands on the Shaffer grading of angles to include a specification of the shape of the peripheral angle and the site of the iris insertion.[14] A concave peripheral iris is denoted *q*, a regularly straight iris *r*, and a steeply convex iris *s*. The implication is that an *s* configuration of the iris brings iris tissue into closer proximity with the functional trabecular meshwork and thereby increases the risk of angle closure. Thus even an iridocorneal angle with a grade-I to -II approach may be at imminent risk of angle closure when a plateau iris configuration is present. The site of iris insertion in this system is specified as *A* if the insertion is *a*nterior to the trabecular meshwork (*e.g.*, synechial closure to Schwalbe's line), *B* if the insertion is just *b*ehind Schwalbe's line, *C* if the insertion is at the sc*l*eral spur, *D* if the angle is *d*eep with a visible face of the ciliary body, and *E* if the angle is *e*xtremely deep (Fig. 4)

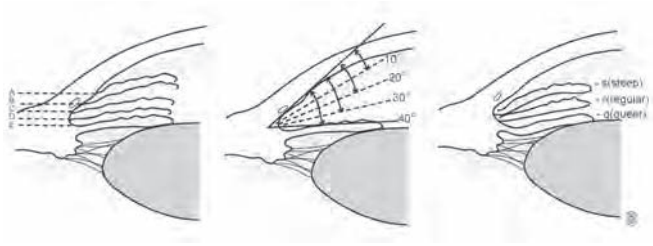

Fig. 4. Spaeth's classification system for grading anterior chamber angle depth. (From: *see* Reference 14)

Grading the degree of pigmentation

Scheie's classification of pigmentation

In childhood, pigment deposition is rarely found in the trabecular meshwork, but the intensity of pigmentation tends to increase in accordance with age. In some pathologic conditions or after undergoing ocular surgery, remarkably intense pigmentation is observed, which is helpful for diagnosing the cause of IOP elevation. Physiological pigmentation is generally denser in the lower portion, so the grade and location of the pigment deposition should be documented in gonio-chart. The color scheme of Scheie's grading system of pigmentation[13] is shown in Figure 5.

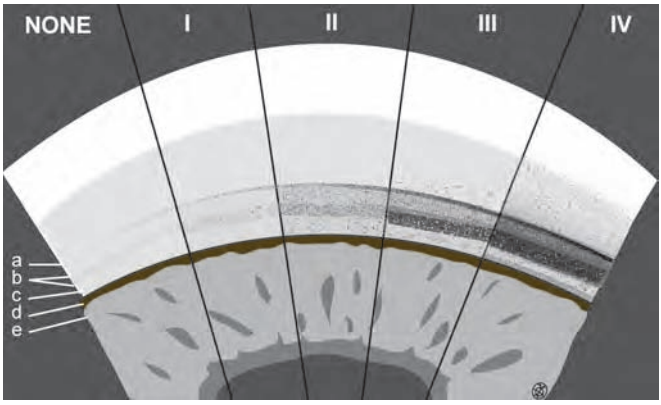

Fig. 5. Scheie's classification system for grading pigmentation of iridocorneal angle. (From: *see* Reference 13)

Gonioscopic findings of ocular disorders

Besides grading angle depth in angle-closure glaucoma (ACG), the essential aim of gonioscopy is to identify the pathological findings and estimate the causative mechanism in secondary glaucoma. (1) PAS are abnormal adhesions of the peripheral iris to the corneoscleral wall in various shapes and degrees. They are not only

caused by relative pupillary block and plateau iris configuration in ACG, but also formed as a result of iridocyclitis, iris bombe, neovascularization of iridocorneal angle, flattening of the anterior chamber, endothelial cell migration in ICE syndrome, trauma, intraocular surgery, laser trabeculoplasty and so on. Each condition presents PAS of its characteristic configuration and location, so careful gonioscopy offers essential information of the etiological mechanism. (2) Pigment deposition is not always pathological, but extremely dense pigmentation of the entire trabeculum is a characteristic finding of pigmentary glaucoma and pigment dispersion syndrome. In the eyes receiving intraocular surgery or laser iridotomy, the anterior chamber angle shows intense pigmentation. Highly pigmented trabecular meshwork with irregular PAS is observed in the eyes of patients with chronic iridocyclitis. Wavy lines of pigment deposition lying beyond Schwalbe's line in the lower portion of iridocorneal angle are seen in the eyes of patients with exfoliation glaucoma, which is named Sampaolesi's line. (3) Neovascularization (NV) of the chamber angle should be distinguished from angle vessels, which are typically broad in character, appear in short segments, do not extend anterior to the scleral spur, and do not arborize in the trabecular meshwork. NV occurs in various ischemic conditions, including diabetic retinopathy, central retinal vein occlusion, occluded internal carotid artery, extremely high IOP in secondary glaucoma, retinopathy of prematurity, tumor, and so on. Small NV seen in the eyes of Fuchs' heterochromic iridocyclitis is a valuable sign for diagnosis. (4) Nodules in the anterior chamber angle accompanied by tentorial PAS are observed in the eyes of glaucomatous uveitis such as ocular sarcoidosis. According to the origin, stage and complication, gonioscopic findings in uveitis are diversified such as nodules, diffuse pigmentation, pigment pellet, PAS, NV, iris bombe, and so on. (5) Blunt ocular trauma may produce partial or broad posterior displacement of the iris root, named traumatic angle recession. On the other hand, angle recess implies a wide ciliary body band, which is generally observed uniformly in both eyes. Injury also results in cyclodialysis cleft, which allows aqueous humor to infiltrate into the suprachoroidal space, causing hypotony. (6) The most common feature of gonio-dysgenesis is a high insertion of a flat iris root, or a wrap-around type insertion, observed in the eyes of developmental glaucoma. Another type of gonio-dysgenetic configuration is a persistent uveal cord/membrane with or without prominent Schwalbe's line, observed in the eyes of Axenfeld-Rieger's syndrome and other congenital anomalies.

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Provocative test

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Introduction

After von Graefe's first success of performing iridectomy for acute inflammatory glaucoma in 1856, Edward Curran introduced the concept of pupillary block and the importance of peripheral iridectomy for glaucoma patients with a narrow anterior chamber in the 1910s. In the 1930s, various gonioscopy techniques were explored by many physicians prior to the establishment of a standard clinical procedure. In the 1970s and 1980s, surgical iridectomy was replaced by peripheral iridotomy using Argon laser and Nd-YAG laser.[1] Studies related to provocative tests had been performed prior to the advent of peripheral laser iridotomy, because angle-closure attack may have been difficult to predict, and to improve decision-making regarding prophylactic surgical iridectomy for the fellow eye of acute angle-closure glaucoma patient. The ease and efficacy of prophylactic laser iridotomy have since reduced the need for provocative testing to be performed.

Primary angle-closure glaucoma is an anatomical disease. As patients were classified into PAC suspect, PAC, and PACG, an occludable angle was defined as an angle in which ≥ 270° of the posterior trabecular meshwork cannot be seen on gonioscopy and, therefore, appositional contact between the peripheral iris and posterior trabecular meshwork is considered possible.[2] In addition to a pupillary block, the occludability of a peripheral anterior chamber angle has been also emphasized in patients for which PAC was suspected, as well as in PAC and PACG patients. Wide variation has been observed in the prevalence of narrow or 'occludable' angles all over the world, with mean prevalence ranging from 2.2 - 47.8%.[3-5] Twenty-two percent of primary angle-closure suspects progressed to primary angle-closure with raised intraocular pressure (IOP) or synechiae over a 5-year period,[6] and 28.5% of known primary angle-closure progressed to glaucoma, as evidenced by optic nerve head damage and visual field defects over the same period.[7]

Narrow or occludable angles are an anatomical trait that predispose an individual to two potential sight-threatening conditions: firstly, an acute angle-closure attack

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as an ophthalmic emergency, which presents relatively commonly in the Western world, and secondly, a chronic angle-closure glaucoma, which is more common in Asian populations.[8] However, gonioscopy, even indentation gonioscopy, does not allow clinicians to predict the potential and progression of PACG. The dynamic complex of peripheral angle, lens, and ciliary body is not reflected in the gonioscopic findings. Therefore, it is still important to predict the occludability of a peripheral anterior chamber angle and acute angle-closure attack in the future.

Dynamics of peripheral anterior chamber angle during provocative test

The force of the dilator and sphincter muscles turn in two directions.[9] The dilator muscle extends beneath the sphincter. Early in dilation, the dilator muscle drags the sphincter posterior to the stroma around the pupil. With increasing dilation, the sphincter force becomes directed more posteriorly.[10] Thus, alpha-adrenergic agonists (especially 10% phenylephrine), which dilate the pupil through a direct effect on the dilator muscle, carry greater risk than other mydriatics. Sphincter activity can also be important in pupillary block. Mydriatics with weak cycloplegic effects (*e.g.*, 0.5% tropicamide) or a dark-room test reduces pupillary block caused by sphincter muscle paresis. This is a probable explanation of false negative results in these tests. Pupillary dilation causes the peripheral iris to be crowded circumferentially. The crowding of the iris may vary in relation to the angle, and can occlude the peripheral angle. In additional, occlusion can start around Schwalbe's line or at the bottom of the iris root.[11]

Types of provocative tests

Pharmacological provocative tests

Mydriatic (tropicamide) provocative test

A short-acting topical mydriatic with a weak cycloplegic effect (*e.g.*, 0.5% tropicamide) is instilled, and a rise in IOP of 8 mmHg or more at 1 to 2 hours is considered to be a positive result.

Pilocarpine/phenylephrine test

After initial measurement of intraocular pressure, 2% pilocarpine and 10% phenylephrine are alternately instilled three times at 1-min intervals. The phenylephrine is repeated half hourly unless the intraocular pressure rises 8 mmHg or more (positive test).[12] After approximately 90 minutes, an additional drop of 2% pilocarpine and 10% phenylephrine is instilled, and the intraocular pressure is again measured. The pressure is finally measured again 1 hour later, and the test is terminated by the instillation of 0.5% thymoxamine drops.

Nonpharmacological (physiologic) provocative tests

Dark-room provocative test

As in the most physiologic tests, mydriasis is induced by placing the patient in a dark room for 60-90 minutes. A rise in pressure of 8 mmHg or more is considered positive when verified by identification of angle-closure on gonioscopy.

Dark-room prone position test

The patient is laying in a dark room in a prone position for 1 hour with instructions to close both eyes but remain awake to avoid the miosis of sleep. A rise of 8 mmHg with gonioscopic confirmation is considered a positive result. This is the most popular of the nonpharmacologic tests. In some subjects, increases in intraocular pressure of ≥ 8 mmHg, 6 or 7 mmHg, and ≤ 5 mmHg are considered to be positive, suspected positive, and negative, respectively.[13] After surgical iridectomy, approximately 7.5% of tests are positive, which suggests that these positive results may be due to a pupillary block with a slight shift of the lens or other factors.[14]

Ultrasound biomicroscopy dark-room provocative test

Gonioscopy does not guarantee a determination of whether an angle is occludable.[15] High frequency ultrasound biomicroscopy (UBM) with high resolution imaging of the anterior segment *in vivo* may be ideally suited for evaluating the anatomy and pathophysiology of anterior segment disease.[16] Palvin *et al*. used UBM as a helpful method in dark-room provocative testing to demonstrate the occludability of peripheral angle.[17] The provocative test of angle-closure performed in a dark room or in a dark room with a prone position for 1 hour is performed by confirming the appositional angle-closure with UBM.

Clinical value of provocative tests

Among 129 predominantly Caucasian individuals with narrow angles or anterior chamber depth less than 2 mm and no symptoms, eight patients (6.2%) developed an acute angle-closure attack with symptoms during a mean of 2.7 years.[18] In addition to issues with the fellow eye after acute PAC attack, the ophthalmologist is frequently faced with a difficult decision of whether or not to perform prophylactic laser iridotomy or laser peripheral iridoplasty. There is still no guideline of management for an individual that is PAC suspect or a PAC patient that has a narrow anterior chamber angle using the van Herick technique. A narrow anterior chamber angle determined by the van Herick technique does not indicate the occludability of angle. Gonioscopy is the current clinical standard for assessing the risk of PACG. However, it is a subjective technique; no uniform gonioscopic criteria exist for identifying the angles that require treatment.[2,19] Therefore, a combined screening method using anterior chamber depth by van Herick and gonioscopy have a low positive predictive value for the development of acute angle-closure attack.

Although iridotomy has proven to be effective as prophylaxis against attacks of

acute angle-closure glaucoma (ACG),[20] it is disputable whether it is effective for long-term control of IOP in eyes with chronic asymptomatic ACG, especially in Asians, [21,22] because the peripheral anterior synechiae can progress even after laser iridotomy.[23] It has been found that laser peripheral iridoplasty is useful in the management of PACG, plateau iris syndrome, and even in phacomorphic glaucoma. However, the long-term effect has not yet been proved.

There are clinical limitations in the application of provocative tests for patients. First, provocative tests may be hazardous, and may trigger an acute angle-closure attack. Therefore, non-pharmacological provocative testing is recommended more often than pharmacological testing. Second, provocative tests are time-consuming and difficult to apply to patients in a routine manner. Third, the sensitivity and specificity of such tests are not high, 48-90% at best, so even when they are negative, they may not rule out the possibility of angle-closure.

Primary angle-closure glaucoma is determined by dynamic movement of the iris. Relative pupillary block and iris crowding in the peripheral AC angle are involved in the development of angle-closure in primary angle-closure glaucoma. In addition to the pupillary block component, it is very important that appositional angle-closure is confirmed morphologically. However, appositional angle-closure is difficult to visualize using conventional methods for observing the anterior chamber angle, such as gonioscopy. Even indentation gonioscopy, another important diagnostic technique for PACG, is theoretically difficult to prove appositional closure.[24] The topography of the iris root is related to the pattern of the appositional angle-closure.[11] Appositional angle-closure can start at around Schwalbe's line or at the bottom of the iris root. Provocative tests such as the dark-room and prone position test have been used for confirming appositional angle-closure and estimating the pupillary block component in angle-closure glaucoma.[25] Even when negative (an increase in IOP of less than 8 mmHg in a dark-room prone position test), it can be clinically useful to visualize appositional angle-closure using various techniques, including UBM and anterior segment OCT. The literature related to the sensitivity and specificity of the provocative test was mostly written prior to the introduction of techniques for visualizing peripheral angles, including UBM and especially OCT. The AC angle dynamics and appositional angle-closure can be visualized with UBM or OCT during provocative tests. UBM has the advantage of allowing the visualization of both peripheral angle and ciliary body morphology, while anterior segment OCT is easy to perform without an eye cup and is more valuable than UBM because it allows for the precise evaluation of peripheral AC angle dynamics in a physiologic position, and does not require the patient to remain in a supine position. Therefore, OCT might be a promising method for screening patients at risk for PACG.

Conclusion

With the possibility that blindness will occur, it is very important to follow up PACG patients closely and to decide which intervention to use at the proper time: such interventions include laser peripheral iridotomy and laser peripheral iridoplasty, as well as others. Although it does not definitively predict angle-closure attack, conversion to PAC glaucoma, or the progression of glaucoma, provocative tests may be valuable for examining the PAC suspect individual and PAC patients when

combined with the new techniques for visualizing the peripheral AC angle such as UBM or OCT; this is especially true of nonpharmacological provocative test.

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Ultrasound biomicroscopy

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Introduction

In the treatment of glaucoma, testing the anterior chamber angle is essential. While gonioscopy is the most common method, ultrasound biomicroscopy (UMB)[1] is useful for assessing areas that cannot be examined by gonioscopy, such as the ciliary body, inside the iris, the posterior chamber, inside filtering blebs following filtering surgery, or the outflow tract for aqueous humor inside the sclera or cases that are difficult to examine using gonioscopy, such as narrow-angle glaucoma. This chapter describes UBM images for common glaucoma conditions.

UBM Characteristics

The following characteristics make UBM suitable for the treatment of glaucoma: 1) a high resolution of 50 μm at a frequency of 50 MHz; 2) cross-sections of the angle can be captured without lighting, so changes in iris shape with or without light can be ascertained; 3) observation is independent of corneal opacity; 4) dynamic changes can be recorded; 5) the technique is noninvasive and can be repeated numerous times; and 6) UBM images can be automatically quantified. However, unlike gonioscopy, UBM cannot detect mild differentiation failure, pigmentation, inflammatory exudate or neovascularization in the angle. Hence, following slit-lamp microscopy or gonioscopy, UBM should be performed to compensate for the shortcomings of gonioscopy.

Equipment

The present article deals with UBM model 840 (Humphrey Instruments, San Leandro, CA) and UD-1000/6000 (UBM probe: UD-6010) (Tomey Corporation, Nagoya, Japan)[2] (Fig. 1). Both systems are based on water immersion and use an eye cup

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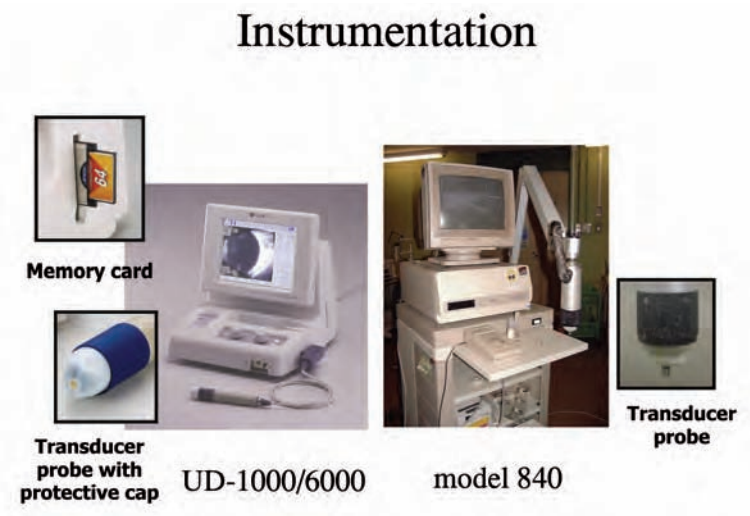

Fig. 1. Left: UD-1000/6000 ultrasound machine and UD-6010 probe. A protective cap covers the probe tip. Right: Model 840 conventional UBM machine and probe.

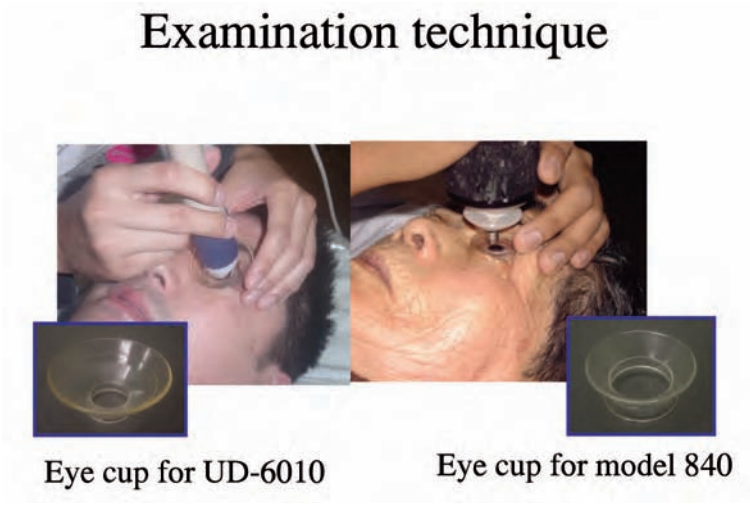

Fig. 2. Left: Testing using UD-6010 and an eye cup. Right: Testing using Model 840 and an eye cup.

for testing (Fig. 2). Ultrasonic frequency is 50 MHz for Model 840 and 40 MHz for UD-6010. Model 840 uses mechanical linear scanning while UD-6010 uses magnetic linear scanning, and while no marked difference is apparent, the scanning range is 5 mm wide × 5 mm deep for Model 840 and 9 mm wide × 6 mm deep for UD-6010. The UD-6010 is thus capable of capturing a larger area from the pupillary

margin to the ciliary body, and allows easy analysis of the posterior pole past the ciliary body. With UD-1000/6000(probe:UD-6010), static images can be stored using compact flash cards, facilitating subsequent imaging processing.

UBM Images

Quality of UBM images

If a probe is positioned perpendicular to the cornea, UBM images show the anterior and posterior surfaces of the cornea as clear reflective lines, along with the scleral spur of the angle (Fig. 3). If the probe is not positioned well, these structures cannot be clearly seen. This is an important point in assessing image quality.

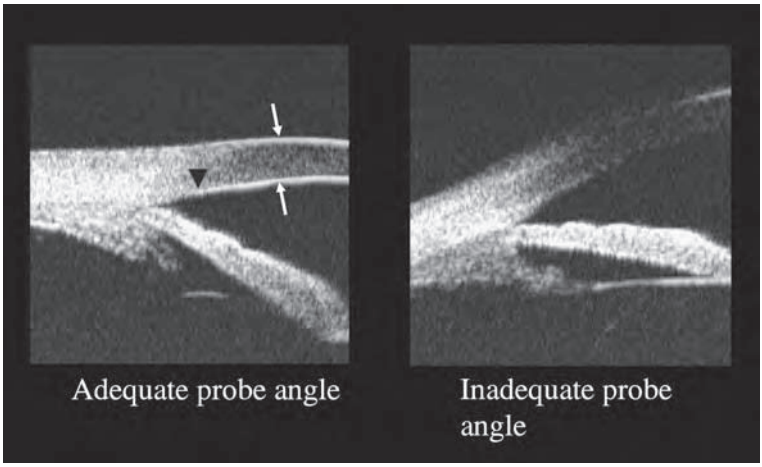

Fig. 3. UBM image clarity and probe angle. Left (UBM image): With proper probe angle, clear reflective lines are seen for the anterior and posterior surfaces of the cornea (arrows). Schwalbe's line is apparent (black triangle). Right (UBM image): Improper probe angle.

Comparison of gonioscopy and UBM images

An UBM-image of the angle merely represents a cross-section, and at this point of time, only captures a single cross-section of 360° of the angle at a specific point in time. UBM does not replace gonioscopy, and comparison of results with slit-lamp microscopy or gonioscopy remains important. Figure 4 compares images from a normal eye between UBM and gonioscopy. With UBM, the scleral spur is the only reference point seen on all images, and represents the cross point between inner surface of the cornea and the boundary between ciliary body and sclera. If the probe angle is appropriate, Schwalbe's line can also be seen nearest to the angle recess of the high-intensity reflective line for the inner surface of the cornea. On normal UBM images, the iris is mildly convex in the anterior direction or flat, and the ciliary sulcus is seen between ciliary processes and iris.

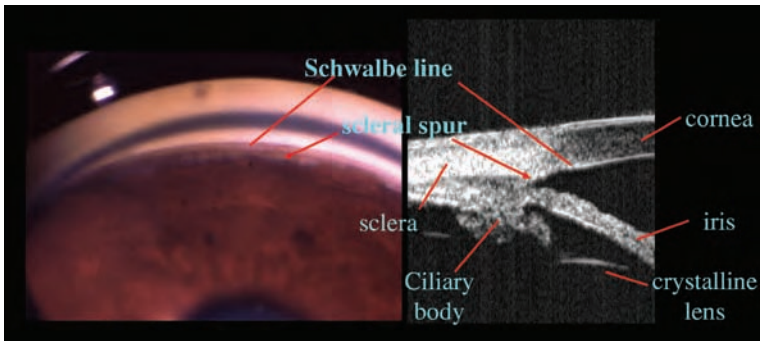

Fig. 4. Comparison of gonioscopy and UBM images.

UBM findings in relative pupillary block

Unlike gonioscopy, which requires lighting, the angle can be observed by UBM without lighting, as is the case with a darkroom test. Figure 5 shows UBM images of relative pupillary block (PRB) captured using the two machines for UBM. With both machines, the iris was pushed up due to increased posterior segment pressure by pupillary block. In addition, angle closure that is absent in bright light may occur in the dark due to pupillary dilatation. In this example, the ciliary sulcus was clearly seen.[3]

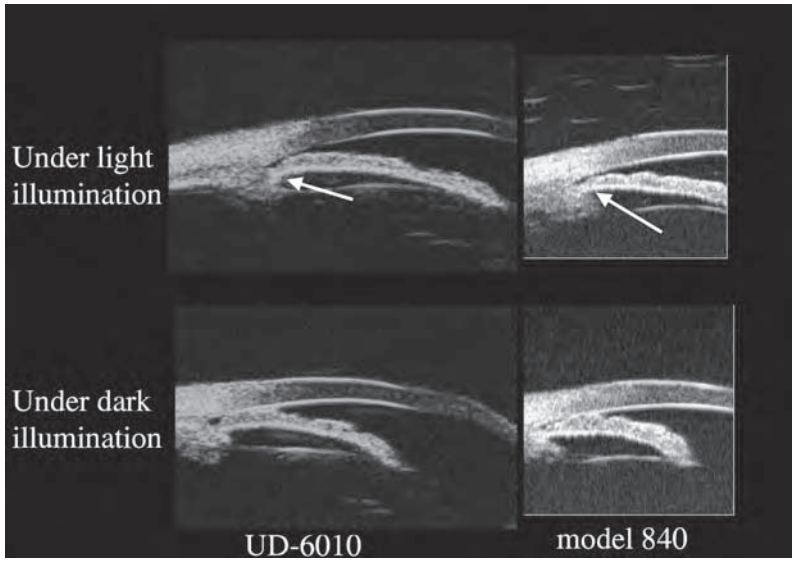

Fig. 5. UBM images of relative pupillary block captured using the two machines in a patient with primary angle-closure glaucoma. Above: with lighting. Below: without lighting. The ciliary sulcus is apparent (arrow).

UBM findings of plateau iris configuration

Figure 6 shows plateau iris configuration (PIC), and while the anterior segment was not shallow, unlike pupillary block, the iris was flat and displayed a thick root. Due to the ciliary process that rotated anteriorly, the iris was pushed up and the ciliary sulcus was lost. In this patient, gonioscopy was difficult to perform, and because the shape of the ciliary body was unique, UBM was extremely useful as a diagnostic tool.[4]

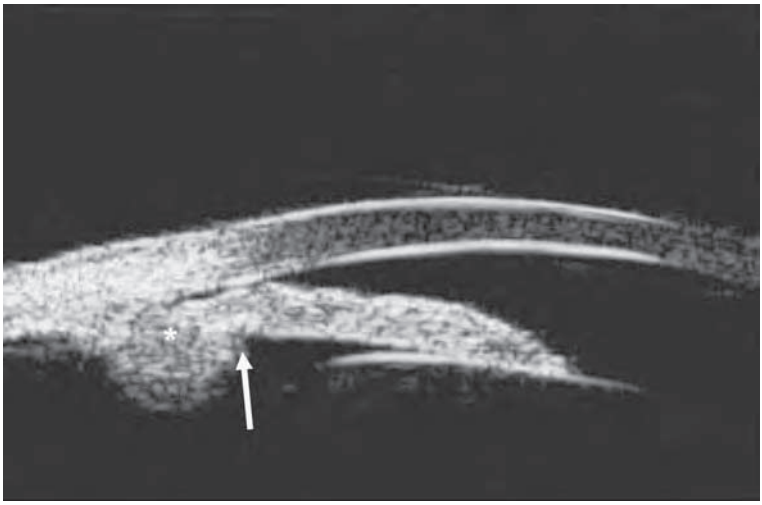

Fig. 6. UBM image of plateau iris configuration in a patient with primary angle-closure glaucoma. The ciliary sulcus is unclear (arrow). The ciliary body can be seen (asterisk).

UBM images before and after laser iridotomy in relative pupillary block

Figure 7 compares UBM images before and after laser iridotomy (LI). LI widened the angle recess, and the iris that initially arched anteriorly became flattened. In this manner, changes in the iris and angle due to surgery can be seen on cross sections.[5]

Indentation UBM

Indentation UBM is an imaging technique to observe the angle by compressing the contralateral cornea using the gonioscopy probe to move the aqueous humor and push down on the iris. With this technique, apposition closure can be differentiated from adhesive closure. The same effect can be achieved by observing the eye by applying slight pressure using a small eye cup, and we have thus performed pressure UBM using an eye cup with a built-in compressor to safely and easily compress the cornea.[6] When angle closure is detected by UBM with lighting,, use of this eye cup allows differentiation of appositional angle closure (Fig. 8) from synechial angle closure (Fig. 9). In other words, compression cannot push and

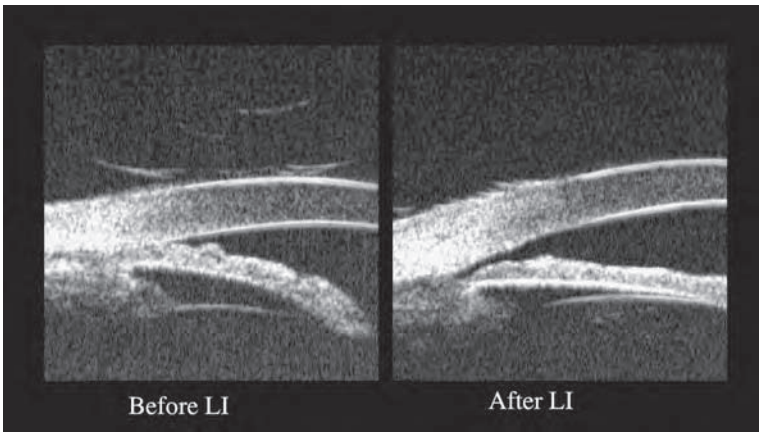

Fig. 7. UBM images before and after laser iridotomy (LI) in a patient with relative pupillary block.

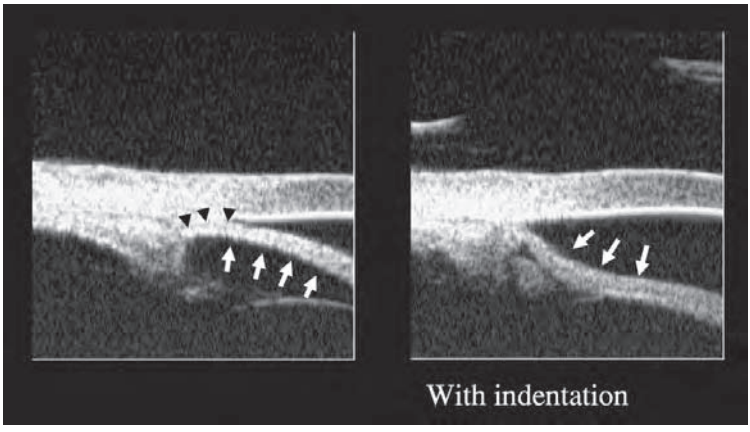

Fig. 8. Indentation UBM in a patient with appositional angle closure. Appositional closure (triangles). Direction of aqueous humor pressure (arrows).

widen iridocorneal adhesion during synechial angle closure. In the case of PIC, compression does not change the shape of the iris root, but state of the angle recess can be observed (Fig. 10).[7]

Iris observation

Angle closure caused by umbrella iris can increase ocular pressure. Whether umbrella iris is caused by a cyst or solid tumor can be assessed on UBM cross-sections of the iris (Fig. 11).[8] Reverse pupillary block can be seen in patients with pigment dispersion syndrome, where the iris is flexed posteriorly (Fig. 11).[9]

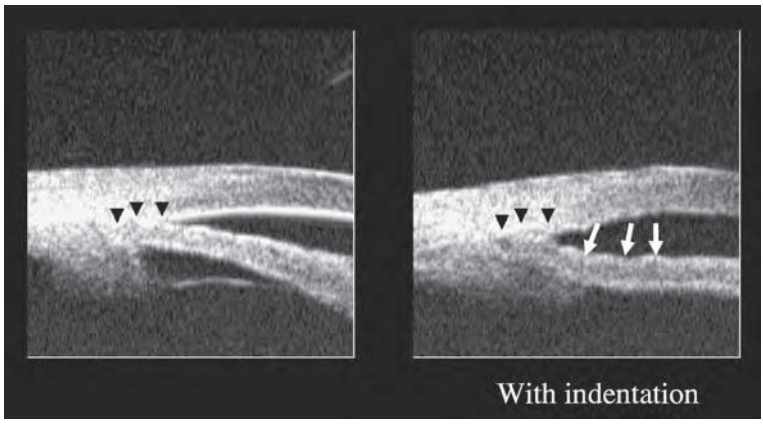

Fig. 9. Indentation UBM in a patient with synechial angle closure. Synechial closure (triangles). Direction of aqueous humor pressure (arrows).

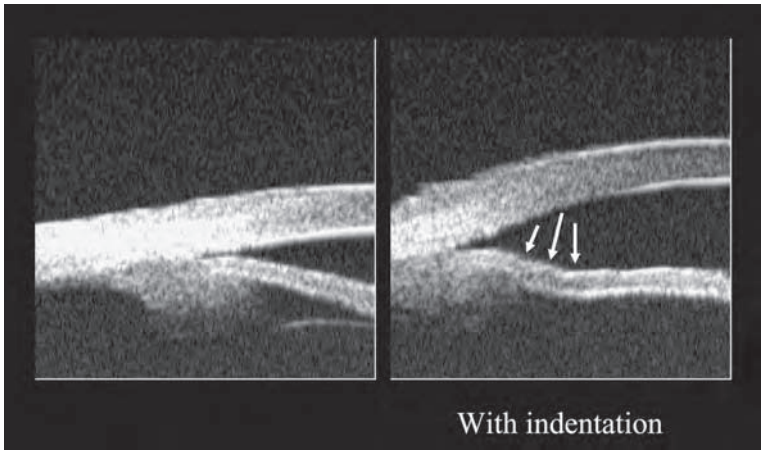

Fig. 10. Indentation UBM in a patient with plateau iris configuration. Direction of aqueous humor pressure is shown (arrows).

UBM images following filtering surgery

Following trabeculectomy, the outflow tract under a scleral flap, inside the filtering bleb, the ciliary body and back surface of the iris cannot be observed optically, but these structures can be assessed by UBM (Figs. 12-14) . This is useful for postoperative management, reoperation and transconjunctival needling procedure under a scleral flap.[10] In addition, following trabeculectomy with MMC, filtering blebs are usually assessed by slit lamp microscopy, but this is sometimes difficult. With UBM, patients can be classified into the following four types: low-reflective type where intensity inside a filtering bleb is low, and ocular pressure control is favorable; high-reflective type where intensity of a filtering bleb is high, and the bleb

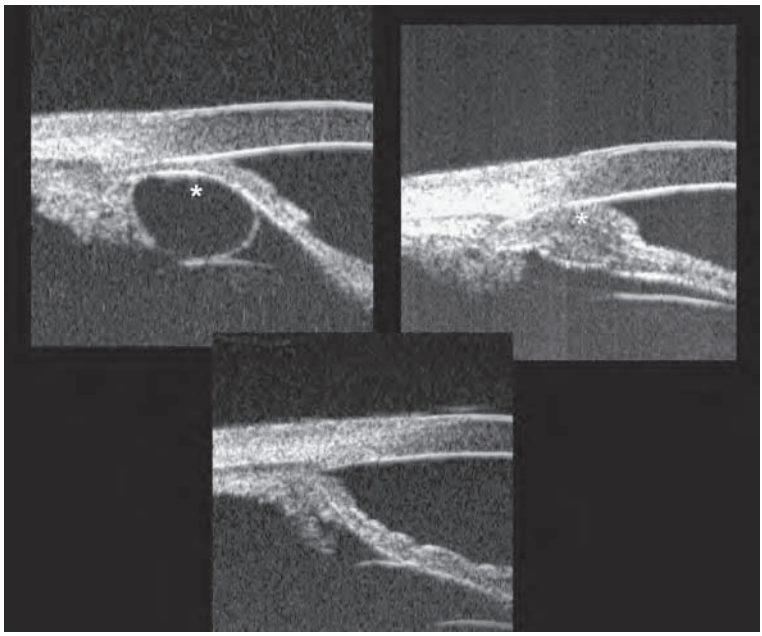

Fig. 11. Above left: Umbrella iris caused by an iris cyst (asterisk). Above right: Umbrella iris caused by an iris tumor (asterisk). Below: A posteriorly flexed iris in pigment dispersion syndrome (From Dr. Hiroshi Ishikawa's data).

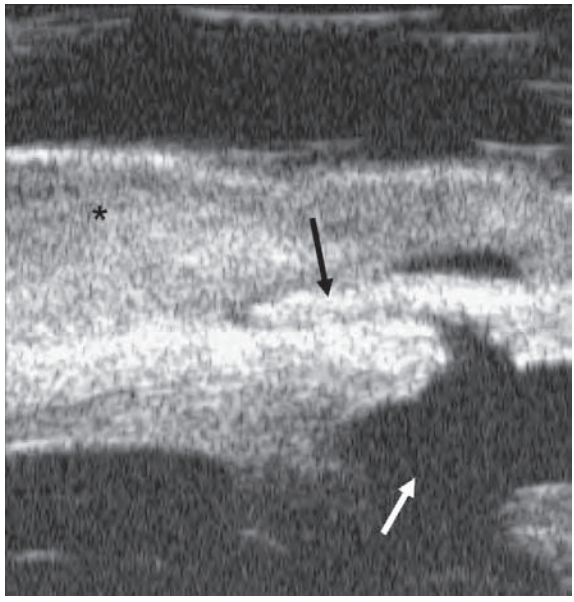

Fig. 12. A UBM image following trabeculectomy. Scleral flap (black arrow), iridectomy (white arrow) and conjunctival filtering bleb (asterisk) are shown.

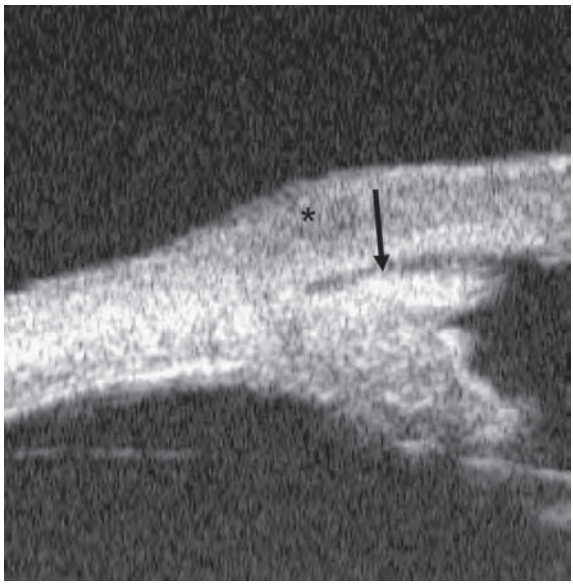

Fig. 13. A UBM image following trabeculectomy. The aqueous humor outflow tract under the scleral flap (arrow) and high-intensity filtering bleb (asterisk) are shown.

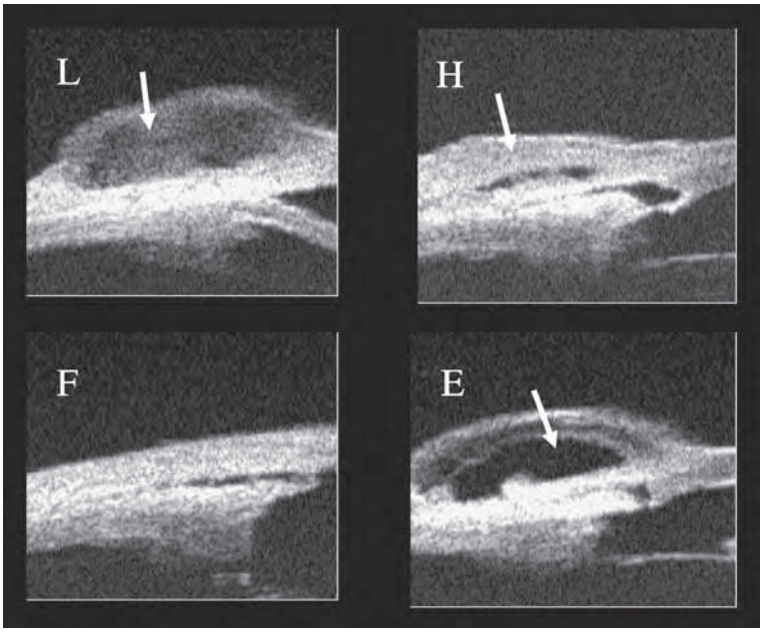

Fig. 14. UBM images of filtering blebs following trabeculectomy with MMC. L: low reflective; H: high reflective; F: flattened; and E: encapsulated.

is clearly seen; flattened type where a filtering bleb is not seen, and ocular pressure control is poor; and encapsulated type where tissue under the scleral flap is scarred and surrounded by Tenon's capsule, blocking function as a filtering bleb[11]. This type of information is important for planning therapy for patients with poor ocular pressure control.

UBM images of the ciliary body

As the ciliary body is difficult to observe through the pupil, cross-sectional imaging by UBM is useful for pathological clarification and therapy planning. Figure 15 shows a patient with malignant glaucoma[12] following filtering surgery. The anterior segment was shallow, and the ciliary process rotated anteriorly and then compressed against the iris. Supraciliary effusion was confirmed. Figure 16 shows a patient with uveal effusion complicated by narrow angle and supraciliary effusion. UBM is also useful for assessing ciliary body dissection or rupture caused by other blunt traumas, supraciliary effusion at low ocular pressure following filtering surgery,[13] or dissection of the ciliary body or choroid in Harada's disease[14] or following laser photocoagulation in diabetic retinopathy.

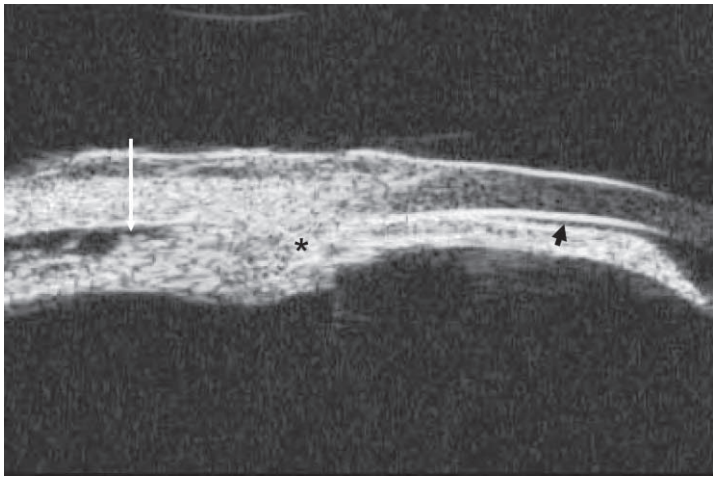

Fig. 15. A UBM image of malignant glaucoma. Supraciliary effusion (white arrow), anterior segment loss (black arrow) and ciliary body (asterisk) are shown.

Quantitative UBM

Measurement of the degree of anterior chamber angle opening is significant in the therapy of closed angle glaucoma. Estimating an angle opening by gonioscopy is subjective and generally gross. But UBM is much better suited for objective measurements and evaluation of the anatomy and pathophysiology of the anterior segment. Pavlin *et al.*[3] proposed several parameters to measure the anterior segment. Angle opening distance (AOD500) is defined as the length of the line drawn from the point

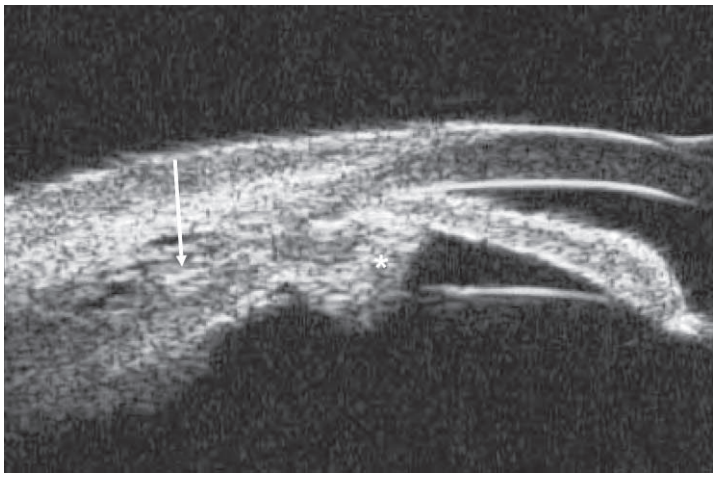

Fig. 16. Shallow anterior segment and narrow angle in a patient with uveal effusion. Supraciliary effusion (arrow) and ciliary body (asterisk) are shown.

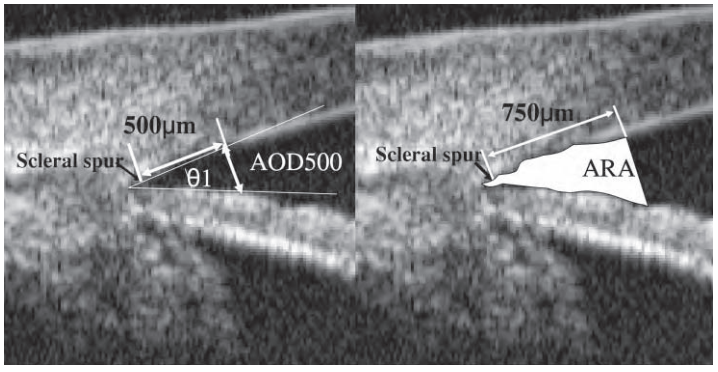

Fig. 17. Parameters to measure the angle. Left: Angle opening distance (AOD500) and angle (θ1). Right: Angle recess area (ARA).

on the endothelial surface 500 μm anterior to the scleral spur to the iris surface perpendicular to the corneal endothelial surface. The trabecular/iris angle (θ1) is measured with the apex in the iris recess and the arms passing through the point 500 μm from the scleral spur and the point perpendicularly opposite on the iris. In addition to these, Pavlin *et al.*[3] presented other parameters to measure the iris and ciliary body configuration, such as the iris thickness, trabecular-ciliary process distance (TCPD), the angle at which the iris leaves the lens surface (θ2), etc.

Ishikawa *et al.*[15,16] introduced angle recess area (ARA) to estimate the anterior chamber angle width. ARA is defined as a triangular area bordered by the anterior iris surface, corneal endothelium, and a line perpendicular to the corneal endothelium drawn from a point 750 μm anterior to the scleral spur to the iris surface. This method faithfully reflects irregularities of iris contour and curvature.

Summary

UBM is capable of generating high-resolution cross-sectional images of the anterior segment and depicting areas that cannot be detected optically. This technique can also be performed without lighting, which is important for testing narrow angle glaucoma. UBM is thus useful for the diagnosis and treatment of glaucoma, but should be combined with techniques such as gonioscopy to maximize usefulness.

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Anterior segment optical coherence tomography

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Introduction

Primary angle closure glaucoma is a visually destructive type of glaucoma that accounts for approximately half of the worldwide blindness caused by glaucoma.[1-5] It is estimated that primary angle closure glaucoma may blind up to five times more people in China than primary open angle glaucoma.[4] The closure of the anterior chamber angle (ACA) seems to be the primary abnormality leading to intra-ocular pressure (IOP) increase and glaucomatous optic neuropathy.[6] The contact between the peripheral iris and the trabecular meshwork may impair aqueous humor drainage from the anterior chamber due to the mechanical obstruction of the functional trabecular meshwork, and/or by abnormalities at the ultra-structural level of the trabecular meshwork due to the prolonged friction/apposition of the iris against the angle wall.[7] Therefore, the detection of angle closure represents an essential step in the prevention of blindness due to angle closure glaucoma, as interventions such as iridotomy and iridoplasty might halt the angle closure process preventing the development of glaucomatous optic neuropathy.

The current reference standard for evaluating ACA configuration is indirect gonioscopy, which is an examination that can be easily and quickly performed by properly trained ophthalmologists. Gonioscopy is not expensive, as it does not require sophisticated and supplementary equipment, but only requires a gonioscopy lens and a slit-lamp. However, gonioscopy requires considerable skill and experience, and mastering gonioscopy can be considered a demanding task with a relatively long learning curve. For some general ophthalmologists, gonioscopy may represent a cumbersome exam which may be neglected in busy daily clinical practice. Furthermore, gonioscopy is a subjective examination in which the ACA assessment may be affected by many variables, such as inadvertent pressure on the cornea, and by light exposure onto the pupil during the examination. Previous studies have shown that even experienced examiners demonstrated only moderate agreement in determining the angle width.[8,9]

In face of the difficulties and limitations of gonioscopy, other methods have been developed in attempt to obtain more objective measures of the ACA. Ultrasound

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biomicroscopy (UBM), Scheimpflug photography, and optical coherence tomography of the anterior segment (AS-OCT) are capable of obtaining high-resolution imaging of the anterior segment. These instruments are able to perform objective measures of the ACA and provide a convenient way to document the ACA configuration. This chapter will focus on the ACA assessment by the AS-OCT.

Anterior segment optical coherence tomography

Optical coherence tomography (OCT) was reported for the first time in 1991,[10] and it was first used in ophthalmology for imaging the posterior segment of the eye. Analogous to ultrasonography, this technology obtains in-vivo cross-sectional images of tissues, but uses light waves to obtain the reflectivity profile of the structure under investigation. Posterior-segment OCT uses a 830 nm superluminescent diode as the light emitting source.[10] No contact medium is required for obtaining the images, as the difference in optical impedance, the refractive index between air and tissue, is not as large as the difference in acoustic impedance between air and tissue.[10] However, since light travels much more quickly than sound, the optical echoes cannot be measured directly. The time delay of the returning light reflection in OCT is determined indirectly by the method of low coherence interferometry, in which the reflection returning from the tissue is allowed to interfere with light that has traveled a known path length (reference arm).[11] The information of different depth of the retina is acquired as a sequence of samples, over time, by changing the path length of the reference arm (time-domain OCT).[11] This technology permitted a particular easy way to obtain real time imaging of the posterior segment structures, and proved to be helpful for elucidating pathological process of some macula diseases, monitoring changes in the macula and retinal thickness, and imaging the vitreoretinal interface, optic nerve head, and retinal nerve fiber layer.

Since 1994, many studies have used optical coherence tomography to image the anterior segment of the eye.[12] To improve the visualization of the anterior segment structures, AS-OCT technology had to undergo several modifications. The two major problems in AS-OCT imaging was that the original 830 nm superluminescent diode failed to penetrate the sclera, and the time for image acquisition was too slow and compromised the quality of the images.[13, 14] The wavelength of light used by the AS-OCT was changed to 1310 nm, due to the fact that this wavelength of light provides an increased penetration through scattering ocular structures, such as the sclera and the iris, resulting in a more detailed visualization of the ACA morphology.[13-15] Furthermore, the 1310 nm wavelength of light is strongly absorbed by water in the ocular media and, therefore, only 10% of the light incident on the cornea reaches the retina.[16] These properties improved retinal protection and allowed the use of higher-power illumination that, in turns, enabled high-speed imaging. The use of a high-speed imaging system reduced motion artifacts in imaging the anterior segment, reduced examination time, allowed the realization of rapid survey of relatively large areas, and enabled imaging dynamics ocular events.[17]

The current version of AS-OCT (such as the Visante OCT, Carl Zeiss Meditec, Dublin, CA) uses a scanning technology 40 times faster than previous anterior segment OCT systems. This technology permits image acquisition at a rate of eight frames per second (2000 A-scans per second) with a transverse resolution of 60 μm, and an axial resolution of 10-20 μm. Furthermore, the use of wide-field scanning

optics (16 mm) and deep axial scan range (8 mm) permitted AS-OCT to cover the entire anterior chamber in one image frame.

All these modifications permitted AS-OCT to acquire good quality images of the anterior segment structures. This device has been used for the evaluation of the cornea morphology,[18,19] to plan the sizing of phakic intra-ocular lenses,[17,20] and to assess the morphology of trabeculectomy blebs.[21-23] From the angle closure perspective, AS-OCT may prove to be useful for assessing the risk of angle closure, particularly because this technology represents a quick and non-contact method capable of acquiring real-time cross-sectional images of the ACA. For these reasons, AS-OCT could be easily integrated into the ancillary exams performed in clinical practice and/or used as a screening tool to prevent blindness from PACG.[15,24] Until the current time, just a few studies have evaluated AS-OCT performance in assessing the ACA configuration. This chapter will provide an overview of previous studies evaluating AS-OCT technology.

Devices and image acquisition

Two devices using anterior segment OCT technology for obtaining images of the anterior segment have been approved by the Food and Drug Administration (United States) until the current time: Visante OCT (Carl-Zeiss Meditech, Dublin, CA, USA), and Slit-lamp OCT (Heildelberg Engineering, Dossenheim,Germany).

Visante OCT system has a motorized chin rest, and an internal fixation target that can be adjusted according to the subject's distance refraction, permitting image acquisition in a non-accommodate state (Fig. 1). Its custom-software uses an intuitive user interface and acquires ACA scans in a highly automated way. In addition, it is capable of acquiring single, dual and quadruple line cross-sectional scans of the ACA at the same time. The current SL-OCT system is incorporated into a slit-lamp, with the scanner unit permanently attached to the slit-lamp illumination. During image acquisition, the patient should firmly place his chin and forehead against the headrest of the slit-lamp, and focus on a point at a distance of two to three meters. The examiner has to position the slit-lamp light beam onto the location to be scan, and precision adjustments to center the image are done manually by moving the joystick of the slit-lamp. The OCT measurement beam is then used to scan from the top to the bottom of the slit produced by the slit-lamp light beam.

After acquisition, the scanned images of both devices have to be processed by a custom-software. This image processing software ('dewarping' software) compensates for index of refraction transition at the air-tear interface and the different group indices in air, cornea, and aqueous to correct the physical dimensions of the images.[17] In contrast to UBM, both AS-OCT devices are able to image the entire cross-section of the anterior segment in a single image frame (Fig. 2).

It is important to note that the infrared light used by both AS-OCT systems cannot image the anterior segment through the eyelids. Thus, the superior and inferior eyelids must be gently moved out of the way before obtaining AS-OCT scans of the superior and inferior ACA, respectively. While the prototype versions of the Visante OCT did not permit imaging the superior quadrant, a properly trained examiner is capable of imaging the superior and inferior ACA with the commercial available device. The image processing performed by the custom 'dewarping' software of the Visante OCT does not seem to require the acquisition of images of the entire cross-section of the anterior segment at one single image frame. There-

Fig. 1. Visante-OCT taking an image of a patient's anterior chamber angle.

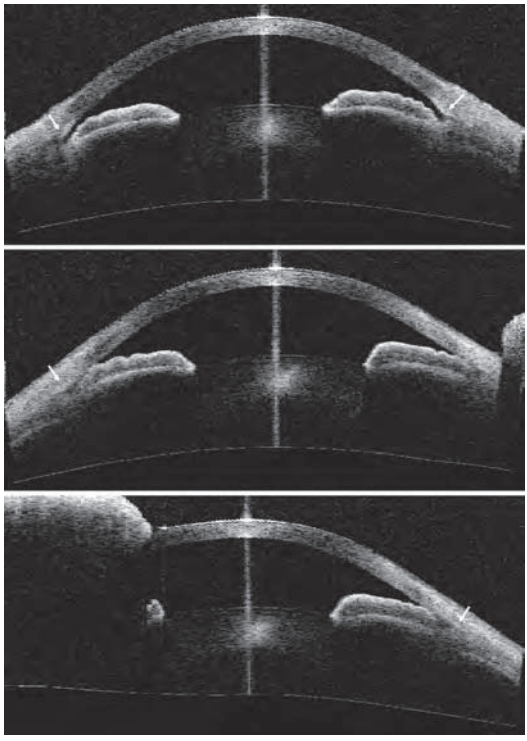

Fig. 2. Visante-OCT images of the anterior chamber angle (ACA). Figure 2A shows the horizontal scan imaging the entire cross-section of the anterior segment in one image frame (ACA of the nasal and temporal quadrants). The ACA is open in both quadrants. Figures 2B and 2C show vertical scans of the ACA of the inferior and superior quadrants, respectively. The ACA is closed in both quadrants. The arrows indicate the location of the scleral spur.

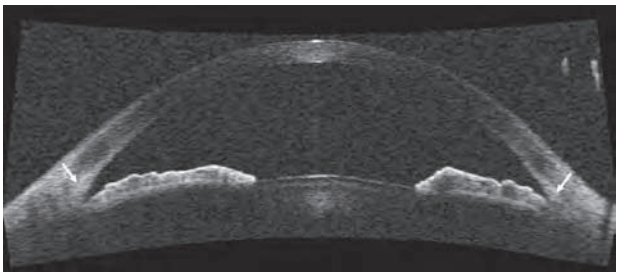

Fig. 3. SL-OCT image of the anterior chamber angle of the nasal and temporal quadrants. The arrows indicate the location of the scleral spur.

fore, the superior and inferior ACA can be imaged separately, avoiding technical difficulties in exposing both superior and inferior ACA at the same time. However, due to the design of the Visante OCT, pulling the inferior and superior eyelids may be cumbersome, particularly on the left eye. On the SL-OCT, since the device is mounted on a slit-lamp, the eyelids are easily moved out of the way. However, it seems that a full cross-section image of the anterior segment has to be acquired in order to SL-OCT images be properly processed by its custom-software. Thus, imaging the superior and inferior quadrant on a single scan requires the examiner to pull both superior and inferior eyelids out of the way at the same time, which might also be considered a cumbersome task. Figures 2 and 3 provide examples of anterior segment images obtained by both devices.

Anterior chamber angle analysis with AS-OCT

The ACA on AS-OCT images can be evaluated qualitatively by subjectively determining the presence of an open or closed ACA, and quantitatively by objectively measuring ACA parameters, such as angle opening distance first described by Pavlin *et al*.[25] Similarly to UBM imaging analysis, the interpretation of the ACA configuration in AS-OCT imaging (qualitatively and quantitatively) is dependent on determining the location of the scleral spur. The scleral spur usually is located on the widest part of the sclera,[25] appearing like an inward protrusion of the sclera where some of the fibers of the longitudinal bundle of the ciliary muscle attaches. It represents an anatomical landmark which reveals the relative location of the trabecular meshwork, which is located approximately between 250-500 μm above the scleral spur along the angle wall.[25]

A previous study compared the performance of UBM and a prototype version of the AS-OCT in detecting eyes with narrow ACA.[15] The authors of this study stated that the scleral spur were more distinct in OCT images, although no further information was provided.[15]

Reproducibility

Previous studies have evaluated the reproducibility of ACA measurements in AS-OCT images.[26,27] Muller *et al*.[27] evaluated the impact of measurement variability on

the reproducibility of ACA parameters in images obtained with a prototype version of the SL-OCT device in 18 eyes of nine healthy volunteers. Evaluating measurement variability is important because AS-OCT measurements can be influenced by the subjective determination of anatomical landmarks (location of the scleral spur). Two observers measured the ACA parameters five times in images obtained on the nasal and temporal quadrants, and a high intra and inter-observer reproducibility in ACA measurements was observed. Of note, the reproducibility analysis was restricted to ACA images obtained in the nasal and temporal quadrants, and only evaluated subjects with open ACA – in whom the location of the scleral spur may be more easily detected, corroborating for the high reproducibility.

Radhakrishnan *et al*.[28] evaluated the reproducibility of ACA measurements in AS-OCT images acquired using a prototype version of Visante OCT. The short-term reproducibility analysis evaluated the intra-observer and inter-observer reproducibility in imaging the ACA in the nasal, temporal, and inferior quadrants of 20 subjects, and the intra-observer long-term reproducibility analysis evaluated the ACA in the same quadrants of 23 subjects. Most of the subjects included in this study had a narrow ACA (33/43), and intraclass correlation coefficient was calculated as a measure of reproducibility. As a third independent examiner measured ACA parameters, this study aimed to focus in the variations induced by the image acquisition and not on variations induced by measuring the ACA parameters. These authors observed that the intra and inter-observer short term reproducibility in measuring all ACA parameters varied from good to excellent in the nasal and temporal quadrants, and from poor to good in the inferior quadrant. Similar results were observed in the intra-observer long term reproducibility analysis. The authors hypothesized that the lower reproducibility observed on the ACA parameters of the inferior quadrant were due to the characteristics of the particular OCT prototype device used in the study, such as the lack of space between the instrument and the patient's face – making it difficult to pull down the inferior eyelid. Furthermore, approximately 12% of the ACA images of the inferior quadrant were excluded from the analysis due to inadequate quality.

It is important to note that these previous studies evaluated the reproducibility of ACA parameters measured on prototype versions of AS-OCT, and further modifications incorporated in newer versions might have altered its reproducibility. Thus, as an important step on the validation process of a new technology, the reproducibility of ACA parameters measured on images acquired using the commercial available AS-OCT remains to be evaluated.

Comparison with UBM

The images provided by both AS-OCT devices are similar to those obtained with UBM. Some of the advantages of the AS-OCT imaging over the UBM are that OCT technology permits a non-contact method of imaging the anterior segment, not requiring immersion of the eye in fluid. Besides, the ability of AS-OCT to image the entire cross-section of the anterior segment in one image frame permits this device to assess and document the profile of the iris, and its relationship to the other anatomical parameters of the eye. However, in contrast to UBM, the infrared light used by AS-OCT is blocked by pigment of the iris, which precludes the assessment of the structures located behind the iris. Furthermore, due to degradation of the light by the sclera, the AS-OCT is not capable of fully imaging the ciliary body.

Radhakrishnan *et al*.[15] compared the accuracy of classification of narrow ACA using quantitative imaging by UBM and a prototype version of Visante OCT. This study evaluated 17 normal subjects and 7 subjects with a narrow ACA determined by gonioscopy. The assessment of the ACA on images obtained in the nasal and temporal quadrants was performed quantitatively by measuring several ACA parameters (angle opening distance, angle recess area, trabecular-iris space area, trabecular-iris contact length). The diagnostic performance of UBM and AS-OCT in detecting narrow ACA was assessed by comparing the areas under the receiver operating curve. The authors observed that both methods had similar discriminatory power to detect eyes with narrow ACA. Both devices provided similar mean values for various ACA parameters, and when a statistically significant difference was present (angle recess area at 500 μm and 750 μm, trabecular-iris space area at 750 μm), UBM tended to give smaller measurements.

Comparison with gonioscopy

Nolan *et al*.[24] evaluated the performance of a prototype version of Visante OCT in detecting angle closure when compared to with gonioscopy in 200 Asian subjects (71% with clinical diagnosis of primary angle closure). In this study, AS-OCT obtained ACA images of the inferior, nasal, and temporal quadrants in light and dark conditions, and gonioscopy angle width was graded using the Spaeth classification for each quadrant in low lighting conditions. An ACA was classified as closed on gonioscopy if the posterior trabecular meshwork could not be seen. A closed ACA on AS-OCT imaging was defined by the presence of any contact anterior to the scleral spur between the iris and angle wall. Angle closure in more than 1 quadrant was detected by AS-OCT in 71% of patients and by gonioscopy in 49.5% of the patients. When performed in dark conditions, AS-OCT identified 98% of those subjects found to have angle closure on gonioscopy, and also detected angle closure on 44.6% of those found to have open angles on gonioscopy.

Thus, AS-OCT tended to identify angle closure in more eyes than gonioscopy. If gonioscopy was considered as the reference standard, AS-OCT would have demonstrated a quite low specificity in detecting angle closure.

Before becoming widely accepted in clinical practice, new technologies have to be validated against existing standard. However, potential limitations of the reference standard technique may impact the evaluation of the new technology. Therefore, potential limitations of the new technology, and also of the existing standard have to be scrutinized in attempt to perform a comprehensive comparison between the two techniques.

Nolan *et al*.[24] have hypothesized that the disagreement between these two techniques may be partially explained by the fact that while AS-OCT uses infrared light and does not require contact with the eye, inadvertent indentation and excessive light during gonioscopy may artificially open the ACA. The authors stated that despite efforts to use as little light as possible and to minimize the length of the slit beam during gonioscopy, the anterior segment and pupil are exposed to light during the exam. This small amount of light may be sufficient to open up an angle that would be closed in the dark. Regarding the distortion of the anterior segment by gonioscopy, the authors stated that placing the Goldmann gonioscopy lens on the globe would possibly cause some displacement of anterior segment structures, resulting in opening of the angle in some quadrants. Furthermore, excessive tilting of the lens, in an attempt to see over the apex of a very convex iris, also may

cause indentation of the cornea, leading to widening of the angle, and the mistaken impression that the angle is wider than it is. On the other hand, pressure from the upper lid on the edge of the gonioscope may result in inadvertent mechanical distortion of the cornea, making the drainage angle appears artificially narrower.

In addition, Nolan *et al*.[24] also hypothesized that the anatomical landmarks considered in the two techniques may not be the same. The authors stated that whereas with gonioscopy it is possible to visualize landmarks such as Schwalbe's line and the posterior area of the trabecular meshwork, the anterior boundaries of the trabecular meshwork are less easy to identify with AS-OCT. Because the position of the scleral spur is easier to determine and the trabecular meshwork lies anterior to this structure, the definition of angle closure on AS-OCT was defined as the presence of any contact between the iris and angle structures anterior to the scleral spur. In gonioscopy, angle closure required apposition between the iris and entire extent of the posterior trabecular meshwork. In short, this difference in definitions could have resulted in AS-OCT detecting more eyes with angle closure than gonioscopy.

It seems that particularities in the methods of assessing and interpreting the ACA configuration of each technique may account for some of the discrepancies between gonioscopy and AS-OCT. Longitudinal studies will be required not only to determine if eyes classified as closed only by AS-OCT are indeed at risk of developing angle-closure glaucoma, but also if those classified as open by AS-OCT and closed by gonioscopy will ever develop the disease.

Future improvements on AS-OCT technology include the development of software to provide ACA parameter measurements automatically, reducing human error when taking measures. Another area of research aims to represent the anterior segment structures imaged by AS-OCT in three dimensions.[20]

Conclusions

In summary, AS-OCT technology represents a quick and non-contact method of obtaining real-time cross-sectional images of the ACA using infra-red light. These characteristics may prevent some of the possible inherent limitations related to ACA assessment by gonioscopy. AS-OCT may be useful for assessing the risk of angle closure. However, as a new technology, AS-OCT has to prove to be an accurate and reproducible instrument for ACA assessment. Longitudinal prospective studies are required to determine the relative values of AS-OCT findings in the management of patients with angle closure. Until then, it is important to emphasize that gonioscopy is a required feature of an eye examination, and glaucoma cannot be evaluated or patient treated properly without it being performed.[29]

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New approaches to visualize the anterior chamber angle

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Why do we need a new technique for gonioscopy?

Routine gonioscopy that utilizes a slit-lamp has some drawbacks for visualizing an angle that is narrow or suspicious of potential closure. Light from the slit-lamp is usually too bright for use in this situation, causing contraction of the peripheral iris and subsequent widening of an occludable angle or flattening of a plateau iris. Bright light also causes constriction of the pupil, which obscures other structures behind the lens, *e.g.*, ciliary body processes (CBP). The distorted view of the angle caused by bright light could bring the observer to an inaccurate conclusion of regarding the angle width and may eventually lead to incorrect diagnosis and treatment. To overcome these drawbacks, two modified techniques will be described: gonioscopy with a slit-lamp using dim light (dim light slit-lamp gonioscopy) and gonioscopy in the dark with infrared light (dark-room infrared gonioscopy (DIG)).

Dim light slit-lamp gonioscopy

By reducing the intensity of light from the slit-lamp, we can visualize the angle in a more physiological state, because under normal conditions our eyes are not exposed to such a high light intensity. With dimmer light, the pupil will be larger and other structures behind the lens such as the CBP could be demonstrated. The detailed procedures of dim light slit-lamp gonioscopy are as follows.

1. A Zeiss-type-4-mirror gonioprism is recommended. This allows indentation gonioscopy to be performed.
2. A narrow slit with reduced light intensity is used.
3. For visualizing the angle recess, the patient is asked to look toward the mirror. Conversely, the examiner could tilt the mirror towards the angle.
4. For visualizing the CBP behind the lens equator, the patient is asked to look away from the mirror or the examiner could tilt the mirror away from the angle. The focus of the slit-lamp should be behind the lens equator.

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5. The superior and inferior mirrors are usually easier to use for visualizing the CBP and should be assessed first.
6. While narrowing the slit and reducing the light intensity, the examiner should look not only at the angle but also through the lens, especially behind the lens equator. The focus should be relatively posterior.
7. To examine the angle structures, the gonioscopic mirror should be tilted towards the angle of interest or the patient should be asked to look towards the gonioscopic mirror. Attention should be given to visualizing the pigmented trabecular meshwork (TM), both with the dim light and when the light is intensified. The examiner could judge an angle to be opened, closed, or occludable by the dynamics of visualization of the pigmented TM.
   – If the pigmented TM could not be seen with both normal and dim light, the angle is 'closed'.
   – If the pigmented TM could be seen with both normal and dim light, the angle is 'opened'.
   – If the pigmented TM could be seen with normal light but not with dim light, the angle is 'occludable'.
8. If the lens is situated at a relatively anterior position, the CBP could be seen through the lens equator.[1] This may be facilitated by tilting the gonioscopic mirror away from the angle of interest or by asking the patient to look away from the mirror. Dimming the light and narrowing the slit beam will also aid in visualization of the CBP, since the pupil will become larger (Fig. 1).

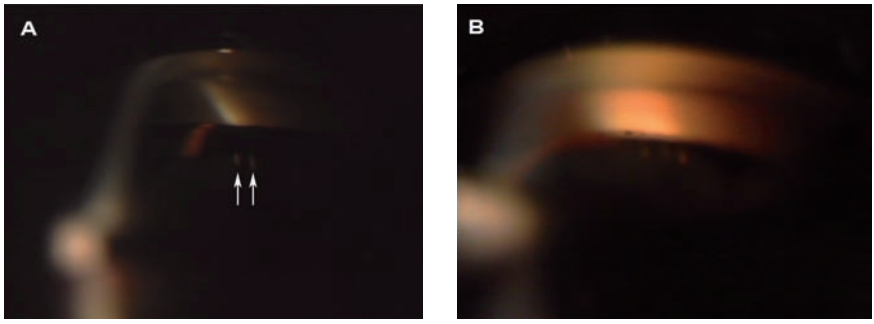

Fig. 1. A: Visualization of ciliary body processes (arrows) by dim light slit-lamp gonioscopy. With small pupil size, the intensity of light should be reduced and the slit is narrowed. B: When the pupil is larger, the ciliary body processes can be demonstrated with higher intensity of light.

The problem with this technique is that angle structures can be difficult to see with dim light. The pupil also can be too small for examiners to look through the structures behind the lens. These problems can be eliminated by using infrared light or gonioscopy with 'no light'.

Dark-room infrared gonioscopy (DIG)

With infrared light, gonioscopy can be performed without 'light'. This means that we can eliminate all of the bright light of the slit-lamp, and will make it possible to

look at the angle and its dynamics in the dark, as well as its response during light or accommodative stimulation. For example, an occludable angle may be opened using normal gonioscopy with a slit-lamp, but it is closed in the dark when using infrared gonioscopy. This may be used as objective evidence to determine whether the angle is occludable. At present, there is no commercial instrument available for infrared gonioscopy. By modifying existing instruments, infrared gonioscopy is possible. Two techniques can be used for DIG: an infrared video camera and the IR mode of HRA (Heidelberg Retinal Angiograph).

DIG with infrared video camera

Infrared gonioscopy can be performed using a cheap, commercially-available infrared video camera. Any infrared video camera that is capable of focusing close-up can be used. The camera that we used was manufactured by Fujiko (model FK-308), and incorporated a Samsung 1/3 inches B/W (0 lux) CCD and a f 3.6 mm/F 2.0

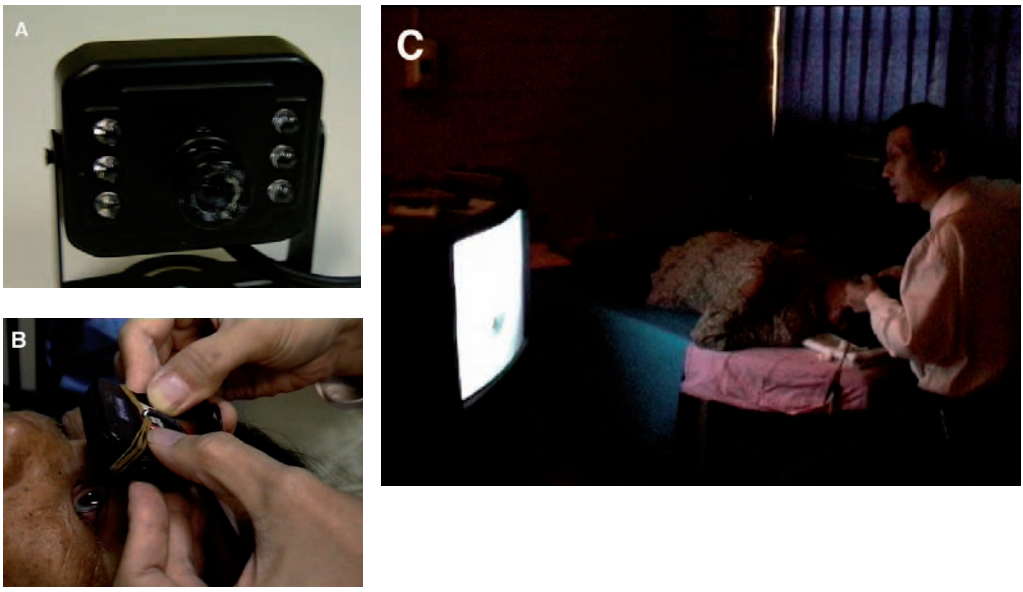

Fig. 2. A: Setting for dark-room infrared gonioscopy with an infrared video camera. B: A Koeppe lens is placed on the eye and the examiner holds the camera close to the lens. C: The examiner looks at the image from the monitor.

lens (Fig. 2). For this procedure, the camera is connected to a TV monitor. The patient has to be in a supine position, and direct gonioscopy with a Koeppe lens is performed. Before the examination, all of the lights in the room are turned off. The examiner holds the camera close to the Koeppe lens, and is adjusted to a position in which the angle structure can be visualized by looking at the monitor (Fig. 2). The examiner can move the focus to different areas around the eye to view all angle positions. During the examination, an assistant can turn a flashlight on and

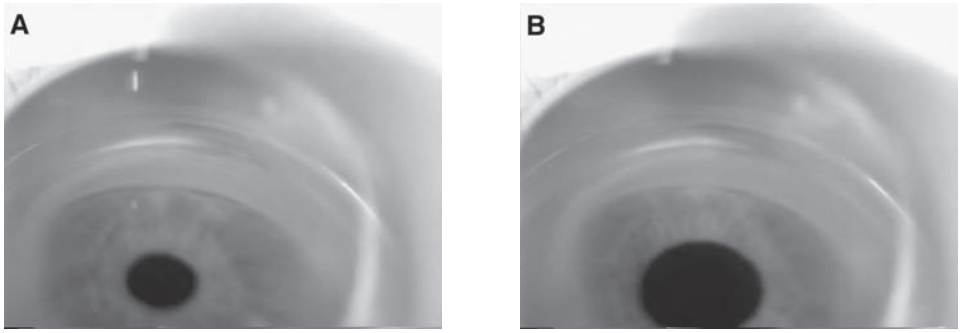

Fig. 3. Dark-room infrared gonioscopy with an infrared video camera and Koeppe lens in an 'occludable angle' eye prior to laser iridotomy. With light stimulation, the pigmented trabecular meshwork can be seen (A). When the light is turned off, the pigmented trabecular meshwork is obscured.

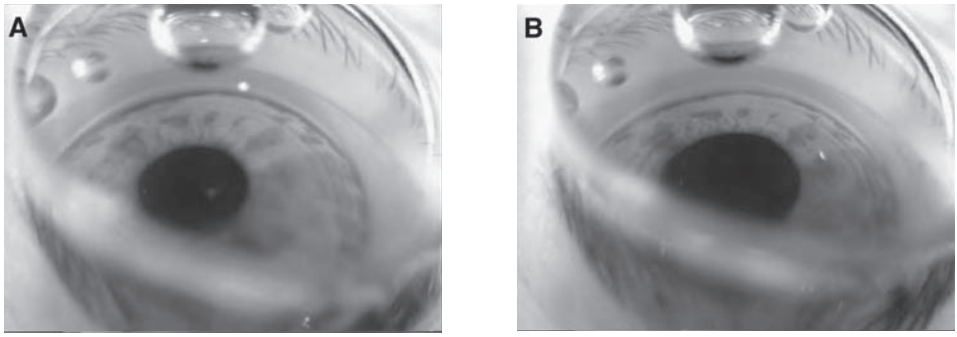

Fig. 4. Dark-room infrared gonioscopy with an infrared video camera and Koeppe lens in a 'non-occludable angle' eye after laser iridotomy and iridoplasty. The pigmented trabecular meshwork can be seen either with (A) or without light stimulation (B).

off in front of the patient's fellow eye to stimulate pupillary constriction and accommodation. The dynamics of the visibility of the angle structure can be studied in dark (with widely dilated pupil) and light (with constricted pupil) conditions.

An example of an eye with an occludable angle is shown in Figure 3. In a light condition, the pupil was constricted and the pigmented trabecular meshwork could be seen. In a dark condition, the pupil was dilated and no trabecular meshwork could be seen. This demonstrated that this eye was occludable and, thus, laser iridotomy and/or iridoplasty were justified. After laser iridotomy and iridoplasty, the pigmented trabecular meshwork could be seen both in light and dark conditions (Fig. 4). This eye is considered non-occludable.

DIG with HRA-IR mode

The IR mode for viewing the retina in the HRA can be used for infrared gonioscopy. The HRA requires an 'iris adapter lens' to focus on the iris (Fig. 5A). The

lens is available from Heidelberg Engineering, GmbH. This lens is designed to cover the built-in HRA lens (Fig. 5B). The lens has a power of +25 diopters (focal length 40 mm) with a working distance of 34 mm. Prior to examination, the iris adapter lens is put on the HRA lens and the HRA mode is turned to IR mode. A Goldmann-type 3-mirror lens is inserted and the HRA is focused on the iris. The examiner views the image of the eye from the computer monitor (Fig. 5C). The angle structure and the structure behind the lens equator can also be visualized by changing the focusing knob. The dynamic of the angle can be observed in dark and light conditions in the same manner as described above.

An example of an 'occludable angle' eye from the anterior lens position is shown in Figure 6. On slit-lamp examination, the anterior chamber was shallow and a mild cataract was observed (Figure 6A). On routine gonioscopy with the slit-lamp, the trabecular meshwork could not be seen, especially when the light was dimmed. The iris configuration was markedly convex. Using the dim light slit-lamp gonioscopy

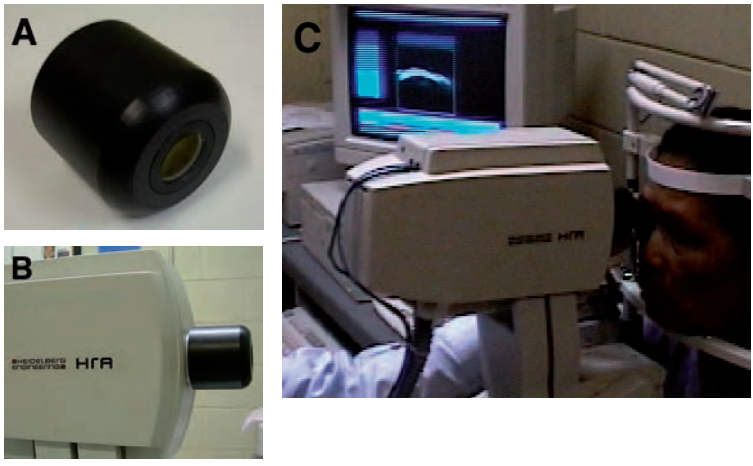

Fig. 5. Setting for dark-room infrared gonioscopy with HRA IR mode. Iris adapter lens (A). HRA with iris adapter lens in place (B). During the examination, the light in the room is turned off. The examiner views the angle structure from the computer monitor (C).

technique, the ciliary body processes (CBP) could be visualized through the lens when the gonioscopic mirror was tilted and the light was reduced with a narrow slit beam (Figure 6B). The CBP could be demonstrated only from the superior mirror. There was no peripheral anterior synechiae (PAS), but some appositional closure could be demonstrated using indentation gonioscopy. When using HRA infrared gonioscopy, the CBP could be demonstrated clearly, even with a small pupil size, but only from the superior mirror (Figure 6C). With a larger pupil size (light turned off), the CBP could be demonstrated in every quadrant (Fig. 7). The trabecular meshwork was obscured only when in the dark. This demonstrated that HRA infrared gonioscopy can facilitate the visualization of CBP in the case of anterior lens position. The visualization of CBP behind the lens is evidence that

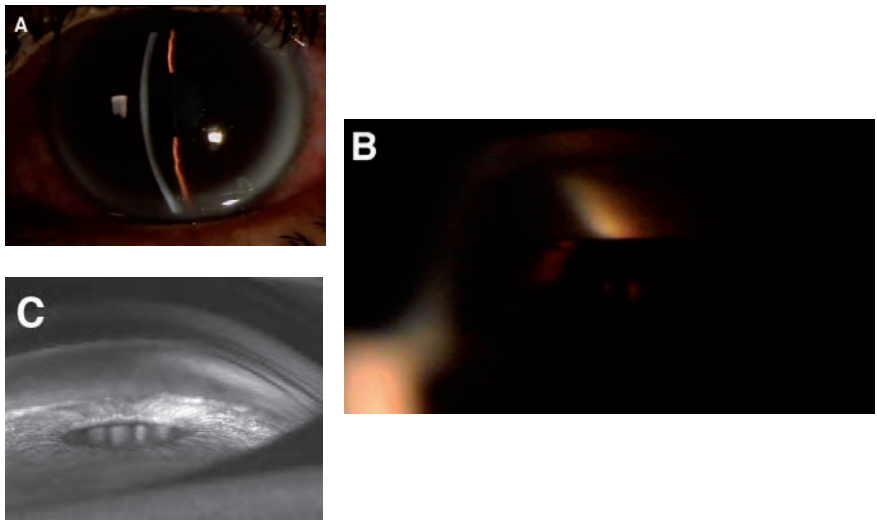

Fig. 6. An eye with anterior lens position and occludable angle. The anterior chamber is shallow (A). Using the dim light slit-lamp gonioscopy technique, the ciliary body processes can be seen behind the lens from the superior mirror (B). With dark-room infrared gonioscopy with HRA, more ciliary body processes can be seen even with a small pupil size (C).

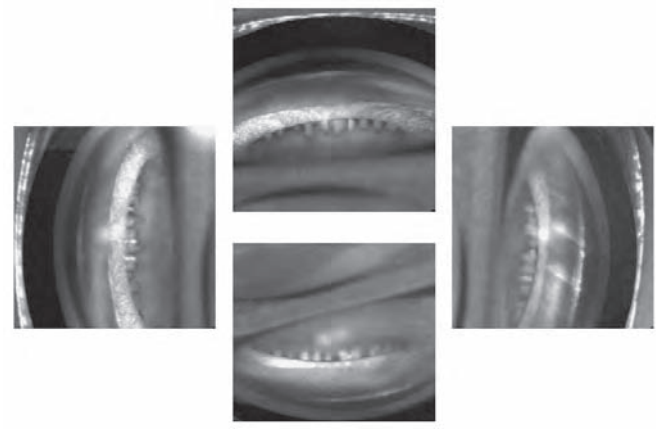

Fig. 7. Dark-room infrared gonioscopy with HRA in an eye with anterior lens position (the same eye as in Fig. 6), the ciliary body processes can be clearly demonstrated in all quadrants. Note that the pupil is dilated in the dark.

the lens is located in an abnormal anterior position, which has been referred to as 'lens forward movement'.

Figure 8 shows another example of an occludable eye in a patient that had already undergone patent iridotomy in both eyes. The anterior chamber was mildly shallow. On routine gonioscopy, the iris configuration was found to be markedly

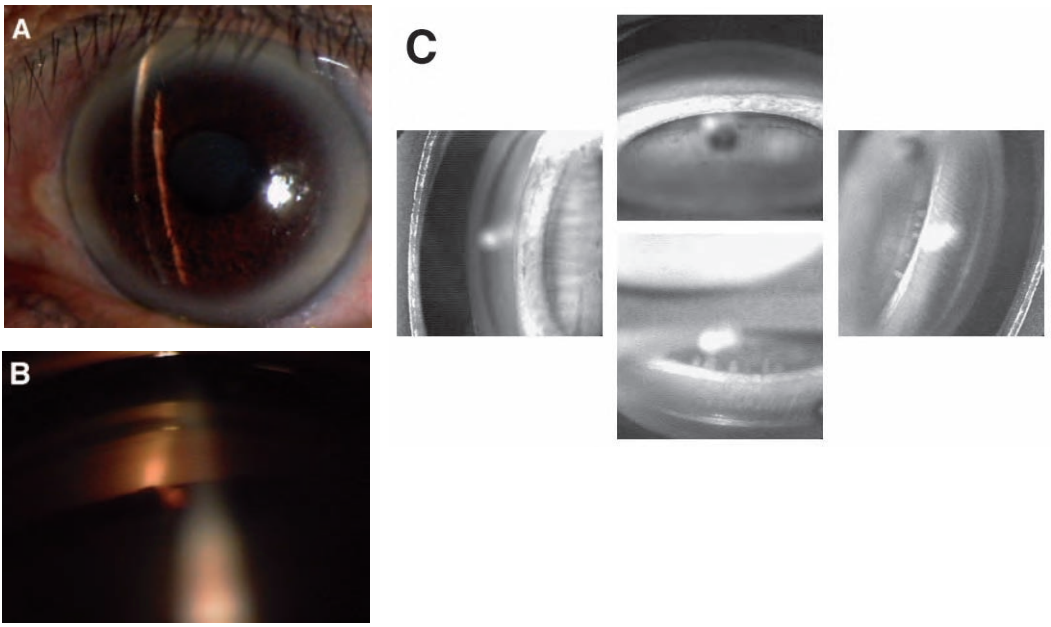

Fig. 8. Right eye of a patient with anterior lens position. Patent iridotomy with shallow anterior chamber (A). Dim light slit-lamp gonioscopy reveals no ciliary body processes (B). However, using dark-room gonioscopy with HRA, ciliary body processes can be demonstrated from the nasal and inferior mirror (C).

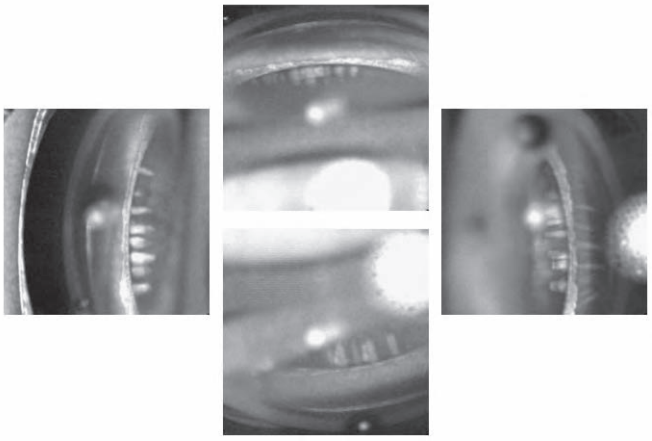

Fig. 9. Left eye of a patient with anterior lens position (the same patient as in Fig. 8). Using dark-room gonioscopy with HRA, ciliary body processes can be demonstrated in all quadrants.

convex, and the trabecular meshwork could not be seen, especially with dim light. Using the dim light slit-lamp gonioscopy technique, the CBP could not be observed in all quadrants (Figure 8B). Using HRA infrared gonioscopy, the CBP could be demonstrated clearly in two quadrants in the right eye (Figure 8C) and all four

quadrants in the left eye (Fig. 9). This is another case of lens forward movement that persisted after laser iridotomy, and the CBP could only be visualized using infrared gonioscopy.

The significance of CBP visualization in angle-closure glaucoma

Normally, the CBP cannot be seen through the lens in an eye with a deep anterior chamber, normal lens thickness, and normal CBP because the light from the CBP could not 'escape' from the eye. In a deep anterior chamber, according to Snell's law,[2] the 'incident angle' of light from CBP that refracted at the lens surface around the pupillary border is larger than the 'critical angle' of the lens-aqueous interface, which causes 'total internal reflection' (Fig. 10). Using figures from the Gullstrand

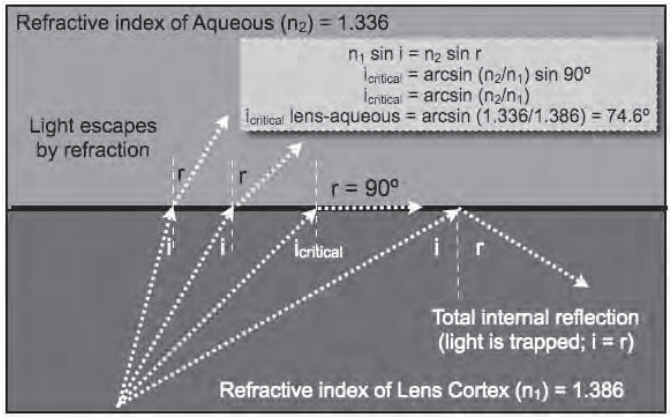

Fig. 10. Snell's law and critical angle. For the anterior lens cortex-aqueous interface, the critical angle for total internal reflection is 74.6°.

Table 1. Conditions in which ciliary body processes may be seen with gonioscopy.

1. Aphakia
2. Anterior lens dislocation
3. Posterior lens dislocation
4. Anterior lens position
5. Increased in anterior lens thickness
6. Combination of increased in anterior lens thickness and anterior lens position

Schematic eye,[3] this critical angle at the lens-aqueous interface is calculated to be 74.6°. For an eye with a deep anterior chamber, light from the tip of the CBP strikes an anterior lens surface that is always larger than the critical angle, so the CBP cannot be visualized regardless of pupil size. However, in some abnormal conditions, the CBP may be seen through the pupil during gonioscopy (Table 1).

Compared to Asian eyes, Western eyes have deeper anterior chamber depth.

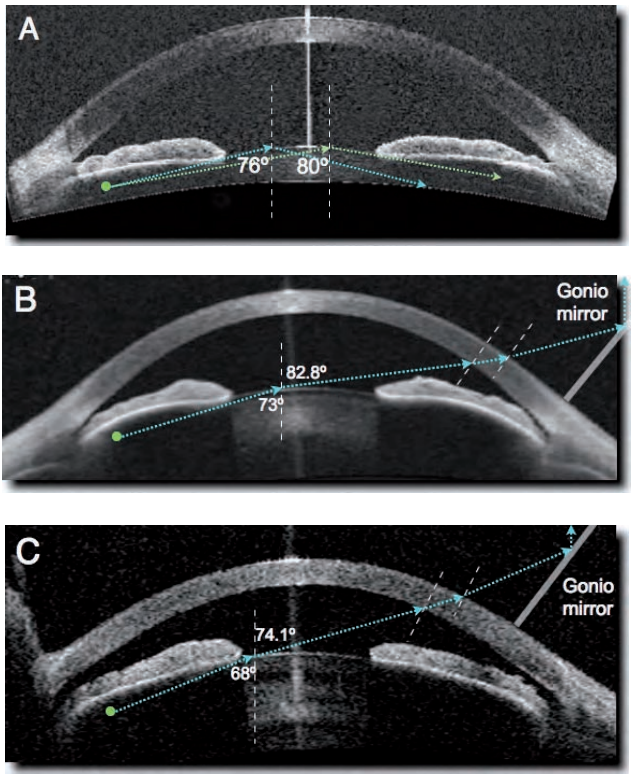

Fig. 11. A: In an eye with a deep anterio chamber, light from the tip of ciliary body processes cannot "escape" from the eye because the incident angle (76°, 80°) at the anterior lens surface is more than the critical angle (74.6°). B: In an eye with a mild shallow anterior chamber from anterior lens position, light from the tip of ciliary body processes can "escape" from the eye because the incident angle (73°) at the anterior lens surface is less than the critical angle (74.6°). By tilting the gonioscopic mirror away from the angle of interest, the tip of ciliary body processes can be demonstrated. C: In an eye with a very shallow anterior chamber from anterior lens position, the ciliary body processes can be demonstrated more easily because light from the ciliary body processes "escape" from the eye with a more acute angle (the incident angle is now 68°).

With aging, the axial thickness of the lens increases and the depth of the anterior chamber is reduced. This may be due to the movement of the lens to a more anterior position, the increased anterior lens thickness, or a combination of both. In a deep anterior chamber, light from the CBP can not escape the eye due to total internal reflection at the lens-aqueous interface (Fig. 11A). When the anterior chamber is shallow due to the anterior lens position and/or increased anterior lens thickness, the amount of incident light from the CBP that strikes an anterior lens surface that is smaller than the critical angle so that light can 'escape' from the eye (Figure 11B). By tilting the gonioscopic mirror in the opposite direction of the angle of interest, the CBP can be visualized. When the anterior chamber is very shallow, the visualization of the CBP is much easier to accomplish and a smaller tilt of the gonioscopic mirror is required (Figure 11C). The same is true for a large pupil (occurring when the patient is in a dark room) compared to a small pupil

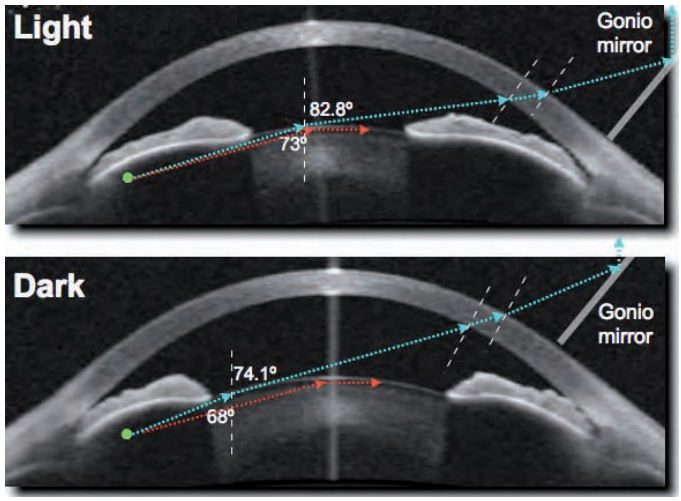

Fig. 12. In an eye with anterior lens position, a dilated pupil (when the patient is in a dark room) will aid in the visualization of the ciliary body processes and marked tilting of the gonioscopic mirror is not required. Note that the incident angle of light at the anterior lens surface when the eye is a in a dark condition (lower) is more acute (68°) than when the eye is in a light condition (73°) (upper). The red line is the incident light that strikes the anterior lens surface at the critical angle (74.6°).

Table 2. Biometry (ultrasound, immersion technique) of eyes that showed acute angle closure and their fellow eyes

	ACD	LT	AL
AACG (pre-PI) n = 1	1.95	4.68	22.26
AACG (post-PI) n = 10	2.13 (0.34)	5.03 (0.25)	22.00 (0.77)
Fellow eye (pre-PI) n = 1	1.84	5.05	21.36
Fellow eye (post-PI) n = 8	2.30 (0.45)	5.04 (0.28)	21.95 (0.73)

(Not all eyes had biometry data. Numbers in parentheses are standard deviations. PI = peripheral iridotomy; AACGC = acute angle-closure glaucoma; ACD = anterior chamber depth; LT = lens thickness; AL = lens thickness)

(occurring when there is light or accommodative stimulation) (Fig. 12).

In our consecutive series of 16 acute angle closure eyes (15 cases, one case had acute angle closure in both eyes), the CBP could be demonstrated in all eyes with DSG. All of the eyes had patent iridotomies at the time of examination. Of the 15 fellow eyes, one eye was blind and could not be examined. In the remaining 14 fellow eyes, CBP could be demonstrated with DSG in all but one eye. In the only eye in which CBP could not be seen, it could be demonstrated with DIG. The biometry (ultrasound, immersion technique) of some eyes had been done (table 2).

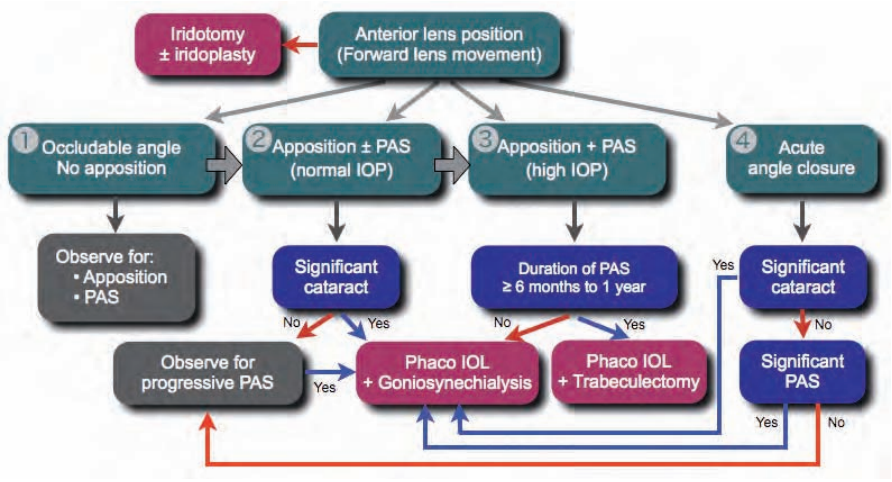

Fig. 13. Diagram showing the clinical categories and stepwise approach for eyes with 'anterior lens position' or 'forward lens movement'. See text for detail discussion.

It can be seen that all eyes had a true anterior chamber depth of less than 2 mm (ACD minus corneal thickness) and a lens thickness of less than 5 mm.

Anterior lens position or 'forward lens movement' as described by Ritch[1] is one of the important causes of angle-closure glaucoma. Although it has been described in the literature, evidence about its clinical course and management were limited. In our experience, patients with anterior lens position can be presented in four categories (Fig. 13): (1) occludable angle (in which ≥ 270° of the posterior TM cannot be seen[4]) without any apposition of the peripheral iris and the posterior (pigmented) TM; (2) apposition of the peripheral iris and the posterior TM with or without some amount of PAS, but with normal IOP; (3) category 2 with a large amount of PAS that causes increased IOP; (4) acute angle closure with signs and symptoms of acute attack angle-closure glaucoma. According to the present classification of angle closure,[4] category 1 can be classified as 'primary angle closure suspect' (PACS), category 2 as 'primary angle closure' (PAC) and category 3 as 'primary angle-closure glaucoma' (PACG). Patients in category 1 can progress to category 2 and 3. The factors that cause patients to develop acute attack angle closure (category 4) are not known.

We recommend a stepwise approach for patients with anterior lens position according to the category of the disease that one encounters (Fig. 13). All categories of anterior lens position have some degree of relative pupillary block, and laser iridotomy with or without iridoplasty should be done in all eyes.[5] After iridotomy, management will be different for each category depending on the amount of appositional closure, PAS and cataract. Patients in category 1 will only need to be followed-up gonioscopically for signs of apposition and/or PAS. Patients in category 2 who have a clear lens should also be closely observed for progression of PAS. Once there is evidence of progressive PAS, removal of the lens by phacoemulsification with intraocular lens implantation (PE IOL), combined with mechanical goniosynechialysis[6] (GSL) is recommended. Although the IOP is normal in this

category, performing GSL will ensure a wide open angle that will not be compromised if there is further PAS in the future. If patients in category 2 have significant cataract, PE IOL with GSL is recommended. Patients in category 3 have PAS that causes high IOP. The duration of PAS is important in these cases. Campbell and Vela[6] reported success of GSL for PAS for up to one year. Teekhasaenee and Ritch[7] reported success of PE IOL with GSL for uncontrolled chronic angle closure glaucoma after acute angle-closure glaucoma with PAS for up to six months. From this evidence, PE IOL with GSL is recommended for patients in category 3 with PAS of six months to one year. If the lens is clear, the risks and benefits of the procedures should be thoroughly discussed with the patients. If the patients have longstanding PAS of more than one year, combined PE IOL with trabeculectomy should be considered instead.

In patients presented with acute angle closure (category 4), iridotomy and/or iridoplasty should be performed.[5] If there is significant cataract, PE IOL with GSL is recommended after the inflammation is controlled. For patients with a clear lens, PE IOL with GSL is recommended if there is a large amount of residual PAS. If there is only a small amount of PAS, close follow-up for progressive PAS and increased IOP is recommended. Once there is evidence of progressive PAS, PE IOL with GSL should be done.

In our case series, PE IOL with GSL were successful in controlling IOP without medication in half of the eyes (eight eyes). One eye required extracapsular cataract extraction with IOL implantation combined with trabeculectomy. The remaining eyes were adequately treated with medication or they were observed. These data suggest that the crystalline lens is an etiology of acute angle closure. Removal of the lens combined with GSL can cure most of the eyes. It should be emphasized that performing only PE IOL without GSL will not work in these cases,[8] because the aqueous outflow is still blocked by PAS.

We would like to emphasize that causes of angle closure should be identified in every case of 'primary' angle closure glaucoma. Since most cases have some degree of relative pupillary block, other causes of angle closure and PAS should be thoroughly evaluated. In our case series, all 16 eyes had been shown to have anterior lens position as a cause of angle closure. This emphasizes that the crystalline lens is an important etiologic factor of 'primary' acute angle closure.

Conclusions

Visualization of CBP is an important, but easily overlooked sign of anterior lens position and/or increased anterior lens thickness. This may be the most common cause of acute angle-closure in Asian eyes. The CBP can be visualized by modifying the technique used in routine slit-lamp gonioscopy, with the dimming of the light and narrowing of the slit beam. Attention should be also paid to regions beyond the angle and into the back of the lens. In some cases with mild anterior lens position, gonioscopy may be performed in a dark room with an infrared light using either a video camera or HRA in IR mode to reveal the CBP more easily.

Removal of the lens by PE IOL combined with GSL is the treatment of choice and can cure most of the affected eyes. For fellow eyes, to prevent the development of angle-closure, appropriate examination and intervention should be done according to the presence of appositional closure, PAS, and cataract.

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Optic nerve and visual field examinations

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Introduction

The characteristic changes in the optic nerve head (or retinal nerve fiber layer) and/or the corresponding visual filed defects are required to differentiate primary angle-closure glaucoma from primary angle closure.[1] Functional loss in visual field or visual acuity must be the most important issue for the patient with shallow anterior chamber or angle closure. Therefore, it is crucial for us, ophthalmologists in Asian countries in which patients with primary angle closure or primary angle closure glaucoma are common,[2-5] to have adequate knowledge about the optic disc and visual field in eyes with primary angle closure or primary angle-closure glaucoma.

Optic nerve head

The characteristics of the optic nerve head in primary angle closure or primary angle closure glaucoma consist of hereditary features in eyes which are likely to develop angle closure and changes secondary to acutely or chronically increased intraocular pressure.

Inherited characteristics in the optic disc of eyes with primary angle closure

It is well known that eyes with primary angle closure have various anatomic features. Biometric studies[6-21] showed that the eyes have the following properties: 1) short axial length; 2) shallower anterior chamber; 3) thicker and more anteriorly located lens with steeper lens surface; and 4) smaller corneal diameters with steeper corneal curvature. Tendency toward hyperopia is also associated with a primary angle closure.[22] Because hyperopic eyes with or without glaucoma commonly have smaller discs, we have the impression that eyes with angle closure should have

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smaller discs or smaller cupping than eyes with open angles. However, to our knowledge, there was only one study which compared optic disc area in eyes with angle closure with those in normal eyes or eyes with open angle glaucoma: Sihota *et al*. reported that disc area in eyes with chronic angle-closure glaucoma had smaller disc area (2.62 mm^2) than eyes with open-angle glaucoma (2.77 mm^2) but disc area in normal eyes was still smaller (2.38 mm^2).[23] Moreover, there is a lack of clinical studies on physiological cupping of the optic disc of eyes with primary angle closure before developing glaucomatous damage or their fellow eyes.

Acquired changes in the optic disc

Acquired changes in the optic disc and surrounding tissues following acute or chronic increase in intraocular pressure have been intensively studied. As an early histological study described in the text by Duke-Elder,[24] the pathological changes in the optic nerve occurred within the first few weeks of an attack of primary angle closure as follows: 24 hours after the onset, the nerve head shows neither papilledema nor cupping, but acute hydropic degeneration of nerve fibers is seen with and just after the lamina cribrosa. The papilledema appears mildly at the third day and apparently at the sixth day after the onset. Deep cupping of the optic disc became evident and the nerve showed commencing cavernous degeneration. In these same cases, the changes in the retinal ganglion cells were minimal at least in the first week after the onset. As significant changes found in human eyes with secondary angle-closure glaucoma, thinner lamina cribrosa, deeper and wider optic cup, finer peripapillary scleral ring, and thinner choroidal vascular bed were reported.[25-27] Pathological changes were studied also in experimental monkey eyes in which intraocular pressure was acutely increased.[28-32] More recently, morphometric changes in the optic disc or retinal nerve fiber layers in monkey eyes of experimental glaucoma were studied using confocal scanning laser tomography[33-40] or scanning laser polarimetry.[35,41,42] One experimental study using monkey eyes[36] showed the time-course changes in the optic nerve head morphology after the acute intraocular pressure rise: intraocular pressure was increased to about 40 mmHg after laser trabeculoplasty and gradually reduced to about 30 mmHg during the following three months; cup volume measured with confocal scanning laser tomography gradually increased and retinal nerve fiber layer thickness evaluated with scanning laser polarimetry gradually decreased during the first month after the laser procedure.

As an early study in the 1970s, Douglas *et al*. reported the changes in the optic disc of eyes following unilateral acute-angle-closure glaucoma or with unilateral chronic angle-closure glaucoma.[43] In their report, none of 18 acute, but five of 11 chronic angle-closure patients, showed asymmetry of cupping, while pallor was seen in seven of the acute and nine of the chronic patients, suggesting that disc pallor should be a dominant change compared to enlargement of the cupping in eyes following acute angle-closure. Recent years, a lot of clinical studies regarding the optic disc in angle-closure glaucoma have been released from Asian countries. Yang *et al*.[44] reviewed 103 patients with 23 acute and 80 chronic primary angle-closure glaucoma and found that concentric steep enlargement of the cupping in 99 (96%) of the eyes, while focal notcing of the neuroretinal rim was seen in only three (3%) eyes. And, both alpha and beta zones of parapapillary atrophy were more frequent in angle-closure glaucoma eyes compared to normal controls.[44] Shen *et*

al.[45] reported that cut-to-disc ratio significantly increased from 0.56 to 0.59 from the second week to the sixth week after the acute angle-closure attack episode and the neuroretinal rim loss was more evident in the superotemporal and inferotemporal portions of the optic disc, although they did not mention which of general or focal enlargement of the cupping was more common. Uhm *et al*.[46] compared the optic disc appearance between acute angle-closure eyes and chronic angle-closure eyes: abnormal disc findings, such as abnormal shaped rim width, bared circumlinear vessel, vessel bayoneting, and zone beta of parapapillary atrophy, were more commonly found in eyes with chronic angle-closure glaucoma than acute one. Thus, in acute angle-closure glaucoma eyes, the changes in optic disc morphology including neuroretinal rim loss and enlargement of the cupping are not necessarily common, while pallor is a dominant finding in the optic disc. On the other hand, intrapapillary changes similar to those in eyes with primary open-angle glaucoma were more often observed in eyes with chronic angle-closure glaucoma.

Vascular aspects in the pathogenesis of optic neuropathy in primary angle-closure glaucoma

As mentioned above, pale appearance of the neuroretinal rim and optic disc edema are characteristic findings for eyes during or following acute angle-closure attack. Frequently seen disc pallor suggests a role of vascular insufficiency in pathogenesis of optic neuropathy following acutely elevated intraocular pressure due to angle-closure attack. Vascular occlusion, as well as hydropic degeneration of the optic disc tissue[24] and axonal swelling from blockage of axoplasmic transport,[47,48] is thought to play a role in developing optic disc edema. A study using color Doppler ultrasonography showed that blood velocity in retrobulbar arteries was lower in eyes with elevated intraocular pressure due to angle-closure in comparison to eyes with normalized pressure following angle-closure attack or to normal control eyes.[49] The same authors also reported that blood velocity in the retrobulbar arteries was significantly decreased in chronic angle-closure eyes with normally controlled intraocular pressure than in age-matched healthy eyes.[50] Reduced choroidal thickness with marked decrease in choroidal vessel diameter[25] may also suggest possible association between blood flow and development of optic neuropathy in angle-closure glaucoma.

Parapapillary atrophy is as usual known to relate to primary open-angle glaucoma: parapapillary atrophy is observed in eyes with glaucoma;[51-53] glaucomatous eyes have larger parapapillary atrophy;[51-55] and parapapillary atrophy is associated with the progression of glaucomatous visual field defect.[56,57] It has been also reported that both alpha and beta zones of parapapillary atrophy were more frequently observed in eyes with acute or chronic primary angle-closure glaucoma than healthy eyes.[44] Uchida *et al*., however, reported that prevalence of parapapillary atrophy was still lower in eyes with angle-closure glaucoma than in those with open-angle glaucoma.[58]

Visual field

Visual field in acute angle-closure glaucoma

The visual field changes are not so frequent in eyes after acute angle-closure. Longstanding or repeated elevation of intraocular pressure is necessary to develop detectable visual field loss.[43,59,60] Douglas *et al*. reported that 11 (61%) of 18 eyes following acute angle-closure had no abnormal visual field, while ten (91%) of 11 eyes with chronic angle-closure showed apparent visual field changes.[43] Bonomi *et al*. showed that abnormal visual fields were found in 19 (86%) of 22 eyes one or two days after acute angle-closure attack, while only 12 (55%) of the same 22 eyes showed field defects one month following the attack.[59] Thus, visual field defects will not remain in about half of the eyes after acute angle closure attack. Recently, however, thinning of the retinal nerve fiber layer in the inferior region evaluated with optical coherence tomography was observed even in eyes after a single acute angle closure attack with normal visual field,[61] suggesting that functional damage in such eyes should exist but it should be below the detectable level with the currently used perimetric techniques.

During acute angle closure attack, the condition of vision is such that reliable visual field testing is impossible. According to the study of Bonomi *et al*.,[59] in eyes one or two days after acute angle closure attack, the most frequent abnormality found in visual field was general depression especially in the upper nasal quadrants; and severity of visual field defects was significantly correlated with maximum level of intraocular pressure during the attack and with the duration of the attack. Irregular depression of all isopters and enlargement of the blind spot, and widening of the angioscotoma, arcuate scotoma, and cecocentral scotoma can be listed as visual field changes during or just after acute angle closure attack.

Visual field in chronic angle-closure glaucoma

As to chronic angle-closure glaucoma, Lau *et al*.[62] made detailed analysis of the patterns of visual field defects. They found that the superior and inferior nasal area was most commonly damaged in the early stage of chronic angle-closure glaucoma and the superior arcuate area was being involved with the deterioration of visual field damage. In comparison with primary open-angle glaucoma, visual filed damage of chronic angle-closure glaucoma shows more generalized pattern[63] and the severity and speed of progression are more closely associated with the level of intraocular pressure.[64,65] Gazzard *et al*.[66] showed that the tendency that the superior hemifield is more severely affected than the inferior was less pronounced in angle-closure glaucoma than in open-angle glaucoma. Severity of visual field loss in chronic angle-closure glaucoma is also correlated with the extent of peripheral anterior synechia.[67]

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Acute angle closure

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Introduction

Acute angle closure is the term for abrupt blockage of the trabecular meshwork by the peripheral iris, which induces a rapid increase of intraocular pressure (IOP) and subsequent characteristic symptoms and signs. Acute angle closure is unique in that it has acute symptoms and is considered to be an ophthalmic emergency.

The incidence of acute angle closure is specifically high in East Asia, with Singaporeans having the highest reported incidence rate in the world (12.2 per 100,000 per year) for individuals age 30 years and older.[1] The prevalence of acute angle closure determined in an outpatient-based multicenter study in the Republic of Korea was estimated to be 0.13% (122 among 96,466 new patients).[2] Acute angle closure is two or three times more common in females than in males.[2-4]

In the clinical field, acute or chronic angle closure is classified by the acuteness of the symptoms. The presentation of symptoms depends on the speed of the rise in IOP, and the abruptness of the increase in IOP depends on how quickly the closure of the angle occurs.

Figure 1 offers a graphical description of the clinical course and features of angle closure. The Y-axis represents IOP, and the X-axis represents time. In intermittent angle closure (IAC), small sub-clinical spikes of IOP occur. This sometimes develops into a big spike, causing acute angle closure (AAC). If the attack is resolved spontaneously or through treatment, the IOP will be diminished. If the attack is not resolved completely or treated properly, it may develop into a slow but progressive chronic angle closure (CAC). Intermittent angle closure may also develop into chronic angle closure with a slow elevation of IOP along with progressive peripheral anterior synechia (PAS) formation. An acute angle closure may even occur during the course of CAC. Therefore, an overlap and interchangeability may be shown between acute and chronic angle closure. The term subacute angle closure is generally considered to be similar to intermittent angle closure. However, this term has been controversially used by some clinicians in cases with larger spikes than those normally seen in intermittent angle closure. Due to these complexities

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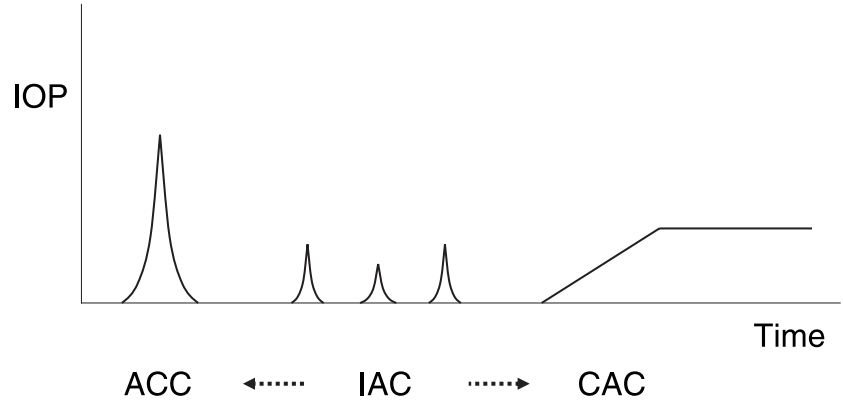

Fig. 1A. Clinical overview of primary angle closure. This diagram helps understanding of the clinical course of the angle closure. The Y-axis is IOP and the X-axis is time. In IAC the small sub-clinical spikes of IOP elevation occur. Sometimes it develops into a big spike and makes an AAC, while also it may develop into a slow but progressive CAC.

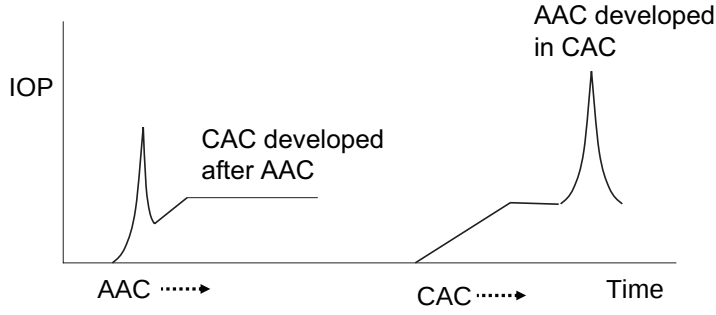

Fig. 1B. CAC may develop even after AAC, and the acute attack may also happen even during the course of CAC. So it seems better to call these complexity of angle closures as primary angle closure or primary angle closure glaucoma depending on the presence of the optic nerve damage.

and the vagueness of classification by symptomatology, the recent suggestion for classification is to use the term 'primary angle closure' rather than dividing the condition into acute, intermittent, and chronic angle closure.

Mechanism

Pupillary block

The potential contact force between the pupil and lens surface increases physiologically and pathologically to create a pressure gradient between the anterior and posterior chambers, with higher pressure in the posterior. This pressure gradient makes the peripheral iris bow anteriorly and results in apposition of the iris onto

the trabecular meshwork. The extent of appositional closure determines the severity of IOP elevation and symptoms. If the appositional closure develops completely around the trabecular meshwork, the acute angle closure occurs. If the appositional closure develops partially the intermittent angle closure may occur.

Plateau iris

In some cases with specific peripheral iris configuration, the angle closure occurs without a pupillary block. The peripheral iris is shaped with an anterior bowing or plateau-like pattern. The problem is present in the peripheral iris and ciliary body. In this case, the pressure gradient between the anterior and posterior chamber is not important.

Lens-induced

In lens-induced mechanism, the problem is caused by the lens. The anterior position or the large size of the lens may increase contact with the iris and push the peripheral iris toward the trabecular meshwork. The loosening of the zonule and aging change of the lens may affect the position and the size of the lens. The inherent disproportion between the eyeball size and lens size, a larger lens compared to the size of the eyeball, can be another factor.

Precipitating factors

Although the mechanism of acute angle closure is not yet fully understood, a number of precipitating factors have been suggested. Near work, intense concentration, emotional stress, and excitement are precipitating factors that have been suggested by previous studies and reports.[5-7]

General illness by systemic infection may induce angle closure. Upper respiratory infection was found to be a risk factor for the attack.[8] Acute angle closure has also been reported in patients with influenza, AIDS, and hemorrhagic fever with renal syndrome.

Choroidal expansion[9] has been suggested as a possible mechanism of glaucoma. Along similar lines, narrowing of the anterior chamber angle and thickening of the ciliary body has been observed during the valsalva maneuver.[10]

Pharmacologic pupillary dilation, miotics, and drugs may precipitate acute attack. The tricyclic antidepressants with anticholinergic properties have been reported to precipitate angle closure glaucoma.[11,12] Recently, an antiepileptic drug, topiramate, has been proven to induce bilateral acute angle closure associated with uveal effusion.[13-15]

Symptoms and signs

Most attacks of acute angle closure are unilateral, with only 5 to 10% being bilateral.[16] The symptoms of acute angle closure are related to the sudden and marked eleva-

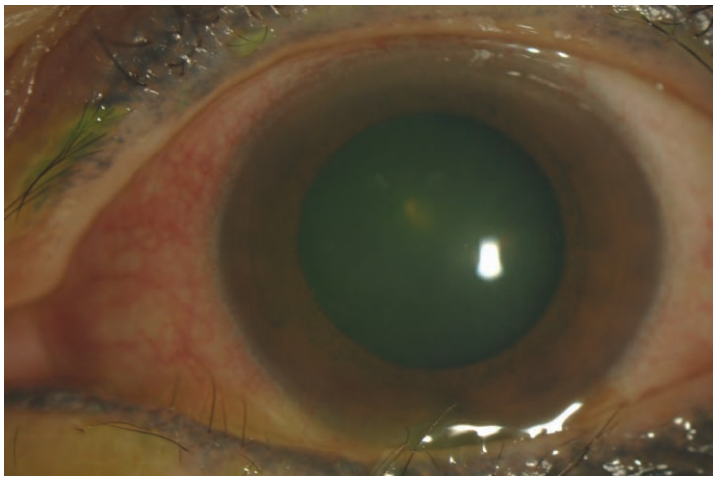

Fig. 2. An anterior segment photograph of 58 year-old female patient with an acute angle closure attack which developed three hours before. The IOP was 54 mmHg. Conjunctival injection is observed around the limbus. In this case the injection in nasal side is more prominent. The pupil is mid-dilated due to sphincter palsy. The corneal edema was not developed due to a relatively short duration of the attack.

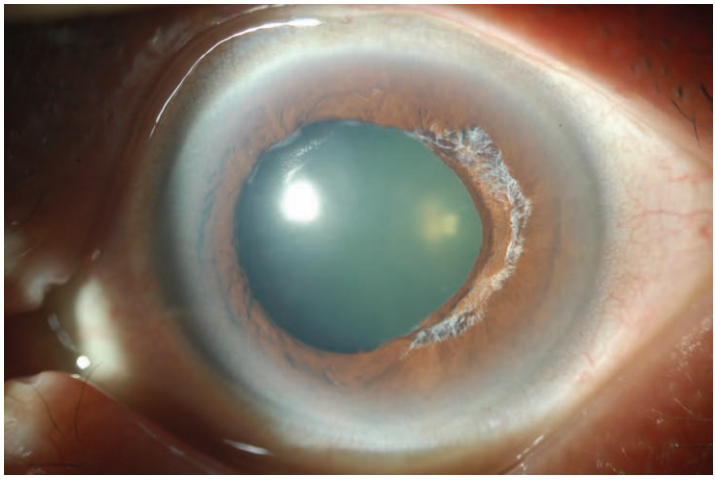

Fig. 3. The iris atrophy (1 to 5 o'clock position) was developed after previous acute angle closure attack.

tion of IOP. Ocular pain is caused by the expansion of ocular tissue, including the cornea, the iris, and the whole globe. A headache usually accompanies ocular pain in the form of a radiating pain.[17] Nausea and vomiting are among the characteristic symptoms of acute IOP elevation. The activation of the vomiting center in the medulla may be triggered by the afferent input from the peripheral pain receptors. Vasovagal responses such as bradycardia and sweating may present. These systemic

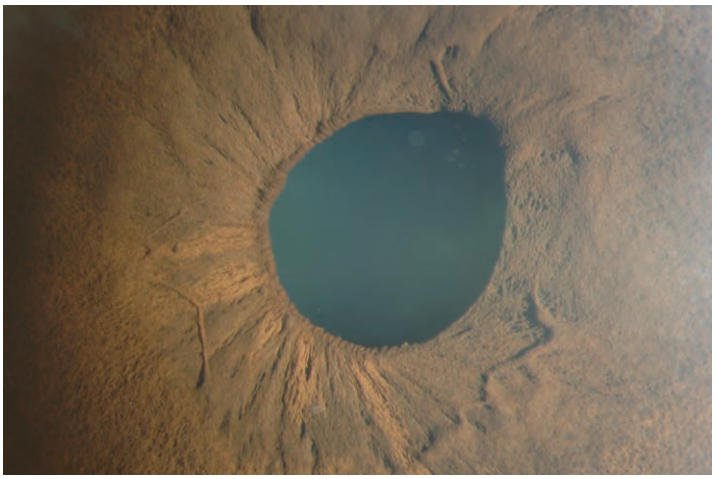

Fig. 4. Pupillary margin may show spiral or whorl appearance (6 and 11 o'clock position) due to a sectoral sphincter damage (3 to 5 and 12 to 1 o'clock) during the acute attack.

symptoms and headache may mislead the general practitioners to refer the patients to internists or neurologists, and may delay proper treatment.[11,18]

The increased IOP affects the endothelial function of the cornea, which induces edema of the cornea. The corneal edema with stretched stromal lamellae causes blurred vision and halo vision around lights, with a blue-green central halo and a yellow-red peripheral halo. Corneal epithelial edema develops and causes the corneal light reflex to become irregular. The conjunctival injection starting around the limbus (ciliary injection) is related to the congestion of the ciliary body (Fig. 2). The conjuctival injection and the leakage from the conjunctival vessels result in chemosis and lid edema. Tearing is increased. The pupil is mid-dilated and fixed due to ischemic damage of the sphincter muscle. If sphincter damage is partial or sectoral, the shape of the dilated pupil may be ovoid or irregular. In severe cases, the iris vessels may also be dilated, and may be mistaken for neovascular glaucoma.

A sequel of an acute attack provides us with information regarding the characteristic features of the condition. The iris showed an atrophic change of depigmentation and thinning at the previous ischemic area of the pupil margin and iris stroma (Fig. 3). A severe attack may create a hole in the atrophic iris stroma. The papillary margin may show a spiral or whorl pattern due to irregular contraction between the areas experiencing sectoral damage (Fig. 4).

The lens showed white anterior subcapsular opacities referred to as 'glaukomflecken' and represented as multiple small white flecks in the pupil area, which develop as a result of ischemia of the anterior lens fibers (Fig. 5).

The focal peripheral anterior synechia and the hyperpigmentation at the area of iris contact during the attack can be observed by gonioscopy.

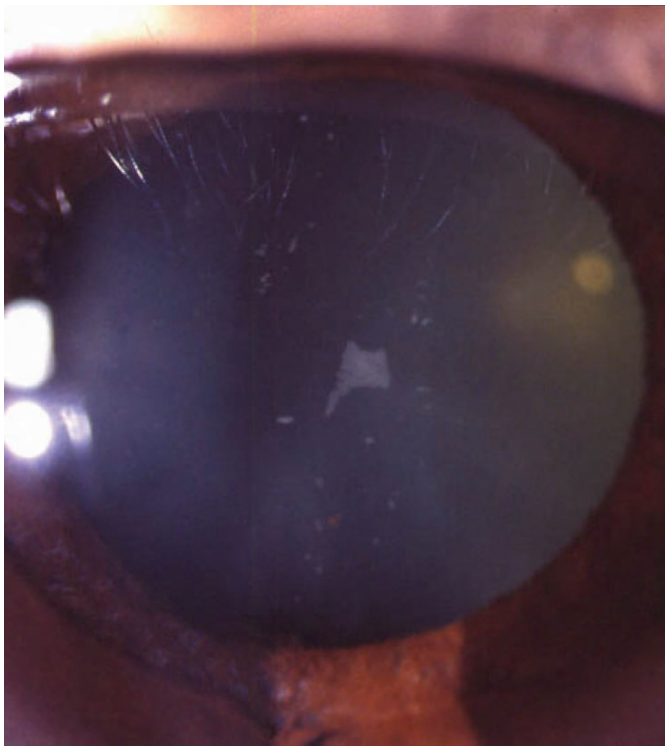

Fig. 5. The photograph shows the glaucomflecken on the lens surface which represents the ischemic change of the anterior lens fibers.

Diagnosis

The diagnosis of acute angle closure is based on the symptoms and signs. Confirmation of the diagnosis and differential diagnosis are done by close examination using slit-lamp biomicroscopy. The IOP is measured most accurately using a Goldmann applanation tonometer. Slit-lamp examination can reveal conjunctival injection, corneal edema, fixed dilated pupil, shallow anterior chamber, and narrow and closed angle.

In the acute stage with corneal edema, the angle is difficult to examine clearly using gonioscopy. Topical application of glycerol or 5% NaCl will make the cornea clear temporarily to allow for an examination of the angle. Opening the angle by indentation gonioscopy may differentiate appositional closure from synechial closure. Gonioscopic examination of the fellow eye provides many clues because the configuration of the chamber angle is similar between two eyes, especially when the corneal edema of the involved eye prevents angular examination.

Ultrasound biomicroscopy may aid in the evaluation of the anterior segment architecture and the mechanism of angle closure.[19,20] It helps to visualize the structures posterior to the iris and provide quantitative measurements. Anterior segment optical coherence tomography was recently developed, and helps investigators to

quantitatively evaluate the angle and the anterior segments rapidly and without causing the discomfort of contacting an eyeball.[21,22] The only major problem is that it cannot be used to visualize the structure posterior to the iris because the laser light does not penetrate the iris.

The fundus cannot be examined clearly due to corneal edema. Indirect ophthalmoscopy with the brightest available light may aid in the examination of the fundus and the optic disc. In a fresh and mild attack, the disc may not show any abnormal changes. In a severe and long-standing attack with congestion of the whole eyeball, the disc will show hyperemia and swelling. If an acute attack occurs during chronic or creeping angle closure, the disc may show atrophic and glaucomatous cupping due to previously accumulated damage.

The visual field examination during the attack is practically and ethically impossible. It can be assessed after the attack is relieved and the risk factors are removed. The results of field examination correlate with the optic disc findings. Field examination should be performed carefully, as it may provoke a new attack if the precipitating risks are not removed.

If the glaucomatous optic nerve head change or visual field change is observed, the diagnosis needs to be changed from acute angle closure to acute angle closure glaucoma. However, in acute angle closure, the optic nerve damage is relatively rare because the duration of IOP elevation is short unless it is missed or develops into the chronic angle closure.

Differential diagnosis of primary acute angle closure

Differential diagnosis is focused on diseases that show acute IOP elevation and similar symptoms.

Uveitic glaucoma

Even though the elevation of IOP is not always acute in glaucoma associated with uveitis, there can be an abrupt elevation of IOP with similar symptoms of acute angle closure. The associated ocular pain may be due to both IOP elevation and uveitis. Ciliary injection by uveitis may mimic acute angle closure. Differential diagnosis is made by observing the chamber reaction, keratic precipitates, and open angle, while focal PAS may be found.[23,24]

Glaucomatocyclitic crisis

A glaucomatocyclitic crisis, or also called Possner-Schlossman syndrome, is one of the specific types of glaucoma associated with uveitis. The elevation of IOP is typically accompanied by a recurrent episode of anterior uveitis. The chamber reaction is usually minimal, with a few keratic precipitates observed in the inferior cornea. Between attacks, the IOP is normal and there is no chamber reaction. Middle-aged men are more frequently affected than other groups. The chamber angle is wide open.[25-27]

Neovascular glaucoma

At the late stages of neovascular glaucoma, the angle can be totally closed by PAS because of the contraction of the fibrovascular membrane at the angle. If the angle is completely closed, the IOP may increase abruptly up to a level that may mimic AAC. Differential diagnosis is made by observing the new vessels on the surface of the iris. However, it should be kept in mind that in case of severe primary angle-closure attack, dilated iris vessels may also appear. The contraction of the fibrovascular membrane may drag the pupil margin and induce ectropion uvea with dilated pupil. At this stage, the fibrovascular membrane on the iris makes the surface of the iris appear glossy. The identification of a disease underlying neovascular glaucoma such as diabetes, central retinal vein occlusion, or ocular ischemic syndrome can aid in differentiation.[28,29]

Malignant glaucoma

The misdirection of aqueous fluid into the vitreous increases the posterior pressure, which in turn pushes the iris, lens, and ciliary body forward, and the angle is closed secondarily. The main differentiation is that both the central and peripheral chambers are shallow or absent in malignant glaucoma due to the pushing force from the vitreous. A detailed description of malignant glaucoma is provided in the chapter by Uranchimeg and Baasankhuu in this volume.

Lens dislocation

The anterior lens dislocation may push the peripheral iris forward to close the angle. Mostly, the patient may have a history of eyeball trauma or pathologic conditions involving the eye, including Marfan's syndrome, homocystinuria, Weill-Marchesani syndrome, acquired syphilis, hyperlysinemia, and sulfite-oxidase deficiency. If the angle is completely closed, it will cause secondary angle closure. The identification of the lens dislocation is a key factor for diagnosis.

Steroid-induced glaucoma

Steroid-induced glaucoma may show an extreme elevation of IOP in a high responder to steroid treatment. In a high responder, the IOP level and speed are quite similar to those of AAC. The chamber is deep in the periphery.[30]

Treatment

Acute angle closure is considered to be an ophthalmic emergency. The key issue of treatment of acute angle closure is to relieve the acute symptoms of the patient by lowering IOP and removing the modifiable risks to prevent additional attacks.[31]

Medication

Medication is used to rapidly reduce IOP and remove the discomfort of the patient. If the attack is fresh (within several hours) and caused by the pupillary block mechanism, miotics can remove the pupillary block. Treatment with 1-2% pilocarpine three times every five minutes is appropriate in this case. It should not be instilled further if the pupil does not respond, because it will also aggravate the attack if the ciliary body rotates forward due to excessive instillation. For the same reason, a patient showing a very shallow anterior chamber should not be treated with pilocarpine. Aqueous suppressant, beta-blocker, carbonic anhydrase inhibitor, and alpha-2 agonist should be applied simultaneously. A hyperosmotic agent like oral glycerol or intravenous mannitol can be administered to rapidly reduce the IOP topical steroid may help to reduce symptoms and acute inflammation caused by an attack.

Laser

When the IOP is normalized or the peripheral chamber is made deep enough for laser treatment, a peripheral laser iridotomy can be performed to remove the risk of an additional attack. This procedure is described in detail in the chapter by Friedman in this volume. Before the application of the laser, the corneal edema may be transiently removed by instillation of glycerol or 5% NaCl. Recently, Argon laser peripheral iridoplasty (ALPI) was suggested as an alternative for the pretreatment of laser iridotomy. ALPI has been found to successfully reduce the IOP and deepen the peripheral chamber faster than conventional medical treatment (*see* the chapter by Tham *et al.* in this volume).

Surgery

Surgical treatment of acute angle closure is saved for rare cases in which medication and laser treatment have not had any effect. Surgical procedures include trabeculectomy, goniosynechiolysis, and phacoemulsification of the lens.

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Intermittent angle closure

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Introduction

Intermittent angle closure designates a condition of primary angle closure in which mild, transient elevation of intraocular pressure occurs sporadically due to pupillary block mechanism and subsides spontaneously. Because the ocular signs and symptoms are intermediate between typical acute primary angle closure and typical chronic angle closure, they vary from one patient to another. Intermittent angle closure is not a single disease entity, but a subdivision of primary angle closure and the border of this subdivision with other ones is relatively arbitrary. The management of intermittent angle closure is basically similar to other clinical types of primary angle closure because pathophysiology is identical.

The Terminology and Guidelines for Glaucoma, published by the European Glaucoma Society, describes intermittent angle-closure glaucoma as milder clinical manifestations than acute angle-closure glaucoma and that it resolves spontaneously.[1]

Signs and symptoms

Mild symptoms are experienced during these attacks described as dull headaches, nonspecific eye pain in and around the involved eye, occasional haloes around light, or transient and mild blurring of vision.[2] The symptoms may last for a quarter hour to several hours and may occur very infrequently once in a couple of years or relatively frequently, several times a month.

The eye is often white and quiet except for the elevated intraocular pressure and a sluggish or mid-dilated pupil that returns to normal once the attack resolves spontaneously. It is believed that the reason why the condition subsides spontaneously is that an environment factor such as bright light and sleep causes miosis before angle closure becomes irreversible. Between repeated attacks, few patients complain of visual symptoms.

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Risk factors

Risk factors for intermittent angle closure are identical to those for primary angle closure which include older age, female sex, Asian parentage, smaller anterior segment dimensions such as shallower limbal and axial anterior chamber depth, thicker lens, more anteriorly positioned lens, hyperopia, and a family history of angle closure.[3-11] The eyeball is smaller in women, Asians, and those with angle closure, making them at risk of getting intermittent angle closure later in life. As the lens enlarges throughout life, the anterior chamber becomes shallower with time and there is a relative anterior chamber-lens disproportion, which is also more pronounced among those with moderate to high hyperopia.

Clinical course

Intermittent angle closure may progress to chronic or acute angle closure (Fig. 1). The mild attacks may be triggered by emotions, fatigue, dim light, or prolonged near reading and tend to recur under similar circumstances.[12] Dilatation of the pupil under these physiologic conditions lead to a narrower anterior chamber angle with resultant elevation of intraocular pressure. The angle may be partially closed to allow moderate elevation of the intraocular pressure with mild symptoms or a

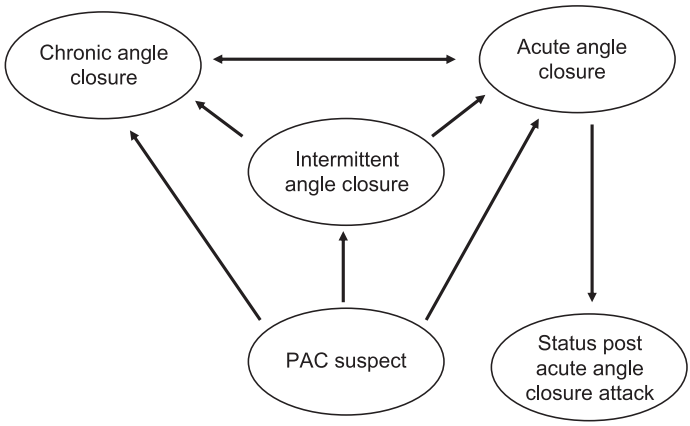

Fig. 1. Progression of angle closure.

near complete closure that spontaneously resolves with a reactive pupil. Sleep has some beneficial effect on intraocular pressure, most likely due to sleep-induced miosis and decreased aqueous secretion.[13]

Some doctors prefer the term *subacute angle closure*. The border of intermittent

and subacute angle closures is again arbitrary. Basically, subacute angle closure glaucoma with pupillary block means attacks which are more severe than intermittent angle closure but milder than acute angle closure. Symptoms of pain, blurred vision, and haloes are more marked than in intermittent angle closure. Racial differences are seen among Caucasians, blacks, and Asians with Asians having shallow anterior chamber than blacks.

Initially, the intermittent attacks occur at intervals of weeks or months that may continue uneventfully for months to years. Some patients avoid or reduce activities, for example reading, frequently associated with the attacks. Eventually, these attacks may become more frequent or lead to a peripheral anterior synechiae (PAS) formation and chronic angle closure glaucoma.[14] It may progress to severe attack.

Diagnosis of this condition is often missed because the eyes appear normal between attacks except for the narrow angle. Moreover, patient's self-diagnosis of similar symptoms such as migraine, sinusitis, or eye strain may confuse the clinical picture.

Management

Recognition of this condition, especially among Asians, is needed to prevent PAS formation and consequent chronic angle closure glaucoma. Periodic gonioscopy must be performed to determine if the angle is 'anatomically narrow' for which laser iridotomy is indicated. Preferably, indentation gonioscopy and ultrasound biomicroscopy should be performed.

All eyes with an established diagnosis of intermittent angle closure should be treated appropriately by releasing relative pupillary block. In most of these cases, laser iridotomy is indicated. In some cases, phacoemulsification with posterior chamber IOL or surgical peripheral iridectomy may be indicated.

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Chronic angle closure

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Introduction

Chronic angle-closure glaucoma (CACG) is the most common form of angle-closure glaucoma (ACG) seen in the clinic or hospital setting,[1-3] as well as in population-based surveys.[4-7] Sadly, it is often misdiagnosed as open angle glaucoma (OAG). Unlike acute or intermittent angle-closure, CACG is usually asymptomatic, although symptomatic episodes may supervene causing episodes of ocular pain and blurred vision. Most patients present in a very similar manner to those with chronic OAG. Careful gonioscopy is necessary to prevent this being misdiagnosed as OAG. This chapter describes the clinical features and important aspects in management of CACG.

What is chronic angle closure?

CACG is composed of two clinical entities, angle-closure and glaucomatous optic neuropathy. Angle-closure precedes the development of glaucomatous optic neuropathy. Angle closure means mechanical obstruction of the trabecular meshwork by the peripheral iris. In the longer term, other pathological changes may occur in the drainage angle, both structural and functional. The structural changes consist of peripheral anterior synechiae (PAS) and pigment clumping on the face of the trabecular meshwork, and may lead eventually to functional changes characterized by increasingly elevated intraocular pressure (IOP). This view is analogous to the concepts of structural and functional changes in the optic nerve, characterized by excavated optic neuropathy and visual field defects characteristic of glaucoma. In cases where angle-closure occurs gradually with an asymptomatic rise in IOP, but without evidence of glaucomatous optic neuropathy, the condition is termed chronic angle closure (CAC). However, this is not commonly seen in hospital or clinic patients, as most cases are not detected or do not present until some damage to the optic nerve has occurred, producing a manifest visual field defect.

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Difference between CAC and CACG

Currently, the term 'glaucoma' is used specifically to signify glaucomatous optic neuropathy. Hence, it indicates that there is evidence of structural and/or functional changes of the nerve fiber and/or optic nerve head that are characteristic of the glaucomatous disease process. Eyes with angle closure that have a normal optic disc and nerve fiber layer, but do not have functionally-significant loss of vision are classified as CAC.

Angle changes in CAC and CACG

Angle changes in CAC and CACG include PAS and acquired pigment on the trabecular meshwork. When these occur in eyes with an anatomically narrow angle they are signs of pathological angle closure. Pigment may be deposited on the surface of the meshwork during periods of contact between the peripheral iris and the trabecular meshwork. This results in coarse, blotchy deposition of pigment. PAS are permanent, pathological adhesions between the peripheral iris and trabecular meshwork. In 'appositional' angle-closure there is physical contact between the iris and the trabecular meshwork, but PAS are absent. Appositional closure is usually more pronounced in low-light conditions when pupil dilates. Consequently, it can be missed if gonioscopy is not properly performed in a dark room using a short, narrow slit illumination beam kept away from the pupil. Care must be taken not to apply pressure to the cornea that could artificially widen the angle. Good gonioscopy technique is very important when examining cases of suspected angle closure. However, since gonioscopy requires the use of visible light , other examination techniques that can be carried out in the dark may offer some advantages in the detection of angle closure. At present, dark room ultrasound biomicroscopy (UBM), anterior segment optical coherence tomography (OCT) with the light off, and infrared gonioscopy are under investigation.

Functional changes in the drainage angle

The sign of significant pathological damage to drainage angle function is raised IOP. An increase in IOP indicates obstruction or significant dysfunction of the trabecular meshwork to the point that aqueous outflow is compromised. It seems likely that this latter stage will be the culmination of many years of intermittent irido-trabecular contact which result in permanent synechial closure or a dysfunctional trabecular meshwork. One histological study has shown that pathological changes in trabecular meshwork can be seen away from visible areas of PAS. A gonioscopic examination alone may not reflect the extent of trabecular meshwork damage in acute and chronic PACG.[8]

Whether PAS are present or not, the impairment of outflow facility leads to increased IOP. A rise in IOP may occur rapidly (within hours in acute cases) or more gradually over years. Although some patients eventually diagnosed as suffering chronic angle-closure may report occasional symptoms consistent with intermittent rises in IOP, most never experience symptomatic attacks.

Natural history of CAC

Angle closure glaucoma cascade

The first stage in the cascade of events that may lead to angle-closure glaucoma occurs when eyes develop irido-trabecular contact. Under the classification system introduced by the International Society of Geographical Epidemiological Organization (ISGEO), this state is termed 'primary angle closure suspect' (PACS). In practical terms, this is analogous to the term 'occludable' angle commonly used in clinical settings. 'Occludable' describes an anatomical configuration in eyes in which angle closure is considered possible, or when the trabecular meshwork is partially occluded, but the IOP is normal, as are the disc and field. Clinicians sometimes use the term 'narrow' angle interchangeably with 'occludable', although these two terms do imply separate, distinct situations. The term 'narrow' reflects what the clinician actually sees with slit lamp biomicroscopy and gonioscopy, whereas the term occludable implies a prediction of likelihood of a future event. There has been much debate on the issue of the most appropriate terminology and classification to describe this condition. Recently, the Association of International Glaucoma Society (AIGS) consensus panel on angle-closure glaucoma proposed that the term 'anatomical narrow angle (ANA)' may be more appropriate as it honestly represents the actual findings. The term 'ANA' emphasizes that the angle inlet appears narrow on gonioscopy, and avoids making any judgment on the risk of closure. More studies are needed in order to clearly define the correct division between the very early stage of angle-closure and eyes that are not at risk of closure. The crucial issue in terms of clinical management is to differentiate between eyes that will progress to sight-threatening sequelae of angle-closure, from those that will not. Once the high risk cases can be effectively identified, it will allow intervention in these people to prevent the cascade of events leading to angle-closure glaucoma.

If the angle-closure process can be halted, most eyes will be effectively 'cured'. If it is not, IOP will probably rise, either acutely or chronically, leading to the next stage – 'primary angle-closure (PAC)'. When the condition reaches this stage, even if angle closure is aborted, it is quite possible that the IOP will remain high. The magnitude of IOP rise depends on the functional reserve in the outflow pathway, and degree of trabecular damage. The underlying mechanism causing angle-closure must be identified and corrected to prevent further trabecular damage, and avoid long-term IOP rises. There may be a single mechanism causing angle-closure, or in some cases, multiple mechanisms are active.

Based upon the ISGEO-classification, PAC is sub-categorized into ischemic and non-ischemic types. The 'ischemic' sub-type has signs including iris whirling, stromal atrophy or glaukomflecken indicating previous acute angle-closure. Anterior segment ischemic sequelae indicate that IOP has previously been sufficiently high to cause pressure-induced damage of the iris and ciliary body. Pathological changes at the optic nerve head are not detectable on clinical examination (or the condition would be classified as primary angle-closure glaucoma). The 'non-ischemic' sub-type describes an eye with angle-closure and raised IOP or PAS, but normal optic disc and visual field, and no signs of ischemic damage.

The final stage of the angle-closure cascade is ACG, signifying the presence of angle closure and glaucomatous optic neuropathy.

Stages of angle closure

Differentiating angle closure into its different stages does have clinical significance. Each stage indicates the presence or absence of end organ damage at a particular site, which in turn implies severity of the disease, and prognosis for the patient. It encourages a systematic approach to treatment, and allows a more evidence-based approach to discussing prognosis, and the risk versus benefit of treatment. For example, the efficacy of laser peripheral iridotomy (LPI) in prevention of an IOP rise depends on the stage of disease. One population-based study in East Asia reported that 97% of PACS will maintain a normal IOP following LPI.[9] Another study[10] showed that 89% of unaffected fellow eyes of those suffering an acute attack maintained a normal IOP following LPI without the need for additional treatment. These fellow eyes can be seen as representative of the highest risk PACS eyes. Considering the situation in eyes with established angle closure, it has been shown[11] that only 42% of eyes which have suffered an acute angle closure attack achieve satisfactory IOP control after LPI alone. The remaining 58% developed an IOP rise requiring further treatment (average follow-up 50 months). Furthermore, in eyes with established glaucomatous optic neuropathy (PACG), most require further treatment to control IOP, despite a patent LPI. In a long-term retrospective review of 83 ACG eyes, only five (6%) did not require any treatment after LPI.[12]

In summary, if LPI is performed early enough (in the PACS stage), it appears very effective in preventing the 'cascade of progression' to the next stages of PAC and PACG. If the condition remains untreated and PAC develops, treatment with LPI may not fully control the condition. And when glaucomatous optic neuropathy has developed, LPI will not be effective on its own. Even with medical therapy, IOP in these eyes is poorly controlled, and they often require filtering surgery.[12] The essence is that staging of angle-closure is important in the choice of appropriate management and in discussing prognosis with the patient.

Predisposing anatomical abnormality and risk factors

It is well known that eyes with relatively smaller anterior segments are more prone to develop angle-closure. Eyes with chronic angle-closure glaucoma have different anterior segment anatomical relationships compared to normals.[13,14] The eye at risk tends to have a shallow anterior chamber, a relatively anteriorly positioned lens and a shorter axial length, and is more likely to be hypermetropic.[15] East or Southeast Asian ethnicity is an important risk factor for the development of chronic angle-closure glaucoma. Other demographic risk factors include older age, female sex and a positive family history.[5,16-20] Both increasing age and female sex are known to be associated with shallower anterior chambers. Such associations have been noted in all races.[21] A shallow anterior chamber is a significant risk factor for angle closure, although research in East Asia suggests the nature of the association is specific to each population.[22] There is still controversy why East Asians suffer a greater prevalence of ACG than other races.[23] A clinic-based study comparing the angle width of Asians, African-Americans and Caucasians found no statistically significant difference in AC depth between the three groups. One possible explanation comes from a report that the iris joins the scleral wall most anteriorly in Asians, slightly more posteriorly in Afro-Americans, and most posteriorly in Caucasians.[21] A thicker, more anteriorly positioned of the lens[24] and a smaller corneal diameter

have also been identified as risk factors.[25-27] The role of the ciliary body anatomy and the position of the ciliary processes in the pathogenesis of this condition requires further investigation. Until now, there have been no conclusive reports of the genetic basis of ACG.[28]

Angle closure mechanisms

'Residual' glaucoma, or 'post-iridectomy' glaucoma, have previously been commonly used to describe raised IOP following an iridotomy or iridectomy.[29] The terminology suggests that several mechanisms may be active in eyes suffering from angle closure. A comprehensive study using biometry, UBM and gonioscopy, demonstrated that approximately half of eyes with CACG may have multiple mechanisms contributing to the angle-closure process.[30] Though pupillary block is the most common mechanism and is present in almost every case, other mechanisms must be sought and excluded. These include plateau iris, lens-related causes, and ciliary block. Classification according to these four levels of obstruction to aqueous flow is widely accepted and of great practical use.[31] By identifying and treating the specific mechanisms responsible for angle-closure, it is possible to convert eyes with angle closure to healthy eyes, provided treatment is given prior to significant damage to the trabecular meshwork or optic nerve.

Clinical presentation

By definition, the onset of CACG is gradual. Symptoms may occur later in the course of the disease, and chronic angle-closure is often the final result of several different processes.[32] CACG can be categorized into two subtypes.

Subtype of CACG

a. **Asymptomatic CACG** This is the more common subtype. The patient has no symptoms of pain or headache and no history of an acute attack. The eye gradually progresses from appositional to synechial angle-closure. 'Creeping' angle closure describes one form of the disease where PAS slowly increase in circumference and height leading to compromised aqueous outflow and a raised IOP. Even in areas without PAS, there may be evidence of loss of corneal endothelial cells and reactive repair processes.[8] The signs and symptoms are similar to those of open angle glaucoma except that angle-closure is present.
b. **Post-symptomatic CACG** This develops after acute angle closure (AAC) or intermittent episodes of pain and headache with or without associated visual symptoms such as haloes or blurred vision. Delayed presentation to hospital (> 24 hours) or an acute attack that is unresponsiveness to medical treatment have been identified as significant risk factors in developing CACG.[33] On slit-lamp examination, anterior segment ischemic sequelae of AAC may be seen. These include distortion of iris tissues (iris whorling) and necrosis of the anterior sub-capsular lens epithelium (glaukomflecken). These are often accompanied by a significant decrease in the corneal endothelial cell density in eyes that have had an acute attack.[34]

A clinic-based study[13] found that patients with asymptomatic CACG were older than patients in the post-symptomatic group, were more often men and were more likely to have either diabetes mellitus or hypertension. Post-symptomatic CACG was more likely to occur in eyes that were more hypermetropic and had more irido-corneal synechiae and large areas where the pupillary ruff was absent.

Diagnosis

The diagnosis of CACG is directed toward detection of angle closure and glaucomatous optic neuropathy. This is described elsewhere in this book with detail description.

Principles of treatment

The basic management principles are as follows:
a. Reverse angle closure by alteration of the angle configuration
b. Control raised IOP and other risk factors
c. Monitor and maintain the structural and functional integrity of the optic disc and the retinal nerve fiber layer.

Steps in management of CACG

The first step is to *document the extent of angle-closure and severity of glaucoma* by examination of the angle structures by slit-lamp examination or gonioscopy. Indentation gonioscopy will help to determine the presence and extent of PAS. UBM provides high resolution images of anterior segment structures and their relationships. UBM is currently the best imaging technique to examine the posterior chamber and ciliary processes, surpassing dynamic gonioscopy.

The second step is to *identify and treat the mechanism causing angle-closure*. Pupillary block is the most common mechanism and responds to laser peripheral iridotomy (LPI). However, other mechanisms should also be considered and excluded. LPI is most effective in the early stages of disease, but is less effective in more advanced cases where AAC has occurred, and or glaucomatous optic neuropathy has developed.

The third step is *reassessment and further treatment if necessary*. Even after successful LPI, most patients with CACG require some further treatment, either because of non-pupil-block mechanisms, or because angle structures have been damaged. Patients therefore need to be reassessed after LPI, to consider further treatment in the form of iridoplasty, medication, or surgery.

Iridoplasty is effective for managing AAC, but is of no proven efficacy in CACG. However, there is some evidence to suggest that it is effective in cases of pure plateau iris syndrome in Caucasians.[35] Glaucoma surgery (trabeculectomy) remains the definitive method of achieving IOP control. However, the success is highly dependent on postoperative management, and the outcome is variable.

Medical therapy has recently become more important for management of CACG

as the IOP may remain high even after iridotomy and iridoplasty have been performed. The efficacy of topical prostaglandin analogues in CACG therapy was demonstrated in a large-scale, randomized, multi-center study. The IOP reduction was 30% to 33% for eyes receiving latanoprost, compared with 20% for eyes receiving timolol.[36]

The final step in the management of CACG is to *monitor IOP, optic disc, and visual field,* and to perform periodic gonioscopy.

Conclusion

In this chapter, the concept of a cascade of events progressing inexorably to angle-closure glaucoma was introduced. There is strong indirect evidence that earlier diagnosis and treatment leads to a better outcome for the patient. Therefore, identifying the stage of disease in each individual patient is important in determining prognosis, and in planning treatment. Laser iridotomy remains a key method of management, although its efficacy is variable and often limited in more advanced cases. Most eyes with CACG need additional treatment to control IOP, which currently means relatively large numbers of patients using conventional glaucoma on medication.

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Occludable angles

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Introduction

In 1938, the first modern classification of glaucoma, differentiating between open angle with deep anterior chamber and closed angle with shallow anterior chamber, and suggesting the terms 'wide angle' and 'narrow angle', was presented by Barkan.[1] Unfortunately, there are various clinical situations which lie between these two groups and classification schemes. Occludable angles belong in this realm. But the inaccuracies of clinical examination and loose usage of this term have lead it to include cases of patent drainage angles which may or may not have increased IOP, and those cases leading to a pathway of iris apposition to the trabecular meshwork before the elevation of IOP.[2] This apposition is caused by one or a combination of abnormalities in the relative or absolute sizes or positions of anterior segment structures, which, in turn, result from abnormal vector forces arising at different anatomic sites.[3]

Definition and classification of an 'occludable' or narrow angle

The terms narrow and occludable angle, are general terms used loosely and interchangeably to indicate the anatomical predisposition to angle closure. Although there is much argument in the definition and use of these terms, this condition describes a state of tapered or tapering angle drainage implying appositional contact between the posterior trabecular meshwork and the peripheral iris.

The phrase 'narrow angle' is a morphologic condition described in the Shaffer System for grading angle widths; 20° for narrow and 10° for extremely narrow.[4] These categories imply a probability and possibility of closure, respectively. This definition is relatively objective and emphasizes that narrow but open angles identified on gonioscopy may or may not occlude permanently. However, a number of Glaucoma guidelines discourage the use of 'narrow angle glaucoma' for being non-specific, as it does not describe whether the main cause of IOP increase is

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primary impairment of trabecular outflow facility, mechanical obstruction of the trabeculum by iris apposition or synechial closure.[5,21]

The occludable angle was first described epidemiologically by Arkell *et al*. in a prevalence study among northwestern Eskimos in Alaska.[6] It was then adopted by Salmon in his prevalence study in South Africa (1993).[7] Foster used the same term in his studies in Northern Mongolia in 1996 and in Singapore in 2000,[8,9] to allow comparison with previous reports. It was defined not as a precise Shaffer angle, but the commonly used clinical derivative based on the visibility of the pigmented trabecular meshwork in the primary position without manipulation or indentation. In the above studies, an occludable angle required no visible meshwork throughout three quarters or more of the angle circumference. In contrast, Thomas used 180° or more of hidden trabecular meshwork, with IOP below 22 mmHg and no peripheral anterior synechiae, in his cross-sectional and longitudinal studies in southern India.[10,11] In another paper, Foster used a definition of an occludable angle as one in which the posterior trabecular meshwork was visible for less than 90° of the angle circumference, with gaze in the primary position.[12]

In 1978, with the developments in the technique of gonioscopy and increased understanding of the mechanism of angle closure, Spaeth introduced a new classification for narrow angles.[12a] In addition to Shaffer's angle, Spaeth included assessment of the convexity of the iris (with a more steeply convex iris configuration implying greater pupil block) and the position of the iris insertion. The apparent iris insertion was a tangent to the most peripheral iris structure seen on primary gonioscopy taken to the wall of the eye. The true iris insertion was that seen when the actual insertion could be visualized (either in primary position, tilting or indentation). This important contribution addressed the major weakness of the Shaffer classification. The irido-trabecular angle is difficult to grade gonioscopically because of the 'en face' view. Instead almost all clinicians grade the apparent iris insertion and infer the Shaffer grade from it. However the most peripheral iris seen on primary gonioscopy is not always the iris adjacent to the trabecular meshwork. Visibility is affected by the convexity of the more proximal iris structures and the angle of view of the particular gonioscope used (Fig 1).

A recent study in Liwan, China has addressed these issues in a population with a high prevalence of angle closure.[12b] Spaeth grading of apparent iris insertion was found to be more reliable than Shaffer grading. The proportion of right eyes which were occludable according to Shaffer grading (an angle of $\leq 10°$, angle closure probable) was 23% and 13% for the superior and inferior parts of the angle. The Spaeth apparent iris insertion of above the trabecular meshwork was 27% and 8% respectively. Increasing numbers of eyes with peripheral anterior synechiae were found with an increasing number of quadrants in which the pigmented trabecular meshwork was not visible as well as narrower average Shaffer angle between superior and inferior quadrants. However, the quadrant that most closely predicted an occludable angle throughout 270° was the nasal angle. Almost all eyes with a Shaffer angle of $\leq 10°$ had a steep or plateau iris configuration.

The most recent classification of angle closure was developed by the International Society of Ophthalmic Epidemiology and published by Foster and colleagues for use in prevalence surveys.[13] It identifies three conceptual stages in the natural history of angle-closure from anatomically narrow angles, to anterior segment signs of disease (raised IOP and/or peripheral anterior synechiae) finally culminating in glaucomatous optic neuropathy:

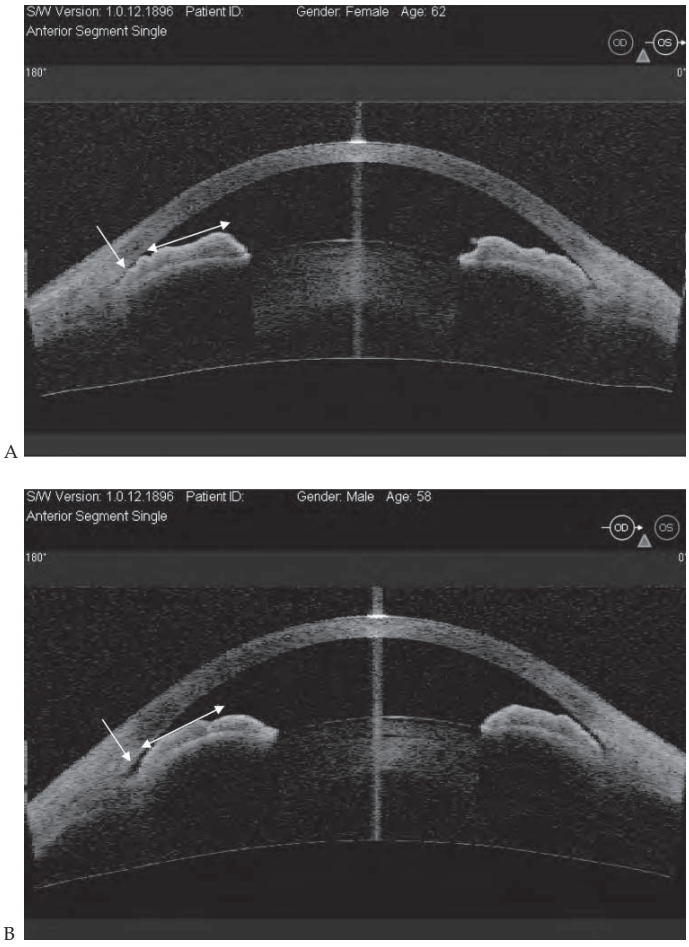

Fig. 1. Two gonioscopically occludable angles seen on AS-OCT. Single-headed arrow shows approximate position of trabecular meshwork. Double-headed arrow shows gonioscopic angle of view to the apparent iris insertion. In both eyes, the apparent iris insertion is anterior to Schwalbe's line. (Courtesy of Tin Aung and Lisandro Sakata of the Singapore National Eye Centre and Singapore Eye Research Institute) A: Below the apparent iris insertion is a large area of appositional closure. Note the prominent last iris roll. The iris configuration is less steep than in B. B: In this eye, the gonioscopic view is very similar. However, the steepest part of the iris centrally hides the wider angle recess. While there is a great deal of pupil block, there is no angle closure.

a. *Primary angle-closure suspect (PACS):* an 'occludable angle', but normal IOP, disc and field, without evidence of peripheral anterior synechiae.
b. *Primary angle-closure (PAC):* an 'occludable angle' with either raised IOP and/or primary peripheral anterior synechiae. Disc and field normal.
c. *Primary angle-closure glaucoma (PACG):* primary angle-closure plus evidence of glaucomatous damage to optic disc and visual field (with similar approaches as those used for POAG).

This approach to classification differs from the scheme found in most textbooks in which eyes with a narrow drainage angle and either raised IOP or peripheral anterior synechiae are said to have primary angle closure 'glaucoma'. This important distinction ensures a constant definition of glaucoma across the spectrum of subtypes of the disease.

Although the ISGEO definition of PACS was no more specific than the possibility of irido-trabecular contact, it recognized that most studies used a definition based on an apparent iris insertion above the posterior trabecular meshwork of an arbitrary circumferential extent.

As yet, few studies have reported the temporal relationship between occludable angles (or PACS) and PAC. In a study by Thomas *et al*.,[10] only 22% of PACS progressed to PAC in five years, a progression rate of 4.4% per year. This was slightly higher than the 35% progression in Eskimos over ten years previously reported by Arkell.[6]

Risk factors

There is evidence in the literature that eyes with angle closure glaucoma or occludable angles have shorter axial lengths, shallower anterior chamber depths, and thicker crystalline lenses.[14-18] A study by George *et al*. among a south Indian population,[19] reported that females were in significantly larger proportion in the groups with occludable angles and ACG than the normal population. Females had significantly shorter eyes, shallower anterior segments and thicker lenses. The association between older age, thicker crystalline lenses and occludable angle are explicable on the basis of a narrow angle configuration in an eye with shorter axial length. The lens thickness/axial length ratio is increased in older age groups, suggesting a disproportionately thick lens or a normal sized lens in an eye with a shorter axial length may predispose to occludable angles.

UBM studies of ciliary body thickness showed that the ciliary body was thinner in narrow-angled eyes than in normal control eyes.[20] Correlation between ciliary body thickness and lens thickness and the anterior chamber depth was also shown. The thinning of the ciliary body may be an age-related change associated with these age-related biometric findings of the anterior segment. Forward rotation of the ciliary processes was also examined in most narrow-angled eyes, but could not be demonstrated statistically.

It has been reported that there are differences in gonioscopic structures amongst different racial groupings.[26] Studies by Oh *et al*. (1994)[27] and Nguyen *et al*. (1996)[28] have shown a more anteriorly inserted iris root among Asian patients, which might account for a higher incidence of angle closure glaucoma among populations of Chinese origin. It also reinforces the importance of assessing iris insertion in gonioscopic grading.

Treatment

Medical treatment

a) Indications for treatment

Patients presenting with elevated IOP due to asymptomatic PAC may need treatment with glaucoma medications prior to laser iridotomy.[21] However, in purely occludable angles and normal IOP, medication may only be needed for laser treatment. Once iridotomy, and when indicated, iridoplasty have been performed to relieve irido-trabecular apposition, any residual elevation of IOP may be controlled by the use of glaucoma medications. All the major classes of topical glaucoma medication can be used in angle-closure patients in the same way as they are used for management of PACG. Topical beta-blockers, carbonic anhydrase inhibitors and alpha-2-agonists can be used when there are no contraindications.[22] However, there has been no extensive study on the use of medication as prophylactic treatment in occludable angles.

b) Specific medications

Pilocarpine
Pilocarpine is the most commonly used and most extensively studied anti-glaucoma agent.[23] In the past it was frequently used in the management of angle-closure as it acts to constrict the pupil and pull the iris away from the trabecular meshwork. But long-term use of pilocarpine can result in the development of posterior synechiae and pupil miosis making cataract surgery technically difficult. Miotic agents have not been shown to prevent progression of angle-closure and should never be used in lieu of an iridotomy.

UBM and Scheimpflug studies have shown that pilocarpine increases angle width in patients with narrow angles, which can be used for the temporal treatment of patients with narrow angles,[23] but paradoxically its use in normal eyes may result in shallowing of the anterior chamber.[24] This effect may be exacerbated in eyes with pseudoexfoliation, phacomorhpic glaucoma and aqueous misdirection. For these reasons, pilocarpine is contra-indicated in cases with level III and IV mechanisms (*i.e.*, lens induced and retro-lenticular mechanisms causing angle-closure).[21] Despite its' complications and side-effects pilocarpine can be very effective in controlling IOP. It is inexpensive and widely available. It can be used in a low dose form in for angle-closure patients with plateau iris syndrome and residual appositional closure following iridotomy and iridoplasty.[25]

Laser

1. Laser periphiral iridotomy (LPI)

There is very little evidence supporting the benefit of LPI for individuals with gonioscopically narrow angles. Little is known about the natural history of eyes with this condition.

Nolan[32] reexamined 164 eyes of 98 participants in Mongolia who had LPI for

an occludable angle or angle closure discovered during two previous prevalence surveys. Median angle width increased by two Shaffer grades after LPI. None of the 74 eyes with PACS developed PAC or PACG by the time of the follow-up examination. In contrast, LPI was judged a failure in 3% of eyes with PAC and 47% of eyes with PACG.

The Liwan Eye Study recruited 74 of 102 Chinese adults with no trabecular meshwork visible for three or more quadrants to study the effect of laser peripheral iridotomy.[29] Eighty-five percent of steep and 65% of plateau iris configurations became regular after treatment, confirming the role of pupil block in iris profile, including plateau configuration. Limbal but not central anterior chamber depth increased after iridotomy and mean IOP decreased by 3 mmHg. Shaffer angle width increased significantly from 0.6 units to 2.4 units after treatment. More than 80% of eyes with Spaeth gradings of A and B outside the superior quadrant converted to D or E after treatment. However, one-fifth of eyes treated still had more than three quadrants of hidden trabecular meshwork following iridotomy.

In the US, anatomically narrow angles are found in 2-6% of eyes. However, the prevalence of angle closure glaucoma is less than 0.2% of the population. This signifies that only about one of ten people with narrow angles will develop angle closure in their lifetime.[26] It is suggested that prophylactic peripheral iridotomy be performed in situations other than in fellow eyes of patients who develop angle closure. These include patients with narrow angles and:

- symptoms of acute angle closure (AAC);
- signs of previous angle closure attacks;
- a well-documented family history of angle-closure glaucoma;
- appositional closure of some portion of the trabecular meshwork with or without an elevated IOP;
- an inability or unwillingness to seek rapid ophthalmic care for an AAC;
- a need for repeated pupillary dilation and extensive retinal treatment.[26]

More research is needed on the natural history of PACS to determine which individuals are likely to benefit from this procedure and whether or not prophylactic LPI is effective at preventing AAC, PAC, and PACG from developing in individuals with gonioscopically narrow angles (PACS). Consideration must be given to the potential adverse outcomes of prophylactic LPI. Treating all individuals with PACS may cause more harm than the disease process itself, and is a strategy that will not be viable in less developed nations where health resources are limited unless there is strong evidence for benefit.

2. Argon laser peripheral iridoplasty

Argon laser peripheral iridoplasty (ALPI) is a method of opening an appositionally closed angle in situations in which laser iridotomy either cannot be performed or does not eliminate appositional angle-closure because mechanisms other than pupillary block are present. The procedure consists of placing contraction burns (long duration, low power, and large spot size) in the extreme iris periphery to contract the iris stroma between the site of the burn and the angle, physically pulling open the angle.

3. Trabeculoplasty

A prospective trial of argon laser trabeculoplasty (ALT) in narrow angle glaucoma has been reported.[30] To achieve relief of pupil block, eyes were randomly assigned to treatment with short pulsed laser iridotomy (LPI) with the YAG or Dye lasers, or surgical peripheral iridectomy (PI). Alternatively, argon laser iridoplasty (ALPI) was performed to widen the anterior chamber angle sufficiently to permit ALT. Fifty-two eyes were treated and follow-up was from 12 to 22 months. A high rate of failure to control IOP with topical medication and progression of visual field loss occurred in all treatment groups. Iridoplasty followed by ALT was particularly unsuccessful as, in 50% of cases, progressive synechial closure of the anterior chamber angle occurred following treatment. In eyes treated with PI/LPI and ALT, the IOP control was improved in 12%, unchanged in 30% and remained uncontrolled in 58%. The authors conclude that iridoplasty followed by ALT is an unsuitable treatment for eyes with narrow angle glaucoma.

Surgery

In an Italian study, occludable angle patients who underwent phacoemulsification showed a reduction in IOP, an increase in anterior chamber depth and angle width.[31] However, this study had a small sample size and a follow up of 15 months.

New devices for detecting narrow and occludable angles

A number of devices to assess the irido-corneal angle have recently been developed. There is little published in the field of screening for angle closure using these instruments. However, they may play a role in PACG screening and management and we therefore discuss them here.

1. IOLMaster (Zeiss). This instrument measures central anterior chamber depth, keratometry and axial length using the combination of partial coherence biometry (infrared light) and optical method.
2. Pentacam (Oculus) uses other methods for central anterior chamber depth measurement. While the optical pachymetry can be performed at the slit lamp the Pentacam has the advantage of rotating Scheimpflug photography, which may offer more insight into angle structures.
3. SPAC – Scanning Peripheral Anterior Chamber depth analyzer (Takagi). This instrument obtains 21 rapid slit photographs of the central and peripheral anterior chamber using optical method and creates an iris anterior surface contour using the measurements. They are graded numerically and categorically compared to a sample database to provide an empirical risk assessment. SPAC appears to identify a high proportion of those with narrow angles.[33] Its usefulness in screening awaits further validation.
4. ASOCT - Anterior Segment Optical Coherence Tomography (Visante, Zeiss). This utilizes infrared light to image the angle and the anterior chamber in real time but not the ciliary body. Recent early research indicates that the AS-OCT identifies a high proportion of subjects felt to be narrow or closed on gonios-

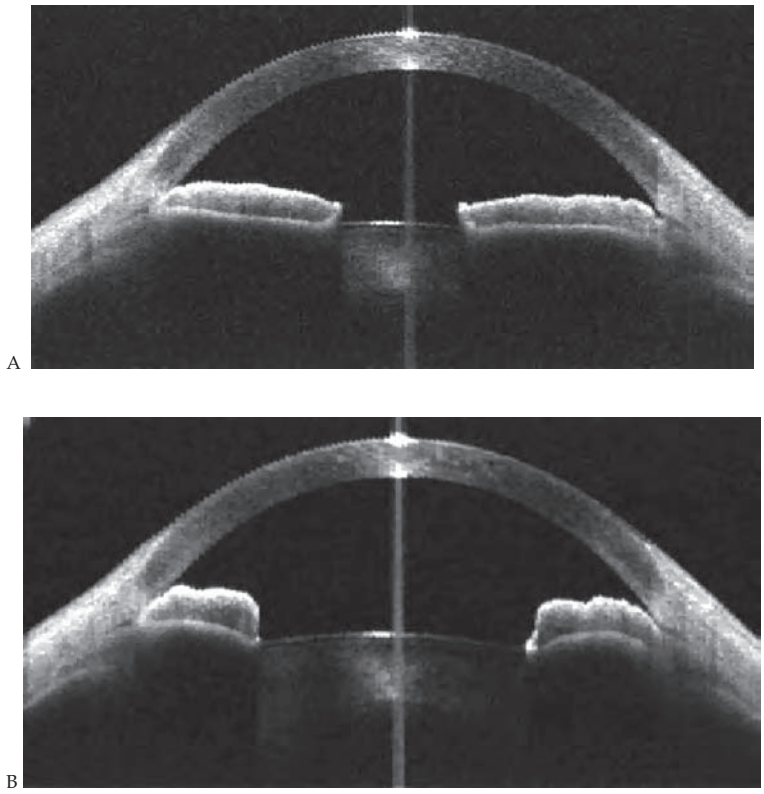

Fig. 2. The effect of ambient illumination on angle configuration shown with AS-OCT imaging. (Courtesy of Tin Aung and Lisandro Sakata of the Singapore National Eye Centre and Singapore Eye Research Institute) A: In the light, the pupil is constricted, rendering the iris profile regular and widening the angle recess. B: In the dark the pupil dilates, dramatically increasing pupil block and appositionally closing the angle.

copy, however, the device identified more subjects as having closed angles than gonioscopy.[34] Further research will be needed to determine the role of AS- OCT in screening.

All the instruments, except the ASOCT, rely on light in the visible spectrum. Theoretically, as with gonioscopy, visible light may affect the angle status during examination (Fig. 2). None of them, however accurately images the trabecular meshwork, ensuring the continued place of gonioscopy in the assessment of the occludable angle.

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Plateau iris

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Introduction

Plateau iris is characterized by closing of the anterior chamber angle secondary to a large or anteriorly positioned ciliary body that mechanically alters the position of the peripheral iris toward the trabecular meshwork.

Gradle and Sugar[1] had initially observed angle closure glaucoma in eyes with normal anterior chamber depths. Tornquist[2] was the first to use the term plateau iris in 1958, when he described the appearance of the iris in a patient with angle closure glaucoma who was having a normal central anterior chamber depth.

Pathophysiology

- In plateau iris configuration, the pars plicata may be large and anteriorly positioned, mechanically positioning the peripheral iris against the trabecular meshwork.
- In addition, the iris root is inserted anteriorly on the ciliary face further crowding the anterior chamber angle.
- There also may be a prominent peripheral roll of iris.

The iris crowding of the angle obstructs aqueous flow via the trabecular meshwork and may lead to angle-closure glaucoma.

The etiology underlying this anterior displacement of the pars plicata is not clear and it probably represents an anatomic variant.

No abnormality of the ciliary body has been found that would cause such forward rotation of the ciliary processes. The possibility that the lens zonule apparatus is pulling the process forward is unlikely because of the observation that even in pseudophakic eyes the iris processes remain in the forwarded position, even though the IOL is in a much posterior position as compared to the crystalline lens.

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Except in the rare younger patients (age 20-30s), some degree of pupillary block may also be present. Because a component of pupillary block may exist in patients with plateau iris configuration, laser iridotomy should be performed as the first intervention.[3] If the angle remains capable of closure despite a patent iridotomy, the condition is termed plateau iris syndrome.

The exact prevalence of plateau iris is unknown. Its diagnosis should be suspected when angle closure occurs in a young myopic patient. Plateau iris is an important cause of angle-closure glaucoma in patients younger than 40 years and is seen most commonly in women and often with a family history of primary angle-closure (relative pupillary block) glaucoma. Barkana *et al.*[4] reviewed retrospectively the data regarding angle closure in high myopes and found plateau iris syndrome in three patients of 17938 patients with high myopia more than -6.0 Diopters.

The racial predisposition to progressive angle closure was analyzed by Hagadus *et al.*,[5] who found that Caucasian eyes have a lesser predisposition to angle closure as compared to Hispanic eyes (46.9% vs 72.7%) even after a laser iridotomy. The frequency of open angles after LI (laser iridotomy) was similarly higher among Caucasians than among Hispanics (75% vs 50%). Choi JS et al[6] analyzed the risk factors of peripheral anterior synechiae progression after laser iridotomy. Over a 3 year period the rate of PAS progression was higher in eyes exhibiting plateau iris.

The effect of mydriatics agents on the anterior segment anatomy was assessed by Sekhar *et al.*,[7] who described a case of plateau iris syndrome who demonstrated a post mydriatic rise in IOP in one eye but not in the other eye. They suggested that plateau iris may be caused by difference in the extent of closure of the angle circumferentially over the 360^0 of the angle.

Clinical presentation[3]

- Patients with plateau iris tend to be female, in their 30-50s with a myopic refractive error. They may present with angle closure, either spontaneously or after pupillary dilation. Usually the diagnosis of plateau iris configuration is made on routine examination. Plateau iris syndrome may be recognized post laser iridotomy when the angle remains persistently narrow in an eye after iridotomy.
- Slit lamp examination of patients with plateau iris usually shows a normal central anterior chamber depth with a flat or slightly convex iris surface.[4] On gonioscopy, the angle is extremely narrow or closed, with a sharp drop-off of the peripheral iris (sine wave configuration). When indentation gonioscopy is performed, the double-hump sign is seen. The more peripheral hump is determined by the ciliary body propping up the iris root, and the more central hump represents the central third of the iris resting over the anterior lens surface. The space between the humps represents the space between the ciliary processes and the endpoint of contact of the iris to the anterior lens capsule. In such eyes much more force is required to open the angle on indentation gonioscopy as compared to cases with pupillary block angle closure.

Plateau iris configuration vs plateau iris syndrome[8]

Plateau iris *configuration* is defined as an anatomically narrow angle as determined by gonioscopy in the presence of a *flat* iris plane and a normal central ACD. This configuration occurs because of large or anteriorly inserted ciliary processes which hold the iris in apposition with the trabecular meshwork and prevent posterior movement of the iris. Relative pupillary block is also believed to play a significant role and laser iridotomy is considered effective in opening up the angle.

Plateau iris syndrome is characterized by the development of angle closure in an eye with a plateau iris configuration even after a patent iridotomy. The level of the iris stroma in relation to the angle structures, referred to as the height of the plateau, differentiates two subtypes of plateau iris syndrome.

1. In the **complete syndrome**, the angle is occluded to the upper trabecular meshwork or the Schwalbe line and intraocular pressure (IOP) rises.
2. In the **incomplete syndrome**, the iris occludes the angle to the mid level, leaving the upper portion of the filtering meshwork open and IOP unchanged. This latter situation is far more common and is clinically important because these patients can develop peripheral anterior synechiae (PAS) and synechial angle closure years after a successful iridotomy. Therefore, patients with an open angle after iridotomy should not be assumed to be cured. The angle can narrow further with age, and angle closure can occur years later.

Differential diagnosis

Pseudoplateau iris[8,9]

In pseudoplateau iris, the anterior displacement of the peripheral iris is not caused by an enlarged or anteriorly positioned ciliary body. Cysts of the iris and/or ciliary body neuroepithelium most often are responsible. This condition is distinguished easily from plateau iris because the angle is usually closed in only one quadrant or, if cysts are multiple, at several focal loculations. Ultrasound biomicroscopy (UBM) is extremely helpful in identifying the underlying mechanism responsible for pseudoplateau iris. The plateau iris also needs to be distinguished from angle closure associated with extensive peripheral anterior synechiae and an incomplete iridotomy.

Imaging studies[10-14]

Ultrasound biomicroscopy

UBM uses high frequency ultrasound (50 MHz) to produce high resolution images of the anterior segment (30-50 μ) This contact procedure is non invasive and can visualize the cornea, iris, angle, anterior chamber, posterior chamber and ciliary body with accuracy. The configuration of the iris surface, iris root insertion, iridocorneal angle, and ciliary processes can be seen in detail to confirm the clinical findings of plateau iris. The UBM characteristics include forward positioned pars plicata,

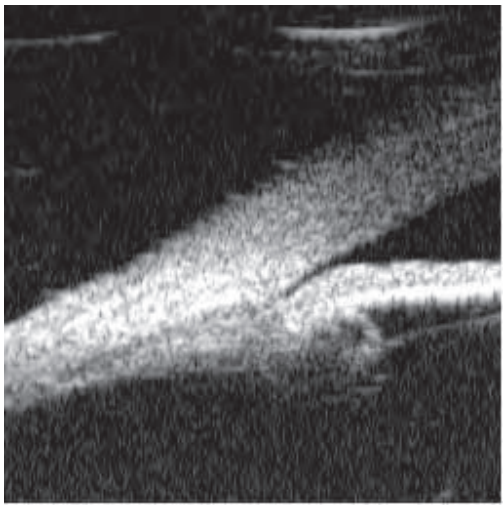

Fig. 1. UBM picture showing anteriorly positioned ciliary processes pushing up the peripheral iris. This has caused a narrowing of the angle recess in the presence of a relatively flat central iris configuration.

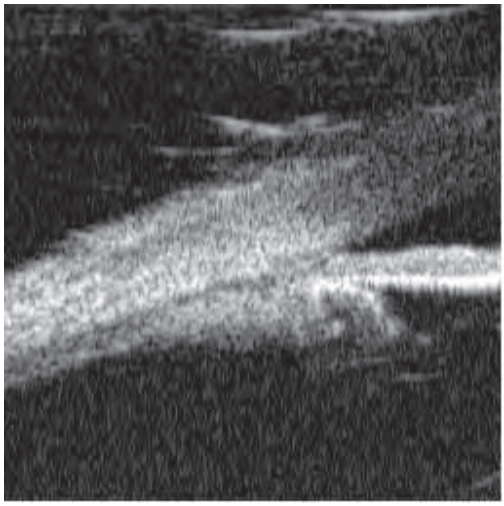

Fig. 2. Second eye of the same patient, again showing an anteriorly placed ciliary process and a closed angle in the presence of a relatively flat central iris configuration.

with a closed ciliary sulcus. This anterior position pushes the root of iris into the trabecular meshwork causing angle closure (Figs 1 and 2). This structural support also prevents the posterior movement of the iris following YAG iridotomy.Any element of pupillary block also may be confirmed with Ultrasound Biomicroscopy (UBM) imaging. Pilocarpine leads to an opening up of the angle.

Polikoff *et al.*[15] studied the various UBM parameters in cases of plateau iris syndrome and assess the effect of laser iridotomy in such eyes. They concluded that

LI did not alter the anterior segment anatomy probably because of fixed anterior insertion of the iris and ciliary body in plateau iris configuration. Matsunaga *et al.*[16] studied the anterior segment anatomy in three groups of patients- relative pupillary block, plateau iris configuration and peripheral anterior synechiae with the use of indentation UBM gonioscopy using a newly deigned cup and found that the angle opened significantly with indentation in eyes with relative pupillary block. Ritch *et al.*[17] evaluated the long term success rates of ALPI in the management of plateau iris syndrome and concluded that ALPI was successful in eliminating residual angle closure after laser iridotomy during the six-year follow-up period even though a small number of patients might require retreatment. A contrasting study regarding the ACD measurement with the use of UBM was presented by Mandell *et al.*,[18] who retrospectively reviewed the Biometric analysis of the UBM measurements of the ACD. The mean ACD in patients with pupillary block was 2.17 ± 0.3 mm, 2.04 ± 0.3 mm in plateau iris, 3.0 mm in normal individuals ($p = 0.0001$). They concluded that ACD associated with plateau iris is shallower than normal and also shallower than pupillary block. A UBM study done on Indian eyes by Garudadri CS *et al.*[19] after laser iridotomy, showed that 66.66% (22 of 33 eyes) of eyes with narrow angles had anteriorly placed ciliary processes after laser iridotomy.

Anterior segment OCT

This new emerging imaging modality is being used more often in the evaluation of anterior segment anatomy in cases of plateau iris syndrome. The chief advantages of this technique being very user friendly and can provide precise information in a non invasive way besides shortening the image acquisition time. The role of OCT in the evaluation of anterior segment anatomy was evaluated by Leung *et al.*,[20] who demonstrated crowding of the peripheral iris in a case of plateau iris syndrome which subsequently opened after ALPI.

Treatment

Laser iridotomy[21] to bypass the pupillary block component is the primary modality in patients with plateau iris configuration or syndrome. However, pilocarpine may produce iris thinning and facilitate angle opening in some cases.

A patent iridotomy may be therapeutic in reducing risks of angle closure. However, in some patients, laser iridotomy[22] may not significantly alter the anterior chamber depth or anatomy. Even after a successful iridotomy produces what appears to be a well-opened angle, periodic gonioscopy remains crucial because these patients may have incomplete plateau iris syndrome or the angle may narrow further with age because of the enlargement of the lens or gradual formation of peripheral anterior synechiae. Although usually recognized in the post iridotomy period, plateau iris syndrome may develop years later. Patients with plateau iris configuration should not be assumed to be cured, even though plateau iris syndrome does not develop immediately.

If persistent iridotrabecular apposition is present despite a patent iridotomy, the diagnosis is consistent with plateau iris syndrome, and peripheral laser iridoplasty (ALPI)[23] is indicated. Argon laser peripheral iridoplasty is the procedure of choice

to effectively open an angle that remains occluded after successful laser iridotomy. The procedure consists of placing laser burns on the surface of the peripheral iris to contract the iris stroma between the site of the burn and the angle. The result is iris stromal tissue contraction and compaction that physically widens the angle and prevents the apposition of the peripheral iris against the trabecular meshwork.

Laser settings in ALPI- 500μ spot size, 200 mW initial power which can be increased in 40 mW increments, duration 0.5 seconds. The end point should consist of adequate peripheral stromal contraction. All four quadrants can be treated in the initial procedure. The use of Abraham lens during the procedure is recommended. The power should be reduced if there is charring of iris or pigment release, formation of gas bubbles, production of a pop sound

The post ALPI care should consist of topical corticosteroids for five days and IOP should be checked 1-2 hours after the procedure to note any post procedure IOP spike. Gonioscopy should be performed after one week to assess the effect of the procedure. However, even after successful opening of the angle, regular gonioscopic examination remains crucial.

A study by Ritch *et al.*[17] has documented the long term success of ALPI (six years) in eliminating the residual appositional closure as well as the need of filtration surgery.

If angle closure persists despite iridotomy and sufficient peripheral laser iridoplasty, miotic therapy may be used to prevent angle closure, or a surgical intervention in the form of trabeculectomy, or tube-shunt implantation surgery may be needed to allow bypass of aqueous flow and to control IOP.

Miotic agents[24] cause the pupillary sphincter to contract, mechanically pulling the iris away from the trabecular meshwork and opening the anterior chamber angle. In addition, these agents also have an IOP-lowering effect by stimulating contraction of the ciliary muscle and thereby increasing trabecular outflow of aqueous humor. Induced myopia, pupillary constriction, brow ache, and retinal detachment are potential adverse effects of this therapy. The concentration of pilocarpine used is 1-2% 3-4 times a day and the incidence of side effects can be decreased with the use of artificial drops instilled after the instillation of pilocarpine drops. Pilocarpine is efficacious because it has been shown to cause peripheral iris thinning and opens up the angle in plateau iris syndrome. Pavlin *et al.*[24] evaluated the efficacy of pilocarpine with the use of UBM biometry in cases of plateau iris syndrome. They found that pilocarpine causes significant peripheral iris stromal thinning (253 ± 48 μ vs 338 ± 34 μ in light conditions, $p = 0.0002$) and is effective in opening the angle. UBM can be used to document this and can be used prior to long term treatment with this drug.

Prognosis

Patients with plateau iris have a good prognosis in general; however, regular follow-up examinations are needed because angle-closure may develop years after successful iridotomy or iridoplasty.

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Lens-associated angle closure

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Introduction

The crystalline lens is involved in causing several forms of glaucoma. These conditions include glaucoma related to: lens swelling or intumescent cataract (phacomorphic glaucoma), lens subluxation or dislocation (ectopia lentis), classical pupillary block, aqueous misdirection or ciliary block (malignant glaucoma), phacoanaphylaxis, lens particle glaucoma and phacolytic glaucoma. Of these, the mechanism for the first four causes listed, is due to angle closure. This chapter will concentrate on secondary angle closure caused by lens swelling and abnormal lens position, the other causes of lens-related angle closure will be elaborated in other chapters.

Lens swelling or intumescent lens

The increase in lens thickness causes progressive reduction in the iridocorneal angle. Pupillary block as the mechanism causing angle closure may be minimal or absent as the swollen lens pushes the peripheral iris forward.

Causes of swollen lens:

1. Age related cataract causing intumescence;
2. Trauma, including surgical trauma;
3. Drug-induced: for example topiramate[1-4] and thiazide diuretics.[5] These are rare and can potentially be reversible;
4. Fanconi's anemia.[6]

History taking

Patients will seek treatment due to symptoms of acute angle closure attack. However they will have preceding symptoms of blurred vision from cataract which can

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occur gradually if it is age related or sudden if it is due to trauma. Those who are drug induced may have symptoms of blurred distant vision from acquired myopia due to lens swelling and a positive history of drug intake.

Ocular findings

There may be signs of acute angle closure attack with corneal oedema, shallow anterior chamber, mid dilated pupil, high IOP and closed angles (Fig. 1). However, the lens would be intumescent and swollen. At times liquefied lens matter may be visible within the lens capsule.

In cases where there is no view of the anterior chamber in the affected eye, a deep anterior chamber and open angles in the fellow eye would negate the diagnosis of primary angle closure.

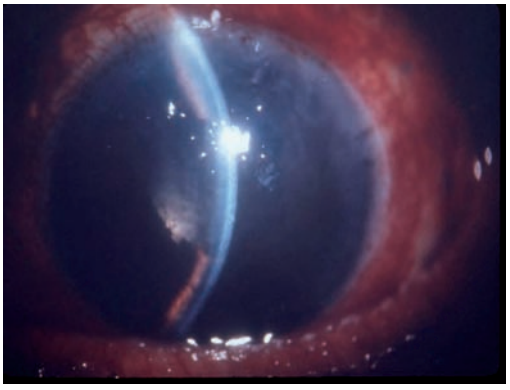

Fig. 1. Anterior segment photograph showing lens intumescence causing secondary acute angle closure with circumciliary congestion, corneal oedema, shallow anterior chamber and intumescent cataract. (Courtesy of Prof. Robert Ritch, New York Eye and Ear Infirmary)

Management

The definitive management is surgical lens removal with or without implantation of intraocular lens.

The IOP should be controlled medically to a safe level prior to surgery. Topical corticosteroids should be given to reduce inflammation. Peripheral iridotomy and/or iridoplasty may be performed to relieve pupillary block and allow time to plan for surgery.[7-9] However, PI may not relieve the angle closure if the mechanism is not due to pupillary block.

Miotics is not helpful as it may aggravate the pupillary block and may cause more inflammation. Surgical lens removal for this type of cases remains a challenge to the surgeon. The difficulty in lens removal could be due to poor visibility from corneal oedema, shallow anterior chamber, posterior synechiae, increased intralenticular pressure and liquefied cortex. The choice of cataract surgery, whether phacoemulsification[10,11] or extracapsular cataract extraction,[12] depends on the experience of the surgeon and on cornea clarity.

Ectopia lentis

Ectopia lentis is defined as displacement or malposition of the crystalline lens from its normal central position within the posterior chamber. The lens is considered dislocated or luxated when all zonular attachments have been broken, although it may still remain behind the iris, it will normally be completely outside the lens patellar fossa. The dislocated lens may migrate anteriorly into the anterior chamber or posteriorly, freely floating in the vitreous or directly on the retina. The lens is described as subluxated when there are loosening or breakage of some of the zonules. The subluxated lens is partially displaced, but still remains partially or entirely within the pupillary space entirely behind the iris. Subluxation or dislocation of the lens can occur after trauma, as an isolated congenital anomaly,[13,14] secondary to pseudoexfoliation[15,16] or as part of the manifestation of systemic diseases such as Marfan's syndrome,[17-19] homocystinuria,[17,20] microspherophakia,[21] Weill-Marchesani syndrome,[22-24] Ehler-Danlos syndrome[25]and hyperlysinemia.[26] There are many other rare heritable conditions reported to be associated with ectopia lentis.[27] Certain ocular conditions such as myopia, congenital glaucoma and aniridia may also cause lens subluxation.

Forward movement of the crystalline lens due to lax or absent zonules causes pupillary block and secondary angle closure, presentation of vitreous in the pupillary area can also cause pupillary block. The degree of zonular impairment determines the degree of lens displacement.

History taking

The patient may present with symptoms of acute angle-closure attack, which may be recurrent. There may be history of ocular trauma which can be recent or in the past. Patients can also present with a history of visual disturbances, including blurring of vision from myopia or astigmatism, reduced near vision from loss of accommodative power or monocular diplopia if the lens is significantly displaced. Uncorrectable poor visual acuity may lead to amblyopia in children and may be the most common cause of diminished visual acuity in patients with ectopia lentis.[28] Those patients due to systemic diseases may have history of systemic problems such as cardiac or skeletal problems and a positive family history.

Ocular findings

Visual acuity varies with the degree of malpositioning of the lens and can be potentially debilitating and amblyogenic. A disparity between the degree of astigmatism found on refraction and that measured by keratometry, as well as a variable amount of astigmatism from one examination to another, should direct the ophthalmologist to consider early subluxation as its cause. The lens subluxation may be subtle with slight localized shallowing of the anterior chamber to gross phacodonesis with displacement of the lens (Figs. 2 and 3). In early stages of subluxation, wide pupillary dilation may be necessary to confirm asymmetry of lens position. Gonioscopy will show varying degrees of narrowing of the angles depending on the degree of lens subluxation (Fig. 4). Intraocular pressure may or may not be raised.

The clinician should be suspicious of microspherophakia when angle closure

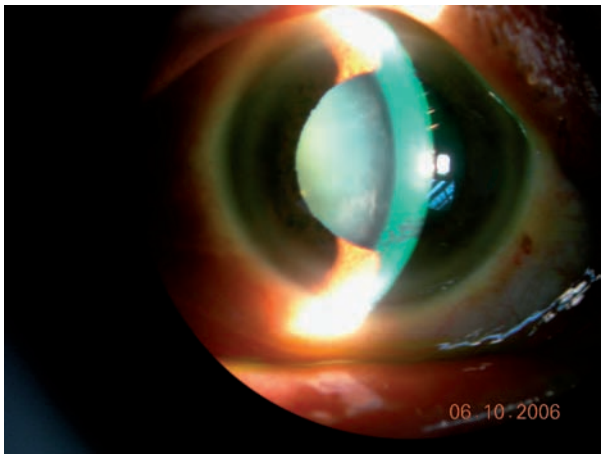

Fig. 2. Anterior segment photograph showing anteriorly subluxated cataractous lens secondary to trauma, the anterior chamber is shallower inferiorly and some vitreous strand is vaguely seen inferiorly. The patient subsequently had intracapsular cataract extraction and scleral fixation of posterior chamber intraocular lens. (Courtesy of Dr S.K. Fang)

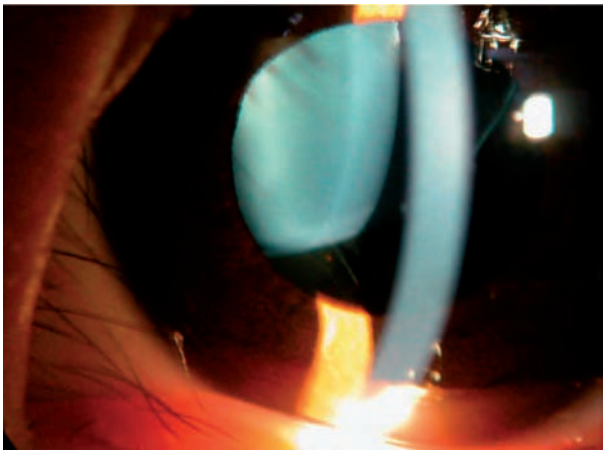

Fig. 3. Anterior segment photograph showing a patient with Marfans syndrome whose crystalline lens is bilaterally subluxated upwards and outwards, zonules are present but stretched, the inferior equator of the lens is clearly seen almost bisecting the pupil. This patient had phacoemulsification cataract surgery with insertion of a Cionni modified capsular tension ring to fix the capsular bag to the sclera and in-the-bag foldable intraocular lens. (Courtesy of Dr S.K. Fang)

occurs in a young myopic individual or the myopic individual has a shallow anterior chamber. One should be also suspicious when angle closure occurs in patients who have history of ocular trauma, and those with presence of other congenital anomalies.

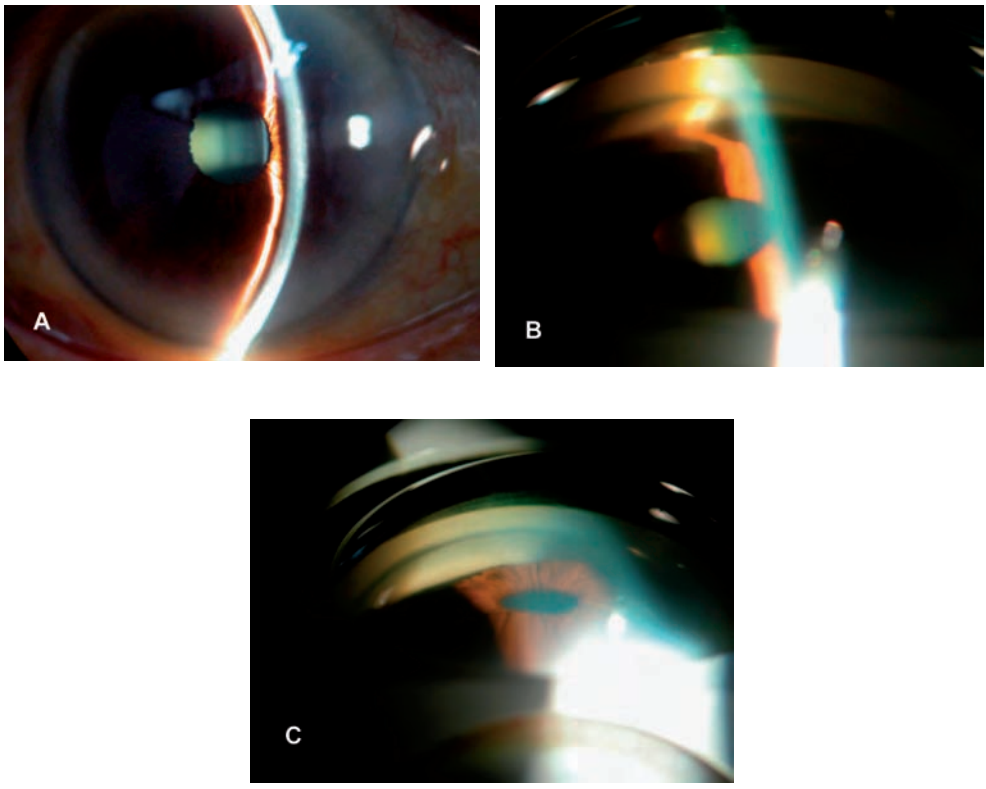

Fig. 4. Anterior segment photographs of the same patient who had secondary angle closure from a subluxated lens. A: shallow anterior chamber with subtle bulge of the lens forward. B and C: gonioscopic photos, showing the forward bulge of the lens. The bulk of the lens is in contact primarily with the middle third of the iris, stretching it and creating a bulge that appears to it the contour of the lens. The patient subsequently had a laser peripheral iridotomy, which relieved the pupillary block and the secondary angle closure. (Courtesy of Dr S.K. Fang and Dr Michael Law)

Management

Medical management to reduce IOP should include the use of a hyperosmotic agent to shrink the vitreous which would allow the lens to move posteriorly. If the lens is caught in the pupil or anterior chamber, a weak mydriatic agent should be administered. If the zonules are known to be intact a cycloplegic drug may be used to pull the lens posteriorly. Putting the patient in a supine position may facilitate the lens to reposit itself in the posterior chamber. Once the lens is in the posterior chamber, the pupil is constricted with a miotic, and peripheral iridotomy is performed.

The definitive management in most cases is laser peripheral iridotomy, which is the treatment of choice especially when angle closure appears imminent. If the condition is bilateral, the fellow eye should receive laser iridotomy prophylacti-

cally. The patient is then treated with a miotic to prevent the forward migration of the lens.

There are a few situations in which surgical removal of the lens is necessary. This includes inability to reposit the lens (especially if dislocated anteriorly), raised IOP even after a successful PI, intolerable monocular diplopia, reduction of visual acuity related to cataract or high astigmatism and phacolytic glaucoma.

The possible surgical options for lens removal are:

1. Intracapsular cataract extraction, anterior vitrectomy with anterior chamber or scleral fixated intraocular lens implant.
2. Phacoemulsification with insertion of capsular tension ring and in-the-bag intraocular lens implant.[29-32]
3. Phacoemulsification with insertion of modified or Cionni type of capsular tension ring (scleral fixation of capsular bag) and in-the-bag intraocular lens implant.[33]
4. Phacoemulsification with small incision scleral fixation of intraocular lens implant in the ciliary sulcus in cases where the capsular support is inadequate.[32]
5. Phacofragmentation of dislocated lens in the vitreous cavity with anterior chamber or scleral fixated intraocular lens implant.[34,35]
6. Pars plana lensectomy with or without intraocular lens implant.[36,37]

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Secondary angle-closure glaucoma

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Introduction

In angle-closure glaucoma, the elevation of intraocular pressure occurs when aqueous outflow to the trabecular meshwork is significantly obstructed by peripheral iris tissue. This physical blockage may either be in the form of permanent tissue adhesion (peripheral anterior synechia) or non-permanent appositional tissue closure. The resulting level of intraocular pressure rise is correlated to the extent of angle closure present and the facility of outflow of the eye.

Traditionally, angle-closure glaucoma is divided into the primary and the secondary types. In primary angle-closure glaucoma, the fundamental and sole underlying mechanism is 'relative pupillary block', resulting in pressure build-up in the posterior chamber causing the peripheral iris to move forward and obstruct aqueous access to the trabecular meshwork. In secondary angle-closure glaucoma, distinct identifiable mechanisms and forces, other than 'relative pupillary block' alone, are at work in bringing about closure of the entire, or portions of, the anterior chamber angle circumference. These act, directly or indirectly, to cause the peripheral iris to obstruct the filtering portion of the trabecular meshwork.

This chapter is divided into sections highlighting various conditions that bring about secondary angle-closure glaucoma.

Nanophthalmos

Pathophysiology and clinical features

Nanophthalmos is a developmental anomaly characterized by a familial form of microphthalmos unaccompanied by other congenital malformations. It is bilateral and affects both sexes in equal numbers.[1-2] Pertinent features include hyperopia, small corneal diameter, thick sclera and narrow angles. All eyes exhibit marked

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convexity of the iris plane and shallow anterior chambers, making the patient susceptible to angle-closure glaucoma.[3,4] The glaucoma usually starts acutely during the fourth to sixth decade of life.[4] Kimbrough *et al*.[5] noted that the thickened sclera of nanophthalmic patients become more sclerotic with age, causing choroidal effusion by increasing resistance to vortex vein outflow. This leads to anterior rotation of the ciliary processes further crowding the angle and resulting to angle-closure glaucoma. Close follow-up of these patients with regular gonioscopic examinations should be done to monitor progression of angle closure.

Management

Medical therapy should include aqueous humor suppressants. Miotics should be used with caution since they may improve some cases but may worsen others.[6] Laser iridectomy should be done in cases of angle closure to eliminate the pupillary block component. If the angles remain appositionally closed after iridectomy, peripheral iridoplasty or gonioplasty should be the next step in angle closure glaucoma control.[3,4] Because of the high rate of disastrous complications, intraocular surgery should be avoided, unless absolutely necessary. If surgical procedures like incisional iridectomy, lensectomy or trabeculectomy become necessary, the patient should be evaluated for the presence of suprachoroidal effusions.[4] It has been suggested by Brockhurst[7] that choroidal effusions result from sudden decrease in intraocular pressure during surgery with relative increase in choroidal venous pressure. It is recommended that posterior sclerotomy be done before entering the anterior segment to prevent choroidal effusion. Vortex vein decompression has also been described by Brockhurst for nanophtahlmic uveal effusion but may be technically difficult to perform.[7,8]

Uveitis with secondary angle-closure glaucoma

Pathophysiology and clinical features

Uveitis describes inflammation of any portion of the uveal tract and may be exogenous or endogenous in etiology.[4] A common complication of uveitis is glaucoma. The associated glaucoma may be an acute severe form or a chronic type. In either case, the iridocorneal angle may be closed or open. The chronic and recurrent nature of the inflammatory process may lead to structural and functional changes in the eye altering the aqueous humor dynamics.[3]

The early stages of secondary glaucoma from uveitis is usually associated with an open angle due to trabeculitis or blockage of the trabecular meshwork from inflammatory cells and tissue debris. At a later stage of the disease, peripheral anterior synechiae develop leading to angle closure glaucoma. Synechiae formation may be related to swelling of the peripheral iris, with accompanying adhesion formation and exudation in the angle, later pulling the iris towards the corneal periphery.[3,4] The synechiae that result from iritis are irregular in shape and in the height of their trabecular meshwork attachment. Cylindric, conical or moundlike areas alternating with areas of open iridocorneal angle have been described.[4] These synechiae differ primarily from the synechiae associated with pupillary block where the iris attachments are in a line parallel to Schwalbe's line.

Posterior synechiae, or the adhesions of the iris to the lens surface is another characteristic feature of uveitis which may lead to angle closure. The pupillary margin may be partially or completely involved. Absolute pupillary block develops when there is complete adhesion of the iris to the lens surface (seclusio pupillae). This closes off the communication between the posterior and anterior chamber through the pupillary area. Forward buldging of the peripheral iris (iris bombe) then results as the pressure in the posterior chamber increases, leading to acute angle-closure glaucoma.[3,4]

Finally, swelling and anterior rotation of the ciliary body may result in angle closure glaucoma without the pupillary block component. This may occur in cylitis[9], swelling of the ciliary body[10] and annular choroidal detachment.[11]

Management

The goal of treatment in patients with uveitis and secondary glaucoma is to1) control inflammation and prevent its compromising effects on the outflow facility of the eye; and 2) decrease intraocular pressure. The anti-inflammatory effect of corticosteroids can be obtained by topical, subconjunctival or systemic administration.[3,4] In cases were corticosteroids are contraindicated, nonsteroidal anti-inflammatory therapy, given topically or orally, may be an alternative. In resistant cases, immunosuppressive therapy (Methotrexate,[12] Azathioprine[13] and Cyclosporin[14]) may be tried. Pupillary dilation using cycloplegic and sympathomimetic agents are employed to break or prevent the formation of posterior synechiae.

Medical anti-glaucoma therapy, consisting of Beta-adrenergic antagonist, alpha-2 adrenergic agonist and topical carbonic anhydrase inhibitors, reduce aqueous humor production thereby controlling the glaucoma.[3,4] Miotics are usually avoided since they may exacerbate ciliary spasm and allow formation of posterior synechiae. The use of prostaglandin analogues and miotics are also discouraged since they aggravate the already inflamed eye.

Laser iridectomy is recommended if pupillary block is precipitating angle closure.[3,4] In cases that are not responsive to laser and medical treatment, filtering surgery with anti-metabolites may be necessary. It should be however emphasized that filtering surgery or trabeculectomy is less successful in these eyes due to the preexisting and postoperative inflammation. Tube surgery[15,16] or cycloablative procedures[17,18] may be employed as well in intractable cases of glaucoma.

Neovascular glaucoma

Neovascular glaucoma results from the growth of a fibrovascular membrane over the trabecular meshwork causing closure of the anterior chamber angle.[3] It is believed that this occurs in response to certain predisposing or pre-existing conditions in the eye associated with hypoxia or diminished perfusion.

The two most common predisposing conditions are central retinal vein occlusion (CRVO) and diabetic retinopathy.[3] Neovascular glaucoma may also occur in association with central retinal artery occlusion, intraocular neoplasm, severe ocular inflammation or infection, and chronic retinal detachment. Less commonly, it is associated with carotid artery occlusive disease, retinopathy of prematurity, carotico-cavernous fistula and Coat's disease.

The non-ischemic type of CRVO rarely develops neovascular glaucoma. The risk in developing this condition lies almost entirely with the ischemic type. About 20% of all CRVO's are initially of the ischemic type[20] and about 50% of these will develop neovascular glaucoma.[21] This occurs 60-90 days after CRVO, hence, the term '90 day glaucoma'. It is also known that 15% of the non-ischemic type can convert to the ischemic type.[20]

The incidence of neovascular glaucoma in diabetic retinopathy is not as well defined as in CRVO. In proliferative diabetic retinopathy however, the incidence of neovascular glaucoma is similar to that found in CRVO and may actually be higher.[22]

Pathophysiology

The various clinical conditions that may lead to neovascular glaucoma appear to act through a common pathway where hypoxia is the stimulus. Any condition resulting in retinal hypoxia and ocular hypoperfusion can initiate the neovascular process. Advances in molecular biology have enabled the identification of several angiogenic factors that may be responsible for new blood vessel formation. One such recognized factor is vascular endothelial growth factor (VGEF).[23]

The neovascular process begins as endothelial budding from capillaries of the minor arterial circle at the pupil. It then progresses sequentially from the pupil to the periphery of the anterior chamber. New endothelial buds may likewise appear from vessels anywhere in the iris, including the major arterial circle in the iris root. These buds eventually become glomerulus-like vascular tufts with thin walls, which characteristically leak fluorescein.[3]

When these neovascular vessels proliferate in the anterior chamber angle, they cause a progressive decrease in outflow facility. Angle neovascularization is associated with a fibrovascular membrane that contracts and pulls peripheral iris towards the trabecular meshwork with eventual synechial closure. These peripheral anterior synechiae can coalesce leading to total angle closure.

Clinical presentation and diagnosis

Initially, intraocular pressure can be normal with new vessels seen first on the papillary border of high-risk eyes. Neovascularization of the iris may progress to total angle closure in days, or it may remain quiescent without angle neovascularization or closure for years.

A full-blown acute clinical presentation usually presents with reduced visual acuity, conjunctival congestion, pain, photophobia, corneal edema, intraocular pressures usually between 40 and 60 mmHg and mid-dilated non-reactive pupils. Common differential diagnosis include acute angle-closure glaucoma and glaucoma secondary to an inflammatory process. Most patients developing neovascular glaucoma after CRVO recall a painless blurring or loss of vision in the affected eye weeks or months prior to developing pain.

Management

The key to successful treatment of neovascular glaucoma involves early diagnosis and institution of appropriate therapy. Regular high-magnification slitlamp examination of the anterior segment and gonioscopy, plus posterior segment evaluation of eyes that are high risk, is mandatory. Recognition of conditions which may lead to neovascular glaucoma is the key.[3]

Retinal ablation by means of photocoagulation or cryotherapy will inhibit and may even reverse neovascular proliferation in the anterior segment. Reducing the mass of viable retinal tissue probably exerts multiple effects on different stages and mechanisms of angiogenesis. This also prepares the eye for eventual surgery.

Medical treatment is directed at controlling elevated intraocular pressure, pain and inflammation. This would involve the use of topical aqueous suppressant drugs, topical or systemic carbonic anhydrase inhibitors, topical steroids and cycloplegics.

Goniophotocoagulation involves direct application of laser energy to the new angle vessels as they cross the scleral spur.[24] This may be useful in an eye with anterior segment neovascularization, but still having open angles, while awaiting the regressive effects on anterior segment neovascularization of panretinal photocoagulation. It does not, however, prevent synechial closure in the long term.

Success of glaucoma filtering surgery in eyes with neovascular glaucoma is dismal. Better success rates are achieved with the adjunctive use of anti-fibrotic agents like mitomycin-C and 5-fluorouracil. Glaucoma drainage implantation or shunt surgery may provide an alternative to filtering surgery.

If the visual prognosis of the involved eye is poor, cyclodestructive procedures can be used to reduce aqueous production and intraocular pressure. In blind and painful eyes, retrobulbar alcohol injections, or even enucleation, may be considered.

Iridocorneal endothelial syndrome

Iridocorneal endothelial (ICE) syndrome is a group of disorders characterized by abnormal corneal endothelium that is responsible for varying degrees of iris atrophy, secondary angle-closure glaucoma in association with characteristic peripheral anterior synechiae (PAS), and corneal edema.[25-27] It is usually unilateral, but may present with subclinical irregularities of the corneal endothelium on the fellow eye. The condition usually affects women whose age may range from 20 to 50 years old. Patients present with pain, decreased vision and abnormal iris appearance. The pain and reduced vision are usually due to corneal edema and secondary angle-closure glaucoma. Patients may also complain of mild blur in the morning hours as a result of the lid closure and mild lid edema that occurs during sleep. Vision then improves throughout the day as the cornea hydrates with exposure to the air. Microcystic corneal edema may be present in other patients, especially those who have Chandler's syndrome. Patients may also present with correctopia or pseudopolycoria.[25,26]

Three clinical variations have been described. Such variations have been differentiated according to the type of iris abnormality. Cogan-Reese Syndrome (Iris nevus) presents with variable and less severe signs and symptoms. Tan and pedunculated

nodules may appear on the anterior iris surface. Chandler's syndrome presents with minimal or no iris stromal atrophy and mild correctopia. Corneal edema and abnormal angle findings predominate this condition and is considered typical of the disorder. Essential (progressive) iris atrophy presents with severe iris atrophy that results in heterochromia. Hallmark findings include marked correctopia, ectropion uveae and pseudopolycoria (hole formation).[25,26]

In each of the three clinical variations of ICE syndrome, corneal endothelial abnormalities such as fine, hammered silver appearance of the posterior cornea are seen. This appearance is similar to the guttata seen in Fuch's corneal endothelial dystrophy. These endothelial abnormalities then results to corneal edema. Angle findings may show PAS that extend beyond Schwalbe's line caused by the contraction of the endothelial cell layer and surrounding collagenous fibrillar tissue resulting to angle-closure glaucoma. The pupil is drawn towards the sector that has the most prominent PAS. Viral etiology such as the Epstein-Barr and Herpes simplex has been postulated.[25,27]

Major concerns for treatment are the corneal edema and secondary glaucoma. The corneal edema may be controlled by hypertonic saline solution. The elevated intraocular pressure (IOP) may be controlled by aqueous suppressants. Filtering surgery may be indicated if IOP is not adequately controlled medically. Success of initial trabeculectomy is 64% for the first year and 34% in three years time. Repeat trabeculectomy presents with lower success rate, 58% for the first year.[25,26]

Iris and ciliary body tumors

The most common tumor affecting the iris and ciliary body are melanomas.[25] Uveal melanomas are primary acquired malignant neoplasm of the uveal melanocytes. They are usually unilateral and unifocal. They have a high tendency to metastasize, especially to the liver. They are seen more often among females, elderly and lighter skinned races. Iris melanomas are asymptomatic and on routine eye examination reveals a visible spot or a discoloration on the iris of one eye. Ciliary body melanomas are also asymptomatic. However, patients complain of blurred vision, visual field defects, flashes and floaters. Secondary angle-closure glaucoma occurs as a result of neovascular closure of the filtration angle as a result of growth invasion of the iris melanoma towards the angle. Ciliary body melanomas may also produce forward displacement of the lens-iris diaphragm producing angle closure glaucoma. Diagnosis of ciliary body melanomas are usually made using B-scan ultrasonography. Treatment consists of excision of the mass. IOP may be controlled by aqueous suppressants.

Glaucoma from forward rotation of the ciliary body

Forward rotation of the ciliary body as a result of choroidal detachment, vitreous hemorrhage, scleral buckling and panretinal photocoagulation (PRP) may produce forward displacement of the lens and iris diaphragm resulting in the development of secondary angle-closure glaucoma.[28-30]

Temporary shallowing of the anterior chamber often occurs after scleral buckling

procedures. Studies by Fiore & Newton,[31] Smith,[32] Sebestyen *et al.*[33] and Perez *et al.*[34] noted different incidences of such condition.

The incidence of angle-closure glaucoma after PRP has been reported to range from 0 to 44%. Multiple treatment sessions, separated by one- to two-week intervals, may reduce its incidence.[35] Cycloplegics will cause a posterior shift of the lens-iris diaphragm, and corticosteroids lessen the chances of synechial formation. In addition, aqueous suppressants, as well as hyperosmotic agents is suggested if the intraocular pressure is considered to be at a dangerous level.[36]

Pathologies affecting vitreous volume

Vitreous volume may be enhanced by various conditions such as malignant glaucoma, persistent hyperplastic primary vitreous, choroidal separation, suprachoroidal hemorrhage and various intraocular tumors of the posterior part of the eye. These conditions create a posterior pushing force that displaces the lens-iris diaphragm forward thus may produce secondary type of angle-closure glaucoma. Management should be directed to the primary cause of the angle closure. However, IOP control may be attained by the use of beta-adrenergic blocking agents, carbonic anhydrase inhibitors and hyperosmotic solutions in full dosage from the very beginning of treatment. In malignant glaucoma, additional mydriatic-cycloplegic drops may prove beneficial to the patient.[37] Vitrectomy has been advocated as treatment to these patients.[38] Steroids have been proven to diminish fluid displacement in patients with choroidal detachment.[39]

Glaucoma after penetrating keratoplasty

Secondary glaucoma is a common complication of penetrating keratoplasty (PKP).[40] The incidence increases further in aphakic and pseudophakic patients, and in those who have repeat grafts.[41] Pre-existing wound distortion of the trabecular meshwork and chronic angle closure are the most common causes of long standing glaucoma in these patients.[42] Frequently encountered causes of elevated IOP include preexisting glaucoma, distortion of the trabecular meshwork, angle closure, postoperative inflammation, retention of viscoelastic substance, malignant glaucoma and steroid induced glaucoma. Progressive synechial angle closure has been suggested as the cause for persistent glaucoma.[42]

The use of an oversized donor button and adjustment of suture tightness are the most significant clinical factors in avoiding elevated pressure postkeratoplasty.[43-46] Suppression of aqueous humor formation with systemic carbonic anhydrase inhibitors and beta-blockers may be effective in lowering the pressure.[47] Cyclodestructive therapy is the usual mode of treatment in aphakic postkeratoplasty glaucoma.[48] Seton tube devices and the use of pharmacologic agents to control wound healing after filtering surgery may increase the rate of filtration success.[4]

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Malignant glaucoma

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Introduction

Malignant glaucoma was initially reported as developing after surgery for glaucoma. Subsequently, associations with trauma, inflammation, and the use of miotic agents, as well as spontaneous occurrence, have been noted. The condition is also regarded as a spectrum of atypical angle-closure glaucomas that have several essential features.

PACG is much more common in East Asian (Mongoloid) ethnic groups than in Europeans or people of African origin.[1] The condition usually follows intraocular surgery, but has also been described following laser iridotomy,[2-5] and has even been associated with miotic therapy.[6]

Terminology

In 1869, Von Graefe described a rare complication of certain ocular procedures, which was characterized by shallowing or flattening of the anterior chamber and elevation of intraocular pressure.[7] He called the condition malignant glaucoma, because of its poor response to conventional therapy. Other terms have been used to describe the condition, including aqueous misdirection glaucoma,[8] ciliary block glaucoma,[9,10] ciliovitreolenticular block,[11] ciliolenticular glaucoma, ciliolenticular block glaucoma,[12] iridociliovitreal block glaucoma,[13] direct lens block angle-closure glaucoma,[14] and hyaloid block glaucoma.[15] However, these terms are based on supposition relating to the underlying aetiology and, until a better understanding of the pathomechanism of the condition is attained, the term 'malignant glaucoma' expresses its seriousness and will continue to be used.

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Pathophysiology

Malignant glaucoma occurs in 0.6-4% of eyes undergoing surgery for angle-closure glaucoma,[16,17] and may occur at any time following surgery, from the first post-operative day to many years later. The exact mechanism that leads to malignant glaucoma is not clearly understood.

Posterior pooling of aqueous fluid

Clinically, the anterior chamber is shallow or flat with anterior displacement of the lens, pseudophakos, or vitreous face. Ciliary processes are seen to be rotated anteriorly, and may be seen through an iridectomy to come in contact with the lens equator. Shaffer[18] hypothesized that an accumulation of aqueous fluid behind a posterior vitreous detachment causes the forward displacement of the iris-lens or iris-vitreous diaphragm, and the concept was expanded to include the pooling of aqueous fluid within vitreous pockets.[19]

Ciliolenticular or ciliovitreal block

Malignant glaucoma is a potentially devastating complication of intraocular surgery that may also occur spontaneously. In this condition, the aqueous fluid is diverted into the vitreous, so the iris-lens diaphragm is moved forward. This causes shallowing of the anterior chamber and increases the intraocular pressure. It is hypothesized that these may be due to more anterior positioning of the lens, which not only causes smaller dimensions of the anterior chamber, but also causes more ciliolenticular blocking and further aqueous diversion into the vitreous cavity.[20,21]

Anterior hyaloid obstruction

The ciliary processes rotate forward and press against the lens equator in the phakic eye or against the anterior hyaloid in aphakia, which might create an obstruction to the forward flow of aqueous fluid. The anterior hyaloid may contribute to ciliolenticular blocking, and that breaks in the hyaloid near the vitreous base, possibly allowing the posterior diversion of aqueous fluid.[15,22]

Weakness of lens zonules

Chandler and Grant suggested that the forward movement of the lens-iris diaphragm in malignant glaucoma might be due to abnormal slackness or weakness of the zonules of the lens, as well as pressure from the vitreous.[12,23]

Ultrasound biomicroscopy

Using the ultrasound biomicroscopy method, the configuration of the anterior segment structures of the eye has been visualized during the malignant glaucoma process. This includes irido-corneal touch, appositional angle closure, and anterior rotation of the ciliary body with apposition to the iris (Fig. 1). Thus, the relative

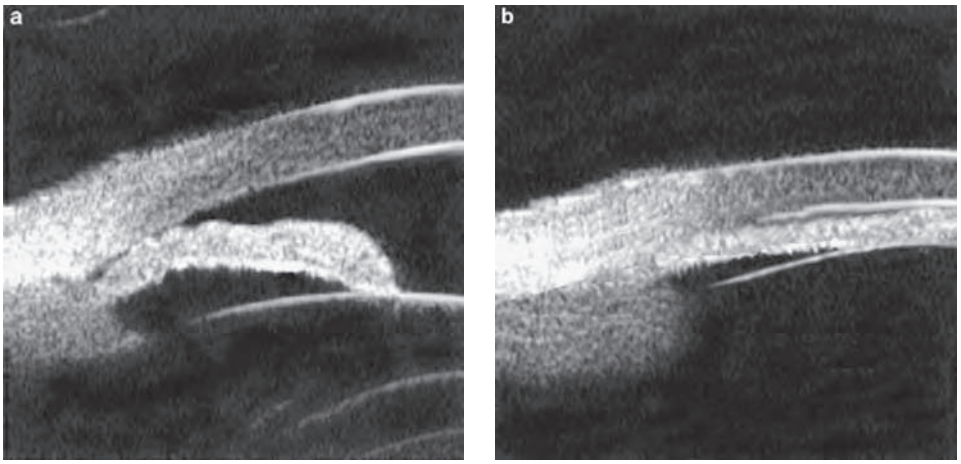

Fig. 1. Ultrasound biomicroscopy images. a: Pupillary block; b: Ciliary block.

positions of the anterior segment structures in malignant glaucoma have been visualized well using high frequency ultrasound biomicroscopy,[24,25] and the images supported the accepted hypotheses regarding its pathogenesis, including anterior rotation of the ciliary processes and forward displacement of the ciliary body and lens. However, while this instrument is useful in attempts to clarify the mechanism of malignant glaucoma, it has not yet been shown to be useful in management of the condition.

Diagnosis and differential diagnosis

This condition can be suspected when a patient has:

1. Flattening or shallowing of both the central and peripheral anterior chamber;
2. Normal or elevated intraocular pressure;
3. No signs of choroidal elevation (clinically and B-scan);
4. Lens displacement (towards the cornea);
5. Iris displacement (towards the cornea);
6. Presence of patent laser or surgical iridectomy;
7. Unresponsiveness to or aggravation by miotics;
8. Frequent relief with cycloplegic-midriatic therapy.

In the early postoperative setting, the diagnosis of aqueous misdirection is often difficult to distinguish from a choroidal effusion, pupillary block, or a suprachoroidal hemorrhage.

Often, the level of intraocular pressure (IOP), time frame following surgery, patency of an iridectomy, or presence of a choroidal effusion may aid the ophthalmologist in making the appropriate diagnosis and initiating treatment.

The diagnosis of malignant glaucoma requires the exclusion of the following conditions: choroidal detachment, suprachoroidal hemorrhage, and pupillary block glaucoma.

Choroidal detachment

Choroidal separation with serous fluid is common after glaucoma filtering procedures, and might be confused with malignant glaucoma resulting from a shallow or flat anterior chamber. Hypotony without a wound leak may be associated with choroidal effusion or with excessive drainage into the subconjunctival space. Choroidal detachments should be ruled out using goniolens mirrors and indirect ophthalmoscopy. The light brown choroidal detachment is easily seen if there is adequate visibility of the posterior ocular segment or, otherwise, could be diagnosed by ultrasonography. Should a detectable ciliochoroidal detachment exist, medical therapy may be sufficient; occasionally, drainage of the suprachoroidal space maybe needed at the time of vitrectomy.

Suprachoroidal hemorrhage

Suprachoroidal hemorrhage may occur after ocular surgery, and may create shallowing or loss of the anterior chamber, which is associated with elevated IOP and pain. The eye shows more inflammation than that seen with choroidal detachment, and the choroidal elevation is frequently dark reddish-brown in color. The prognosis can be significantly improved by prompt drainage of the suprachoroidal blood and reformation of the anterior chamber.[26]

Pupillary-block glaucoma

Pupillary block is the most frequent cause of angle closure. The flow of the aqueous fluid from the posterior chamber through the pupil is impeded, and this obstruction creates a pressure gradient between the posterior and anterior chambers, causing the peripheral iris to bow forward against the trabecular meshwork. This pupillary block is broken by an unobstructed peripheral iridectomy. In malignant glaucoma, the entire lens-iris diaphragm is shifted forward, with marked shallowing or loss of the central anterior chamber, and patent peripheral iridectomy may be present.

Clinical forms

Phakic malignant glaucoma

Phakic malignant glaucoma presents as peripheral and central anterior chamber shallowing because of the higher pressure gradient posterior to the hyaloid face. As a result, the lens and ciliary zonular interface are cramped anteriorly.[19,27]

Partial or total closure of the anterior chamber angle at the time of surgery is associated with an increased incidence of this complication (Fig. 2). However, the condition rarely, if ever, follows a prophylactic iridectomy when the angle is open at the time of surgery.

The causes of phakic malignant glaucoma include a component of chronic subacute angle closure and miotics. In addition, certain conditions can trigger the attack, including laser surgery to the iris, uveitis, ciliary spasm, and trauma.[28]

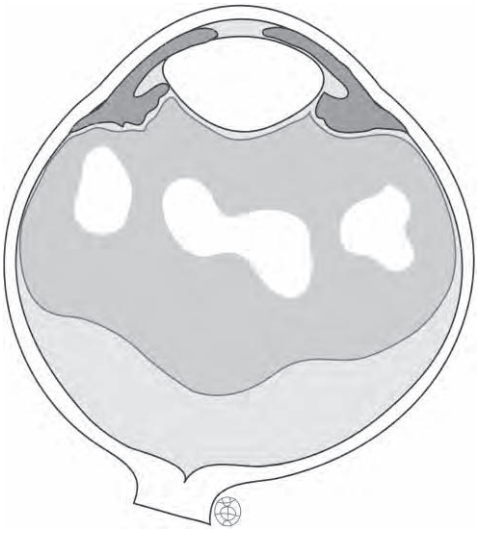

Fig. 2. Phakic malignant glaucoma.

Malignant glaucoma in aphakia and pseudophakia

Malignant glaucoma may occur in pseudophakic or aphakic eyes.[9,22,29] Malignant glaucoma may persist after lens removal for treatment of the disease, or may develop after cataract extraction in eyes without preexisting glaucoma. Malignant glaucoma may occur in association with anterior and posterior chamber intraocular lenses. A large posterior chamber intraocular lens optic (7 mm) in a small eye (axial length of 21.7 mm) was thought to be responsible for malignant glaucoma in one case, and caution is advised in these patients.[30,31]

Malignant glaucoma associated with laser treatment

Laser iridotomy has been utilized to avoid the risk of subsequent malignant glaucoma in eyes with angle-closure glaucoma by avoiding surgical incision of the eye (Fig. 3). However, Cashwell and Robinson reported cases of malignant glaucoma after prophylactic laser iridotomy. In all but two cases, medical therapy for the malignant glaucoma resulted in deepening of the anterior chamber and normalization of the intraocular pressure.[2,3]

Some authors have reported malignant glaucoma as a complication of Nd:YAG laser posterior capsulotomy.[32,33] There have also been reports of the condition occurring following Nd:YAG cyclophotocoagulation,[34] laser sclerostomy,[35] and diode laser cyclophotocoagulation.[36]

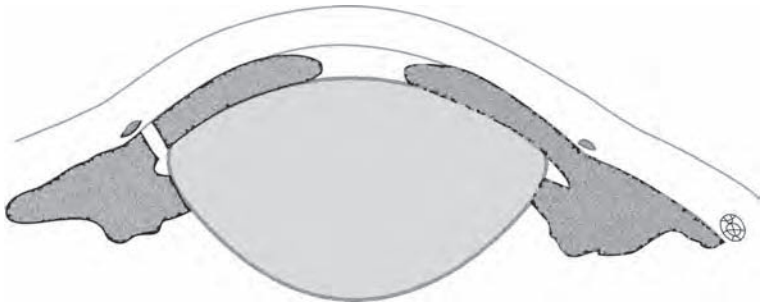

Fig. 3. Malignant glaucoma associated with Nd:YAG laser iridotomy.

Miotic induced malignant glaucoma

Malignant glaucoma may correspond to the institution of miotic therapy, which suggests a potential causal relationship.[37] This kind of clinical picture has been described in eyes that were not operated on but were receiving miotic therapy[38] and in an eye treated with miotics after a filtering procedure for open-angle glaucoma.[39] The systemic use of miotics is ineffective for treating this condition, and may affect intraocular fluid dynamics.

Malignant glaucoma associated with other condition

Predisposing anatomical features in patients with chronic angle-closure glaucoma associated with sudden anterior chamber decompression and increased postoperative inflammation may facilitate the development of malignant glaucoma following combined glaucoma implant and phacoemulsification surgery.[40]

Inflammation and trauma have also been reported as precipitating factors of malignant glaucoma.[41] A form of this condition has been reported in association with endophthalmitis.[42] Malignant glaucoma is associated with a pseudoexfoliation, retinal detachment,[18,43] and cessation of aqueous suppressants. This condition has also been reported in children with retinopathy of prematurity.[44]

Management

Medical

Management of this condition is, in the first instance, medical. The goal is to decrease aqueous fluid and move the iris-lens diaphragm backward. Descriptions of currently used treatment options follow.

Installation of cycloplegic + mydriatics: Use of cycloplegic agents, including tropicamide, cyclopentolate, and topical atropine, tightens the zonules, retracts the lens-iris diaphragm, and maximizes the annular surface of the anterior hyaloid face.

Mydriatics such as phenylephrine may both enhance the cycloplegic effect on the zonules by stimulating the longitudinal muscle of the ciliary body, as well as preventing pupillary block by keeping the pupil as wide as possible.[45,46]

Aqueous suppression: Topical beta-blockers, alpha-adrenergic agonists, and topical and oral carbonic anhydrase inhibitors are effective in decreasing aqueous humor production and lowering intraocular pressure, presumably decreasing aqueous misdirection.

Vitreal dehydration: Osmotic agents such as oral glycerol, isosorbie, or intravenous mannitol are used to decrease vitreous volume. Hyperosmotic agents can significantly contribute to reducing the accumulation of inappropriate fluid within the vitreous, and should be used with caution due to possible metabolic disorders and intravascular volume overload; they are contraindicated in patients with renal or heart failure.

Anti-inflammatory agents: Especially in postsurgical or uveitic cases of malignant glaucoma, topical corticosteroids can minimize intraciliary inflammation, as well as interrupting adhesion consolidation between either the peripheral hyaloid and cilliary processes or the posterior lens surface and adjacent structures (*e.g.*, capsule, intraocular lens, hyaloid). Such a short time regimen is unlikely to induce a corticosteroid-induced response in IOP.

Discontinuation of miotics: If a patent iridectomy has been conducted, a pupillary block is unlikely and miotic can not contribute to maximizing outflow.
Prostaglandin analogues reduce intraocular pressure by increasing uveoscleral aqueous outflow. However, their roles in the treatment of malignant glaucoma are not clearly defined. The exact combination of drugs will depend on the preferences of individual clinicians and facility at which the patient is being treated.

Medical management should be continued, unless intraocular pressure is higher than acceptable, given the state of the optic nerve. Once the condition is resolved, medications can be withdrawn gradually. The condition may recur when therapy is decreased. Atropine may be required indefinitely to prevent recurrences. Long-term use of atropine, possibly for years, may be required.[47,48]

Surgical

Medical treatment works within four to five days in approximately 50% of cases. If high pressure continues after this time, or if lens-corneal touch occurs, surgical intervention should be considered, as prolonged shallowing of the anterior chamber will lead to the formation of peripheral anterior synechiae, posterior synechiae, cataract, and damage to the corneal endothelium. There is no clear-cut evidence as to which of several surgical approaches for malignant glaucoma is superior.[28]

Laser

The outcome of the argon and Nd:YAG lasers depend entirely on the visual accessibility of the structure that needs to be treated. Clear media is required to perform

laser treatment for optimal focusing. Patients that do not respond to medical treatment may benefit from argon laser ciliary body partial destruction.[49]

Argon laser can be used during a peripheral iridectomy to diminish the volume of ciliary processes and, therefore, relieve ciliolenticular block. In 1980, Herschler reported that transpupillary laser shrinkage of ciliary processes in aphakic patients was successful in reversing the posterior secretion of aqueous humor and restoring anterior chamber depth.[50,51] Concomitant and postlaser medical therapy is advised.

The Nd:YAG laser is useful in a variety of settings:

Peripheral iriotomies: These processes can be performed easily to eliminate pupillary block glaucoma, as pupilloplasties and iridoplasties cannot always be done safely.

Hyaloidotomies: Depending on accessibility, consideration must be given to performing both peripheral and central (pupillary) hyaloidotomies in post-cataract malignant glaucoma. A combination of applications may be needed, with significant deepening of the anterior chamber. If the expected result is not achieved, further laser attempts should be undertaken concomitant with medical therapy. Aphakic patients with clear media may temporarily benefit from the disruption of anterior and posterior hyaloid with the Nd:YAG laser–hyaloidotomy.[11,52]

Capsulotomies: In the eyes following extracapsular cataract extraction (ECCE) with or without an intraocular lens, the potential barrier role of the persistent posterior capsule easily compromised the anterior flow of aqueous fluid. Capsulotomy is usually performed in conjunction with hyaloidotomies, and retrocapsular block has been described. Both peripheral and central sites must be entertained because of the possibility of vitreous hernia and the plugging of capsulotomies.[53,54]

Surgery

In the event of failed medical and laser therapies, surgical intervention is needed.

Posterior sclerotomies and air injection: A pars plana incision with aspiration of fluid from the vitreous and reformation of the anterior chamber with an air bubble (Fig. 4) is considered by some to be the procedure of choice for classic malignant glaucoma.

It has been suggested that the sclerotomy should be placed three mm posterior to the limbus to break the anterior hyaloid, thereby reducing its contribution to the blockade.

Postoperatively, patients are generally maintained on atropine to prevent recurrence.

Vitreous aspiration: Using the temporal sclerotomy site, diathermy is applied; a sharp blade is used to perforate into the vitreous, and an 18-gauge needle is inserted at a maximal depth of 10 mm, pointed posteriorly away from the lens and toward the optic nerve, and swept back and forth in a small arc until 1 to 1.5 ml of liquid is aspirated.[28,55-58]

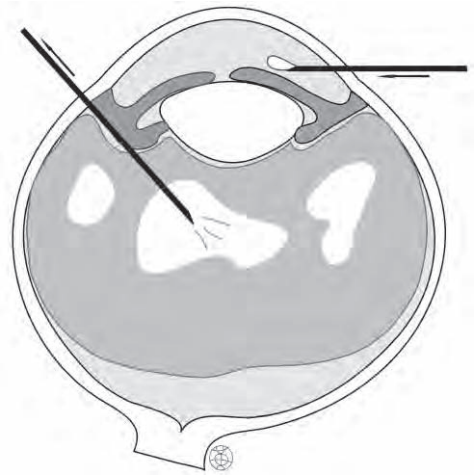

Fig. 4. Posterior sclerotomies and air injection.

Anterior chamber deepening: With care not to cause excessive reinflation of the hypotonous globe with a balanced saline infusion, a large air bubble is then introduced through the paracentesis and injected in order to force the iris diaphragm decidedly posterior to its original position. The bubble should be observed carefully. In the event that it goes behind the iris, anterior chamber shallowing may be temporarily observed, and should not be confused with recurrent malignant glaucoma.

Pars-plana vitrectomy: Pars plana vitrectomy is effective in treating phakic and pseudophakic malignant glaucoma. In 1983, Momoeda[59] reported successful reversal of malignant glaucoma in five eyes using anterior pars plana vitrectomy combined with intracapsular lens extraction through a corneal incision, although intraocular pressure required medical treatment in all five eyes, and two required further filtration surgery. The goal is to create a pathway for aqueous flow into the anterior chamber, which usually is accompanied by intraoperative deepening of the anterior chamber.[60-64]

Lens extraction: In the phakic eye, vitrectomy alone may not relieve the ciliolenticular block because of the difficulty in adequately removing the anterior vitreous without simultaneously damaging the lens. For this reason, the vitrectomy is likely to be accompanied by cataract formation. Therefore, combined ECCE or phacoemulsification with posterior capsulotomy and hyaloidotomy in any patient with even mild lens opacity should be considered.[65] Intraocular lens implantation and cataract removal should be combined only for compelling reasons of visual rehabilitation, or if intraocular fluid dynamics have so definitely restored to normal that no complications are anticipated. In this case, lens extraction is among the effective procedures, but it should be combined with an incision of the anterior hyaloid and possibly with deep incisions into fluid pockets in the vitreous.[12,16]

Others surgical approaches: Cyclocryotherapy has also been advocated, with the presumed mechanism being alteration in the ciliary body or vitreous.[66] Perilenticular incision of the vitreous was described by Chandler,[67] but the procedure has generally been abandoned because of the significant risks involved.

Management of the fellow eye

There is a significant chance that malignant glaucoma will develop in the fellow eye, when it has occurred previously in one eye. For this reason, it is often appropriate to perform a prophylactic laser peripheral iridotomy prior to the development of symptoms in the fellow eye. It is still important to determine whether angle closure contributed to the malignant glaucoma in the first involved eye, or if any peripheral synechiae or angle-closure glaucoma was evident in the fellow eye. However, if angle-closure glaucoma is present, every effort should be made to halt the attack prior to surgery and, if the attack can not be halted, mydriatic-cycloplegic therapy is strongly recommended after iridotomy and should be continued indefinitely.

Finding of malignant glaucoma should be pre-emptively treated with cycloplegics and osmotic agents in the unfortunate event that the fellow eye also requires surgery (*e.g.*, cataract or filtration surgery).

Conclusion

The precise mechanism of malignant glaucoma remains unclear, but it is almost certainly closely related to the anatomical relationships between the lens, zonules, anterior vitreous face, and ciliary body. Reversal of aqueous misdirection appears to be dependent on the existence of direct continuity between the vitreous cavity and the anterior chamber, which is difficult to achieve in the presence of a lens, as the lens is often relatively large. The management of this difficult condition is likely to remain controversial until the exact mechanism is more clearly understood. However, in light of modern microsurgical techniques, reversal of ciliary block glaucoma can be achieved with preservation of good visual acuity and control of intraocular pressure.

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Medical treatment

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Primary angle-closure glaucoma

Acute angle closure

The goal of initial medical treatment of acute angle closure is the preparation of the patient for laser iridotomy. In doing so, medical treatment is used to lower the IOP, to constrict pupil, to clear cornea edema, and to reduce inflammation. The medications available to achieve these objectives include oral or intravenous hyperosmotic agents and carbonic anhydrase inhibitors and topical agents, such as beta-blockers, topical carbonic anhydrase inhibitors, and alpha-2-adrenergic agonists, all of which lower IOP by reducing the aqueous production. However, pilocarpine remains the key agent in the initial management of acute angle closure because of its ability to constrict the pupil, pulling the peripheral iris away from the trabecular meshwork. Oral glycerin or intravenous mannitol may be used in unresponsive episodes of elevated IOP. Such hyperosmotic agents lower the IOP by increasing the plasma osmolarity, resulting in transient dehydration and shrinkage of the vitreous. Topical steroids are used to reduce ocular inflammation. In some cases, the pupil may become paretic, and fixed in a mid-dilated position as a consequence of ischemia caused by increased IOP. In this situation, pilocarpine may have little or no effect on pupil size. Laser iridotomy should be performed as soon as possible after temporarily reducing the IOP and clearing cornea edema.

The fellow eye typically shares the anatomic predisposition to angle closure. Such eyes are at increased risk of an acute attack itself as a result of exposure to environmental agents that may have precipitated the contra-lateral episode of angle closure. Fellow eyes should be treated with pilocarpine 1% q.i.d. in the short term, until prophylactic laser iridotomy has been performed. Such untreated fellow eyes have a 40-80% chance of developing an acute attack over the next five to ten years. Long-term pilocarpine administration is not effective in preventing such attacks in many cases.[1,2]

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Pilocarpine is a cholinomimetic alkaloid which acts by direct stimulation of muscarinic receptors. The onset of miosis with a 1% solution occurs 10 to 30 minutes after administration, and reaches maximal IOP lowering effect at around 75 minutes. The duration of action for miosis is about four to eight hours, and the reduction in IOP lasts for between 4 and 14 hours after administration.[3] Intensive administration of pilocarpine in initial management of acute angle-closure is controversial. Some authorities recommend 1% or 2% pilocarpine is administered two or three times over a 30-minute period to encourage miosis.[3] However, one study which compared an intensive regime with a single doses of pilocarpine given at one and six hours revealed no difference in IOP reduction between the two regimes of treatment.[4] Stronger miotics, such as pilocarpine 4%, should be avoided, as they may increase the vascular congestion of the iris, or rotate the lens-iris diaphragm more anteriorly, increasing the pupillary block. Table 1 summarizes the medical therapy of acute primary angle closure. Contra-indications and hypersensitivity to drugs should be excluded prior to starting treatment.

Table 1. Immediate medical therapy for acute primary angle closure*

1. Acetazolamide (250-500mg) IV stat, then 125 to 250 mg q.i.d. P.O. until symptoms subside.
2. Topical pilocarpine 2% every 10 minutes for 3 times,[3] then q.i.d.
3. Topical beta-blocker and/or alpha-2-agonist stat, then regularly.
4. Mannitol 10% or 20% solution with a dosage of 1 to 1.5 g/kg body weight (5-8 cc/kg) IV at a delivery rate of 3 to 5 ml per minute[6,7] or Glycerol 50% solution orally with a dosage of 1 to 1.5 g/kg (2-3 cc/kg) body weight.[8,9]
5. Topical steroid, such as prednisolone acetate, 1% q.i.d.
6. Analgesics and antiemetics as required.

* (Modified from Foster PJ and Chew PTK.[5])

Medical treatment of other symptomatic forms of primary angle closure, such as intermittent angle closure, should follow these principles mentioned above. Initial pilocarpine therapy to induce miosis is necessary until a laser iridotomy is performed.

Chronic angle-closure

Evidence suggests that chronic angle-closure is the consequence of multiple contributory mechanisms, including pupillary block, a thick peripheral iris, and abnormal arrangements of the ciliary processes, causing plateau iris configuration.[1,10,11] Prior to performing a laser iridotomy, pilocarpine is still a logical choice of therapeutic agent, in view of its ability to widen the drainage angle. After successful laser iridotomy (which has resulted in an open angle), treatment of chronic angle closure is essentially the same as that of POAG. In cases where residual angle closure is present, the management must still be directed towards opening the drainage angle. Miotics or laser peripheral iridoplasty are useful in this role.

Secondary angle-closure glaucoma

Lens induced angle-closure glaucoma

Glaucoma associated with lens swelling (phacomorphic glaucoma)

Scenarios which may result in an eye developing phacomorphic glaucoma include an age-related cataract becoming rapidly intumescent, or a traumatic cataract developing after a perforating injury. In phacomorphic glaucoma, an increase in lens thickness pushes the iris forward and increases the amount of lens-iris contact. This in turn causes an increase in resistance to aqueous flow from posterior to anterior chamber via the pupil.

Beta-blockers, carbonic anhydrase inhibitors, α-agonists and hyperosmotic agents may all be used to lower the IOP in the short term. Topical steroids are used to control the accompanying inflammatory reaction. Urgent lens extraction should be performed if IOP cannot be lowered by medical means. Usually cataract surgery is carried out when the IOP has been controlled, corneal edema has cleared, and the eye is less inflamed.[12-14]

Glaucoma associated with lens subluxation and dislocation

Subluxation or dislocation of lens may present with identical symptoms and similar signs to those seen in acute primary angle closure. One should be extremely cautious in treating any patient with angle-closure who is suspected of having an anteriorly subluxated lens. Miotics constrict the ciliary ring and loosen the remaining zonular fibers, allowing further anterior displacement of the lens.

If the angle can be successfully opened with the use of pilocarpine (*i.e.*, it does not further shallow the anterior chamber), one should suspect a complete dislocation of the lens. Mydritics should only be used in this situation with great caution. In the acute phase, pressure rises occurring as a result of angle closure associated with lens subluxation is managed by placing the patient in a supine position and giving an oral hyperosmotic agent and topical beta-blocker. The hyperosmotic agent will reduce the volume of the vitreous, and may permit posterior movement of the lens, thus relieving pupillary block. Laser iridotomy helps prevent subsequent attacks. After iridotomy, miotics can be used to constrict the pupil to prevent dislocation of the lens into anterior chamber.

Anterior dislocation of the lens into the pupillary aperture, into the anterior chamber, or vitreous herniation through the pupil, may cause pupillary block. This is characteristically worsened by miotics. Cycloplegic mydriatics dilate the pupil and tighten the intact zunules, pulling the lens backward. Thus cycloplegics may help alleviate pupillary block.[12-14]

Neovascular glaucoma

In its latter stages, neovascular glaucoma (NVG) results from secondary angle closure caused by the contraction of a fibrovascular membrane in the anterior chamber angle. Initially, the fibrovascular membrane occludes the open angle, covering

the trabecular meshwork. This progresses to the formation of peripheral anterior synechia, leading to irreversible angle closure.

The goals in treatmemt of patients with NVG are the preservation of vision and the globe, as well as relief of ocular pain, and control of ocular inflammation. Medical treatment of NVG can be frustrating and is often ineffective. Panretinal photocoagulation (PRP) for proliferative retinopathy should be performed as soon as possible if the ocular media are clear enough. When adequate PRP is performed early, there is a possibility of regression of anterior segment neovascularization in eyes that have suffered a central retinal vein occlusion or proliferative diabetic retinopathy.

When extensive synechial angle closure has developed, miotics and/or epinephrine are of little use to control intraocular pressure. Both increase the permeability of the blood-aqueous barrier and aggravate inflammation, and should be avoided. If total synechial angle closure has developed, a combination of aqueous suppressants such as beta-blockers, carbonic anhydrase inhibitors (topically and/or systemically), and topical steroids may help improve comfort and offer some reduction in IOP. However, medical treatment rarely gives satisfactory pressure control. Hyperosmotic agents can be used intermittently. Cycloplegics help to decrease ocular congestion and pain, and may improve uveoscleral outflow.[12-16]

Iridocorneal endothelial syndrome

Iridocorneal endothelial syndrome (ICE) denotes a spectrum of diseases characterized by a corneal endothelial abnormality associated with corneal edema, anterior chamber angle changes, alterations in the iris, and secondary angle-closure glaucoma. Approximately half of the cases of ICE syndrome develop glaucoma. Aqueous outflow may be impaired by either the abnormal membrane covering the trabecular meshwork, or by synechial closure of the anterior chamber angle. However, in ICE syndrome, the severity of glaucoma does not correlate precisely with the degree of synechial angle closure.

Patients with ICE syndrome may require treatment for corneal edema, glaucoma or both. The glaucoma can often be controlled medically in the early stages with aqueous suppressants. Miotics are ineffective when the angle is covered by a membrane or closed by synechiae. Lowering IOP may also control the corneal edema, although the additional use of hypertonic saline solution and soft contact lenses are often required.

Medical control becomes ineffective as the disease progresses, and surgical intervention is ultimately required. Late failure of a functioning trabeculectomy bleb may occur, owing to proliferation of a cellular membrane that covers and occludes the internal aspect of the sclerotomy. Argon laser trabeculoplasty is contraindicated.[12-15,17,18]

Glaucoma associated with uveitis (inflammatory glaucoma)

Angle-closure glaucoma without pupillary block

Intraocular inflammation may lead to an accumulation of inflammatory debris and exudate in the angle. Neovascularization of the iris and anterior chamber angle may

occur after long-standing intraocular inflammation. Contraction of the fibrovascular membrane covering the trabecular meshwork causes PAS and obliteration of the iridocorneal angle. Forward rotation of the ciliary body can occur, with cyclitis, swelling of the ciliary body, and annular choroids detachment.

Angle-closure glaucoma with pupillary block

Fibrinous adhesions between the iris and lens may cause partial or complete papillary block, with resultant anterior bowing of the iris (iris bombe). The axial anterior chamber depth is typically normal, although the periphery is usually shallow. The relatively anterior position of the peripheral iris leads to peripheral iridocorneal contact and active inflammation leads to the development of PAS. Laser iridotomy is considered the treatment of choice in cases of inflammatory glaucoma with pupillary block.

Cycloplegic mydriatics can be used to prevent or break posterior synechiae in inflammatory glaucoma- both with and without papillary block. These drugs may also increase uveoscleral outflow, helping lower IOP. Steroids are usually applied topically or by periocular injection, with systemic administration being reserved for severe cases, or when other routes are not effective. Steroids are associated with ocular complications, particularly elevated IOP. Other complications include cataract formation, ptosis, and mydriasis. Systemic complications compromise peptic ulcer, hyperglycemia, infectious diseases flare-ups, osteoporosis, Cushing syndrome, and aseptic necrosis of the head of the femur. Nonsteroidal anti-inflammatory drugs may be used to treat mild to moderate inflammation, when corticosteroids are contraindicated or not tolerated by the patient. In certain types of uveitis, immunosuppressive treatment may be appropriate. Aqueous suppressants are also employed to control IOP (beta-blockers, alpha-2-agonist, and carbonic anhydrase inhibitors). Miotics should be avoided because they increase ciliary spasm, posterior synechiae formation and aggravate the inflammatory reactions. Prostaglandin analogues should be avoided if possible.[12-15,19]

Angle-closure glaucoma secondary to posterior scleritis

Differentiating angle-closure glaucoma secondary to posterior scleritis from primary angle-closure glaucoma is important, as medical treatment is markedly different, and surgical treatment is not required in cases of scleritis. Posterior scleritis may be difficult to diagnose, although proptosis, limitation of eye movements secondary to scleral thickening, unilateral signs of diffuse anterior scleritis, or an exudative retinal detachment are all suggest the diagnosis. B-mode ultrasound may demonstrate the 'T-sign' supporting the diagnosis of posterior scleritis.

Treatment of angle-closure associated with posterior scleritis is aimed at the managing the underlying inflammatory condition – topical steroids, oxyphen-butazone, cycloplegics and where necessary, systemic steroids. In addition, glaucoma medication is required to control IOP – where necessary using acetazolamide.[20]

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Laser iridotomy

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Introduction

Laser iridotomy has become the procedure of choice for relief of, or prophylaxis against, pupillary block, having largely supplanted surgical iridectomy.[1] Producing iridotomies with radiant energy was accomplished as far back as 1956, when Meyer-Schwickerath used a xenon arc coagulator to perforate the iris.[2] While frequent iridotomy closure and corneal and lenticular damage prevented its widespread usage, the subsequent introduction of Argon and Nd:YAG lasers have transformed laser iridotomy into a routine office procedure.

Though the technical aspects of iridotomy have changed little in recent years, fundamental questions remain unanswered, including who will benefit from prophylactic iridotomy, why iridotomy fails in certain eyes, and what the long-term risks of laser iridotomy are, particularly with respect to cataract formation. Addressing these questions will help define the role of laser peripheral iridotomy (LPI) in preventing the 21 million cases of PACG and 5.3 million cases of resultant blindness that are expected to be found by 2020.[3] In this chapter, we review the technical aspects of LPI, the indications for its use, the complications of treatment, and alternative and adjunctive treatments.

Performing laser peripheral iridotomy

Choice of laser

Head-to-head trials comparing argon to Nd:YAG laser iridotomy support the use of the Nd:YAG laser. Several studies in mainly white populations have demonstrated more frequent closure of argon laser iridotomies.[4-6] Over variable follow-up ranging from 20-42 months, Del Priore found closure in no eyes receiving Nd:YAG iridotomy, while 21% of contralateral eyes from the same patients treated with argon iridotomy required retreatment for iridotomy closure.[4] Additionally, Nd:

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YAG iridotomy requires far fewer applications of laser and less total laser energy, resulting in a quicker, better tolerated procedure.[5,6]

The rates of most short-term complications, i.e. non-progressive corneal opacification and intraocular pressure (IOP) spikes, are similar with both lasers.[5,6] Hyphemas, however, do occur more frequently in Nd:YAG treated eyes, occurring in 30% or more of Nd:YAG treated eyes, and rarely when using the argon laser (though no long-term complications of these small hyphemas have been reported).[4,5] Hyphema rates can be reduced by pre-treating patients for Nd:YAG LPI with argon laser at the intended iridotomy site. In one study, argon pre-treated eyes had a 17% rate of bleeding compared to a 67% rate in eyes treated with Nd:YAG alone.[7] Combining these two lasers also allows for iris perforation with fewer Nd:YAG pulses, particularly in patients with dark irises,[8] and is a common practice in parts of Asia.

Laser settings

For argon laser iridotomy, settings typically involve a spot size of 50 microns, power of 500-1000 mW, and duration of 0.02 to 0.2 seconds, while for Nd:YAG laser iridotomy, energy levels between 2-10 mJ are administered. In studies from primarily white populations, total energies needed for argon laser iridotomy averaged between 10 and 20 J, while total energies for Nd:YAG laser iridotomy averaged 30 to 40 mJ.[5,6] Substantially more Nd:YAG laser energy may be required in populations with darker irises, as was reported from a large case series of patients treated in Saudi Arabia, who required over 100 mJ on average to create a patent Nd:YAG LPI.[9]

The energy required to create a patent Nd:YAG LPI may be higher in acute angle closure, with one study from Saudi Arabia noting an average of 152 mJ in AAC eyes, compared to means of 123 mJ in eyes with occludable angles, and 98 mJ in eyes with chronic angle closure.[9]

Application of laser

Laser is best applied through a focusing lens, such as a 66 D Abraham lens or a 103 D Wise lens, which helps apply energy directly on the iris surface, increasing the power applied per pulse, and decreasing exposure to the cornea, lens, and retina.[10] Laser energy is ideally applied to the superior iris in such a location that the iridotomy site will be covered by the upper eyelid, minimizing the potential for glare disability. The iridotomy should be placed as peripheral as possible, though less peripheral iridotomies may be necessary with peripheral corneal opacities (*i.e.*, arcus senilis) or iris-cornea apposition. An iris crypt or a region of thinned or atrophic iris should be chosen for the iridotomy site, minimizing the energy necessary to create a patent hole. Placement of an iridotomy directly at 12 o'clock has been discouraged, as air bubbles created during the procedure (typically seen when using the argon laser) tend to accumulate at the 12 o'clock position, obscuring the view for further laser application.[11] (Figs. 1 and 2)

Perforation of the iris is often marked by a gush of fluid along with iris epithelium pigment into the anterior chamber. Further laser to enlarge the iridotomy is usually still desired at this point, but the view to the iris may be limited because of pigment in the anterior chamber or corneal clouding. Waiting for pigment set-

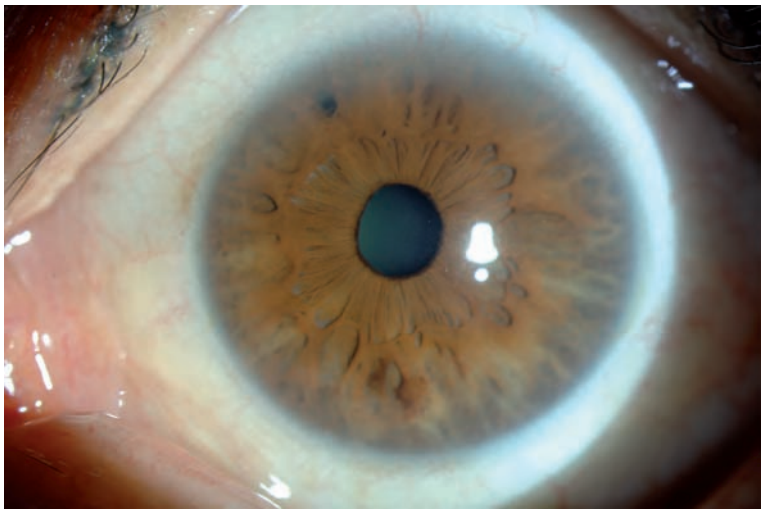

Fig. 1. Anterior segment photograph after argon laser iridotomy. (Photo courtesy by Ki Ho Park, MD, PhD)

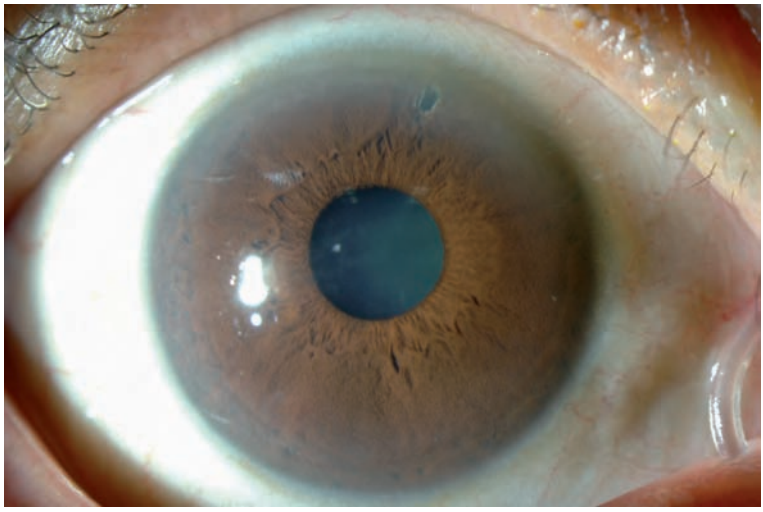

Fig. 2. Anterior segment photograph after Nd:YAG laser iridotomy. (Photo courtesy by Ki Ho Park, MD, PhD)

tling, or having the patient return for a second visit to complete the iridotomy may facilitate treatment while not subjecting the patient to large amounts of ineffective laser energy. Once a patent hole is achieved, care should be taken to focus on remaining iris tissue, as application of laser through a patent iridotomy can injure the lens[12,13] and result in retinal, and possibly foveal burns.[14,15]

Pre- and post-treatment medications

Fifteen to sixty minutes prior to iridotomy, eyes may be treated with pilocarpine (1-4%) to achieve miosis and thin the iris. Topical apraclonidine should be used at the same time to prevent post-operative pressure spikes,[16,17] though other pressure lowering agents, including brimonidine and dorzolamide, are also effective, and may be used if apraclonidine is not available.[18,19] Apraclonidine may also reduce the risk of hyphema due to its vasoconstrictive effects. The absence of a pressure spike is confirmed by retesting intraocular pressure one to two hours after the procedure. After treatment, patients are placed on a topical steroid such as 1% prednisolone acetate four times daily until the next follow-up visit, typically a week later. In eyes with active inflammation at the time of LPI, or eyes which may have a significant inflammatory response to the procedure (because of previous uveitis or recent surgery or trauma to the eye), more frequent dosing of the topical steroid would be advisable. Other pressure lowering medicines are typically maintained until it is determined whether the LPI has resulted in lower IOP.

Indications for LPI

Acute angle closure

The most clear-cut indication for LPI is an acute attack of angle closure (AAC), marked by a mid-dilated pupil, redness and severe elevations of intraocular pressure. Corneal edema, resulting in decreased vision and haloes, can occur, and may prohibit gonioscopic confirmation of a closed angle in the affected eye. Fellow eyes will have very narrow angles as well,[20] and gonioscopy of fellow eyes should confirm the diagnosis. If the fellow eye is not narrow, other secondary causes of AAC need to be considered including uveitis and neovascularization.

Intraocular pressures (IOPs) in the context of AAC are typically quite high, with median IOPs in case series ranging from 50-56 mmHg.[9,21-23] Prior to LPI in eyes with AAC, IOP must be lowered enough to ensure a clear cornea through which the LPI may be performed. In a study of Asian eyes, at least one-third of patients had sufficient corneal edema to obscure iris details, with very few eyes having no corneal edema whatsoever.[24]

'Adequate' reduction of IOP prior to LPI was achieved in 36 of 40 patients (90%) by Suanders, who used a combination of oral and IV acetazolamide, pilocarpine, timolol, and topical steroids.[23] Of the four remaining patients, two responded to IV mannitol, while the remaining two underwent primary extracapsular cataract extraction. In a study from England, Choong evaluated the ability of a standardized protocol to reduce IOP in AAC by 25%, or to below 35 mmHg, in 63 subjects.[22] Forty-four percent of patients had successful IOP reduction with a combination of acetazolamide (PO and IV), pilocarpine, carteolol, topical steroids, and supine positioning; with an additional 51% of patients achieving successful IOP reduction with the addition of a single osmotic agent (glycerin or mannitol); and 5% of patients requiring a second osmotic agent. IOP reduction was achieved in seven hours or less in all patients, with a median time of three hours to achieve the specified IOP endpoint.

Several studies confirm that nearly all eyes with AAC can successfully undergo LPI despite the concerns of corneal clouding.[5,6,21] In one study of 111 eyes receiving sequential Argon and Nd:YAG LPI for acute angle closure, a patent iridotomy was created in 110 eyes, with the lone remaining eye undergoing trabeculectomy because of persistent corneal edema.[21] However, a study in which LPI was performed by less experienced personnel found a 58% rate of failure in the original treatment, suggesting that results may be operator-dependent.[25]

Immediate IOP lowering with LPI in AAC is frequently dramatic. All 110 Asian eyes treated by Aung had the IOP drop below 21mm Hg after a patent LPI was achieved.[21] In another study from Saudi Arabia, mean IOP decreased after LPI from a mean of 49 mmHg to only a mean of 26 mmHg, with 81% of patients having an IOP less than 22 mmHg after a median follow-up period of four months.[9]

Long-term IOP control after LPI for AAC is frequently an issue, with most studies showing a need for additional IOP-lowering treatment in the months or years after LPI. Over half the patients in a study from Singapore with mean follow-up greater than four years required additional treatment, including 32% who went on to trabeculectomy.[21] Most requiring additional treatment did so in the first month after LPI – though long-term follow-up proved useful, as 16% of those requiring additional pressure-lowering treatment did so after one year. A second study from Singapore showed similar results, with 41% of patients undergoing additional treatment within a year for an IOP rise to above 21 mmHg.[20] Two British studies also found a significant need for additional treatment in AAC eyes after LPI. Saunders reported that 63% of such eyes required additional treatment within eight months of follow-up, including 41% of eyes needing additional surgery,[23] while Choong found that 56% of eyes required additional treatment (including surgery in 25%) after a follow-up period of six months.[22]

In a report from Singapore, serial gonioscopy in eyes with AAC after LPI demonstrated a widening of the angle in the first month after the procedure, but no significant change in the amount of PAS.[20] Eyes that subsequently needed additional pressure-lowering treatment started with more PAS and narrower angles than eyes that did not need subsequent treatment, although after 12 months of follow-up these groups did not differ in angle opening (measured by Shaffer score) or the extent of PAS.[20] Reporting from Taiwan, Hsiao noted a more significant impact of pre-operative PAS, with 5/6 eyes going on to trabeculectomy having greater than 270 degrees of pre-operative PAS.[26]

Others have looked at AC angle opening after LPI with ultrasound biomicroscopy (UBM). Kashiwagi noted a significant increase in peripheral anterior chamber depth (ACD) after LPI, though a less-pronounced change than that noted in PACG eyes or eyes receiving prophylactic LPI for occludable angles.[27] Yeung performed dark UBM in 16 AAC patients with patent LPIs, finding persistent appositional closure in nine patients, and significantly narrower ACD than controls (1660 vs 2300 microns).[28] UBM also documented anteriorly positioned ciliary bodies in these patients which could result in a 'plateau iris' configuration, pushing the peripheral iris forward against the TM even in the presence of a patent LPI.

Short-term visual outcomes after LPI are generally good, with Choong showing recovery of visual acuity to 6/24 or better in 76% of treated eyes in the months after LPI.[22] However, AAC eyes receiving LPI need good long-term follow-up given the high rates of blindness and glaucomatous optic neuropathy in the years after LPI.[29]

Fellow eyes in unilateral acute angle closure

Most large cases studies show that approximately ten percent of patients presenting with AAC present bilaterally.[30,31] Lowe followed the fellow eyes of patients who had a unilateral AAC attack, and found that over half developed AAC in the second eye over a follow-up period as long as 25 years. Of fellow eyes experiencing an attack of AAC, 36% had their attack in the first year, 52% within five years, and the remaining 48% between five and 25 years after the initial attack.[31] Snow looked at 72 patients not receiving prophylactic LPI in the fellow eye after unilateral AAC, and found that 60% had AAC in the fellow eye, with 77% of these eyes affected within six years.[32] Provocative testing failed to identify the fellow eyes which went on to AAC.[32]

Prophylaxis against AAC with LPI or surgical iridectomy is highly effective. In Lowe's longitudinal study, none of the 64 patients receiving prophylactic surgical iridectomy in the fellow eye went on to develop AAC (Lowe 1962). Ang followed eighty LPI-treated fellow eyes of Asians with unilateral AAC for an average of 51 months, and found no cases of AAC.[33] However, Saunders reported a low rate (6%) of AAC in 36 fellow eyes, despite what appeared to be a patent LPI, over a mean follow-up period of eight months.[23]

Gazzard used ultrasound biomicroscopy to describe deepening of the peripheral anterior chamber in fellow eyes after LPI.[34] However, mean central anterior chamber depth remained unchanged, and one-third of eyes were still gonioscopically classified as occludable after LPI (compared to 73% prior to LPI), with no more than 90° of pigmented trabecular meshwork visible without indentation.[34] Compared to eyes with AAC, deepening of the peripheral anterior chamber with LPI is more pronounced.[27] However, as in AAC eyes, almost one-half of fellow eyes of patients with unilateral AAC show dark-room appositional angle closure by UBM even after a patent LPI has been placed.[28] These eyes also possess anteriorly positioned ciliary bodies and shallow anterior chamber depths, explaining their potential for AAC even with a patent LPI.[28]

Intraocular pressure in fellow eyes of patients with unilateral AAC is usually low at presentation, and remains low after LPI. Ang found only ten of 80 eyes to have an IOP of greater than 21 mmHg at presentation (including two eyes with PACG), with a mean IOP of 15.6 mmHg.[33] After LPI in these eyes, only nine required additional IOP-lowering treatment, including the two eyes with PACG, and seven other eyes which had an IOP of less than 21 prior to LPI. Each of these nine eyes required additional treatment within one year despite a patent LPI, including one eye that went on to trabeculectomy three years after LPI.

Long-term follow-up in this cohort showed low rates of glaucoma, with only five additional eyes (6.5%) developing glaucoma after a mean follow-up of six years, and over 80% of eyes retaining vision of at least 6/12, with unoperated cataract accounting for most of the visual impairment.[35]

There should be no delay in performing LPI in fellow eyes of patients presenting with AAC, as several studies have reported AAC occurring in unaffected contralateral eye within the first week of presentation.[30,31,33] If the second eye is not treated immediately on presentation, pilocarpine prophylaxis may be beneficial.[30]

Chronic angle-closure glaucoma

Several studies in multiple ethnic backgrounds have found lowering of IOP after LPI in eyes with primary angle closure glaucoma (PACG).[9,26,36-41] Twelve months after Nd:YAG LPI, 187 Saudi Arabian eyes with PACG or primary angle closure showed a drop in mean IOP from 24.8 to 17.5, with equal numbers of patients receiving more and less medical therapy after treatment.[9] A British study of 64 patients receiving argon LPI compared the results in those with visual field loss to those without definite visual field loss and reported greater intraocular pressure lowering (16% vs 12%) in eyes with visual field loss, though these eyes also had a significantly higher intraocular pressure prior to LPI (25.0 vs 20.7 mmHg).[39]

A mostly white population treated with argon LPI for PACG was followed for 53 months, with a decrease in mean IOP from 28 to 18.5 mmHg, and a decrease in medications used from 1.5 to 0.9.[40] However, one cannot determine what the true effect of LPI was in this population, because ten of the 98 treated eyes required trabeculectomy during the follow-up period. Similar long-term follow-up results were obtained in a study of 58 Taiwanese eyes with PACG, in which mean IOP decreased from 25.4 pre-op to 14.1 post-op after a mean follow-up of 51 months.[26] All but 7% of eyes needed the same or fewer medicines to achieve this lower pressure, though nearly half were still on some medical therapy at the end of the follow-up period, and four of the 58 eyes (7%) required trabeculectomy.

Other studies have shown substantially higher rates of trabeculectomy after LPI for PACG, including 30% of South Africans treated with Nd:YAG LPI and followed for a mean of 22 months,[41] and 34% of British patients treated with argon LPI.[39] Nolan and colleagues treated 164 Mongolian subjects with occludable angles, angle closure with elevated IOP or PAS, and PACG, and reported the proportion of eyes who failed treatment (*i.e.*, requiring surgery to control IOP, or with a drop in acuity to less than 3/60).[42] Failure was noted in 48% of eyes with glaucomatous optic neuropathy at baseline, while only 3% of those without glaucoma failed. A multivariate analysis identified vertical cup to disc ratio of 0.8 or more, and IOP above 19 as important risk factors for failure, though these could easily be explained by lead-time bias, or the need for more aggressive treatment and lower target pressures in these eyes.

LPI outside of AAC generally causes widening of the anterior chamber angle, with 98% of the 164 Mongolian subjects treated by Nolan having less than 270 degrees of appositional closure after the procedure.[42] However, PAS were often still present post-operatively, with 64% of eyes having PAS in the same number of quadrants, 17% of eyes having PAS in additional quadrants, and 19% of eyes having PAS in fewer quadrants. PAS were also noted not to change substantially in 140 Japanese eyes treated with argon LPI.[43] In this study, 83% of eyes had PAS in the same number of clock hours, while 6% of patients had fewer clock hours of PAS, and 11% had more clock hours of PAS. LPI in a selected group of South Indian PACG patients (without cataract lowering vision below 6/12, or advanced disk or field damage) was noted to open at least 180 degrees of the angle to the point where the posterior third of the TM was visible in 73% of eyes.[44] PAS prior to LPI was not associated with whether the angle achieved this degree of opening. However, eyes with more extensive PAS, as well as those with higher IOP and greater optic nerve damage at presentation, require more interventions to control IOP after LPI.[26,37,41,42]

Primary angle closure suspects (occludable angles)

There is very little literature to guide decision-making on who is at risk for angle closure, and would benefit from a LPI solely on the basis of iridotrabecular contact. A study in Greenland Eskimos, found that seven of 20 (35%) individuals with occludable angles (as determined by gonioscopy, with no specified criteria) developed ACG, while four or 49 eyes with non-occludable angles went on to ACG.[45] One hundred twenty-nine American patients deemed to be at risk for angle closure glaucoma on the basis of a central ACD less than 2.0 mm or an anatomically narrow AC angle were followed for an average of 2.7 years.[46] Eight patients (6 %) developed AAC attacks in the follow-up period, while another 17 patients (13%) developed primary angle closure, defined as appositional or synechial closure of 0.5 to 3 clock hours in the superior angle. Dark room prone provocative testing was unable to accurately predict those patients who went on to angle closure.[46] Unfortunately, no long-term data exist following eyes with occludable angles, nor is there data following angles defined as occludable through rigid criteria. Thus, the true ability of gonioscopic findings to predict future angle closure remains largely unknown.

LPI in 148 Asian eyes with 'anatomically narrow angles' lowered the average IOP from 14.0 to 11.7 mmHg after six months), and over a mean follow-up period of 51 months, only six eyes required medications to control IOP, and none required glaucoma surgery.[26] None of the 74 Mongolian eyes treated with LPI for iridotrabecular contact over three-quarters or more of the angle lost visual acuity to below 3/60 or required glaucoma surgery after a mean follow-up period of three years.[38]

While LPI appears to have few adverse sequelae, one recent report documented a possible increase in cataract in eyes undergoing LPI.[12] If this is indeed the case, LPI in all persons with iridotrabecular contact may not be indicated, and further research will be needed to determine optimal screening and treatment strategies for such persons.

Reverse pupillary block

It has been suggested that pigment dispersion syndrome (PDS) occurs as a result of 'reverse pupillary block', in which backward bowing of the iris results in rubbing of the iris pigment epithelium against the lens zonules, leading to the dispersion of pigment granules which disrupt flow through the trabecular meshwork.[47,48] These early reports suggested that laser iridotomy could change this posterior bowing of the iris to a more planar configuration. Gandolfi treated one eye of 21 patients with bilateral PDS, and found that fewer LPI treated eyes had IOP elevations over the following 2 years.[49] However, a retrospective study of 46 patients with bilateral PDS followed for at least two years after one eye received LPI showed no lowering of intraocular pressure, though iris configuration was not studied in this case.[50] At this point, the efficacy of LPI in PDS remains unclear, and additional studies are necessary to determine whether this is a worthwhile indication for LPI.

Other indications for LPI

Laser peripheral iridotomy functions to relieve any method of pupillary block, including secondary pupillary block from a variety of causes. In aphakic pupillary block, the vitreous humor forms circumferential adhesions to the iris margin, and laser iridotomy has been used to allow redirection of aqueous humor into the anterior chamber.[51,52] Pupillary block can also occur in aphakic eyes which have had silicone oil or gas bubbles placed as part of retinal surgery, particularly if no surgical iridectomy was placed.[53, 54] Jackson and colleagues also describe seven phakic patients and one pseudophakic patients that had pupillary block after silicone oil placement, arguing that silicone oil can come through areas of zonular dehiscence to create pupillary block.[53] LPI was successful in some patients at relieving this pupillary block, though all patients eventually required removal of silicone oil. Reddy and colleagues tried using Nd:YAG LPI to reopen closed surgical iridectomies performed with Silicone oil placement, but were successful in only 22% of cases.[55]

Pseudophakic pupillary block has been described with anterior chamber intraocular lenses (ACIOLs), posterior chamber intraocular lenses (PCIOLs), and iris fixation lenses.[56,57] Pupillary block with anterior chamber intraocular lenses should be anticipated with a surgical iridectomy at the time of surgery. Several mechanisms for pseudophakic pupillary block have been described for posterior chamber IOLs, including traumatic IOL dislocation, optic capture with in-the-bag haptics,[58] and iris-anterior capsular adhesions.[59,60] Definitive treatment usually requires replacing and/or repositioning the IOL. However, short-term pressure lowering may be achieved through mydriasis to dilate the pupil beyond the edges of the IOL, or aqueous redirection into the anterior chamber by LPI. Recurrent closure of laser iridotomy has been reported for pseudophakic pupillary block,[61] and generating larger iridotomies, or placing multiple iridotomies, may increase the chance of maintaining aqueous flow into the anterior chamber.

Uveitic glaucoma can produce pupillary block by producing 360 degrees of posterior synechiae and iris bombe. A retrospective review of 15 eyes in 11 patients treated with Nd:YAG LPI for iris bombe from uveitis showed that 7/15 eyes needed between 2-5 treatments over a follow-up period averaging 14 months.[62] A total of 28 iridotomies were performed in these 15 eyes, with failure in 17 of these LPIs and a mean time to failure of 85 days. In a control group of 66 patients without uveitis, no treatment failures were noted. Failure rates of 40-60% were seen both for eyes with severe inflammation at the time of the LPI, as well as eyes with no active inflammation at the time of LPI. No notes were made on the size or number of iridotomies performed with each treatment, and it remains unknown whether placing larger or greater than one LPI would be successful in this setting. While larger or more numerous LPIs may be more difficult to close off, there is also the concern of generating more inflammation which might increase the likelihood of closure.

Complications of therapy

Pressure spike

Transient pressure spikes were a significant problem in the early days of LPI,[63] but have become much less common since Robin and colleagues described the utility of apraclonidine in preventing pressure spikes after laser iridotomy.[17] Krupin showed that 28 of 100 eyes receiving argon LPI after pretreatment with only pilocarpine had IOP elevations to greater than 30 mmHg, with IOP rising to a mean of 40 mmHg in these eyes.[63] Similar rates of IOP spikes have been noted for Nd:YAG LPI.[5,6] In contrast, Robin showed that none of 14 eyes treated with apraclonidine prior to argon laser iridotomy experienced an IOP rise of greater than 10 mmHg after treatment, compared to six of 14 placebo-treated eyes.[17] In Japanese eyes treated with Nd:YAG iridotomy, only one of 29 eyes (3.4%) treated with preoperative apraclonidine experienced a pressure rise of 10 mmHg or more, as compared to 5 of 29 (17.2%) of eyes not receiving preoperative apraclonidine.[64] Lewis and colleagues retrospectively looked at 289 eyes with occludable angles, OHTN or CACG, and found that only two eyes had pressure rises of 10 mmHg or more with apraclonidine and pilocarpine pretreatment, suggesting that pressure monitoring for routine LPI in eyes without significant GON may not even be necessary.[16] Other topical agents, including dorzolamide and brimonidine, have also been shown to have similar efficacies in preventing post-operative IOP rise after LPI, suggesting that the effect of apraclonidine may not be unique, and that other agents may be substituted when apraclonidine is not available.[18,19]

Lenticular damage

Several lines of evidence suggest that LPI may speed up cataract progression. Welch and colleagues studied eight lenses removed by intracapsular cataract extraction one day after Nd:YAG LPI, and found five cases of superficial damage to the anterior lens capsule and cortex which likely resulted from the treatment.[13] Cases of lens rupture with Nd:YAG LPI have also been reported, leading to cortical material in the anterior chamber[65] or a sterile granulomatous endophthalmitis.[66] Furthermore, LPI has been noted to result in flattening of the iris and increased iris lens contact, presumably from redirection of aqueous flow.[67] Theoretically, the increased iris-lens contact or redirected flow of aqueous humor could lead to cataractous change.

Lim and colleagues prospectively observed 60 mostly Chinese LPI-treated fellow eyes of patients with unilateral AAC, and noted that after one year 23% had progression of cataract using a lens opacity classification system, with two-thirds of those progressing demonstrating worsening or incident posterior subcapsular cataract.[12] While there was no control group in this study, and the natural progression of cataract in these eyes is not known, this finding in combination with the findings of anterior equatorial cortical damage after LPI, is suggestive, and should give pause to the implementation of widespread programs to prevent angle closure through LPI, particularly in areas where access to cataract surgery is limited. It has been noted previously that Asian countries such as India and China may have tens of millions of individuals with occludable angles, and speeding cataract progression in even a small percentage of these patients could significantly increase the volume

of necessary cataract surgery in regions where there is already a large volume of unoperated, visually significant cataracts.[68]

Corneal damage

In experimental rabbits, laser iridotomy has been shown to focally denude endothelium when laser was applied within 1.0 mm of the endothelial surface using a spherical contact lens.[61] When laser spots were applied within 0.1 mm of the endothelium, Descemet's membrane was disrupted as well. Electron microscopy was also performed in a human eye receiving laser iridotomy just prior to enucleation for melanoma.[69] When the iridotomy was performed with no contact lens, a 500-micron diameter area of corneal endothelial denuding was produced along with a Descemet's membrane tear. When an Abraham contact lens was used, a 50% smaller area of corneal denuding was produced, with no disruption of Descemet's membrane.

Wilhelmus described a series of five patients who went on to penetrating keratoplasty 0 to 5 years after argon laser iridotomy in eyes with narrow angles and corneal guttae. Corneal buttons showed generalized endothelial cell loss, suggesting that patients had an underlying endothelial dystrophy, whose progression may have been more rapid due to the iridotomy.[70]

Hyphema

Bleeding at the site of iridotomies can occur in up to 67% of eyes receiving Nd:YAG LPI.[4,5,7] Bleeding with argon iridotomy is rare, and pre-treatment of the iridotomy site with argon laser prior to Nd:YAG iridotomy may also decrease less bleeding.[7] There is little consequence to bleeding or hyphema after iridotomy, with blood spontaneously resolving without sequelae in virtually every instance.

Retinal burns

Retinal burns have been reported with argon laser iridotomy. Three of six monkeys treated with argon LPI with no contact lens had peripheral retinal burns, with the area of the retinal burn as high as 3.7 optic disc areas with a power of 1000 mW.[15] Two of six monkey eyes still showed evidence of retinal burns when an Abraham contact lens was used, though the size of the burn was smaller, particularly when the power was also decreased to 600 mW. A single case of foveal photocoagulation has been reported in a patient receiving argon laser iridotomy with an Abraham contact lens.[14] Visual acuity ultimately decreased to 20/400 with a visible area of foveal RPE depigmentation and early hypofluorescence and late staining on fluorescein angiography. No reports of this complication have been noted with Nd:YAG LPI.

Glare

Patients with patent iridotomies not covered by the eyelids may describe seeing a blurred or hazy line in front of the treated eye. This line is typically horizontal, is worse with bright light, and disappears when the eyelid is lowered to cover the

iridotomy site. Murphy and colleagues noted this visual symptom in 11 of 480 patients receiving Nd:YAG iridotomies over a three-year period.[71]

Alternative and adjunctive therapies

Several alternatives to LPI exist, both as primary treatment for the conditions discussed above, as well as for cases in which LPI is unsuccessful. These are discussed briefly below, with further discussion found elsewhere in this book.

Surgical iridectomy

Laser iridotomy has become the standard of care for angle closure, with recent Medicare data revealing over 50 laser iridotomies performed for every surgical iridectomy.[1] While laser iridotomy can be performed in the office, and carries no risk of intraocular infection, its efficacy is probably no better than the procedure it replaced. Fleck and colleagues carried out a prospective, randomized trial comparing operative iridectomy to Nd:YAG iridectomy, and followed patients for three years.[72,73] Though the numbers in the study were somewhat limited (21 patients received bilateral LPI, and 27 bilateral surgical iridectomies), there appeared to be no difference in visual acuity or intraocular pressure control after three years. However, one patient who had a small, but patent LPI did suffer an attack of AAC, while no AAC attacks were noted in the surgical iridectomy group.[72] A retrospective study from Japan found that similar numbers of angle closure patients achieved an IOP of less than 21 when treated with LPI or surgical iridectomy.[74]

Cataract extraction

Cataract extraction has been described as a primary procedure in patients with iridotrabecular contact or PACG, or as a secondary procedure that may produce additional angle opening and pressure lowering in eyes with persistently elevated pressures after LPI. This topic is covered elsewhere in this book.

Laser iridoplasty

Residual angle closure can persist even after placement of a patent LPI. Some of these eyes will have a plateau iris configuration, in which large or anterior ciliary processes push the peripheral iris against the trabecular meshwork.[75,76] Polikoff looked at ten patients having a suspected plateau iris configuration with UBM before and after LPI, and found that anterior chamber anatomy was largely unchanged, with anterior chamber depth, angle opening distance at 500 microns from the scleral spur, TM to ciliary process distance, and trabecular-iris angle all unchanged before and after LPI.[77] However, such eyes may not routinely be identifiable without techniques such as UBM or anterior segment OCT, and are often only identified by residual angle closure after LPI. These eyes may achieve further IOP lowering as well as opening of the peripheral angle with argon laser iridoplasty, which is covered in a separate section in this book.

Argon laser iridoplasty has also been reported to decrease IOP in the acute at-

tack of angle closure, and may be useful in cases where persistent corneal edema prohibits LPI.[78]

Trabeculectomy

As mentioned above, trabeculectomy can be necessary in some patients with PACG even after successful creation of a patent PI, and may rarely be necessary as a primary procedure in eyes where unresolved corneal edema prohibits LPI.

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Argon laser peripheral iridoplasty (ALPI)

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Introduction

Argon laser peripheral iridoplasty (ALPI) is a simple and effective means of opening an appositionally closed angle in situations in which laser iridotomy either cannot be performed or does not physically eliminate appositional angle-closure because mechanisms other than pupillary block are present. The procedure consists of placing contraction burns (long duration, low power, and large spot size) in the extreme iris periphery to contract the iris stroma between the site of the burn and the angle, physically pulling open the angle (Fig 1).[1-5] ALPI is extremely useful in reversing an attack of acute angle-closure (AAC), either as a primary measure or when systemic medications fail to control intraocular pressure (IOP).

Indications

Acute angle closure (AAC)

An attack of AAC that is unresponsive to medical therapy and in which corneal edema, a shallow anterior chamber, or marked inflammation precludes immediate laser iridotomy, or which is unresponsive to successful iridotomy, may be broken with ALPI.[1,6-7] Circumferential treatment of the iris opens the angle in those areas in which there are no peripheral anterior synechiae (PAS). All published series have reported virtually 100% success. In a prospective study of ten eyes with medically unbreakable attacks of two to five days' duration, mean pre-laser IOP was

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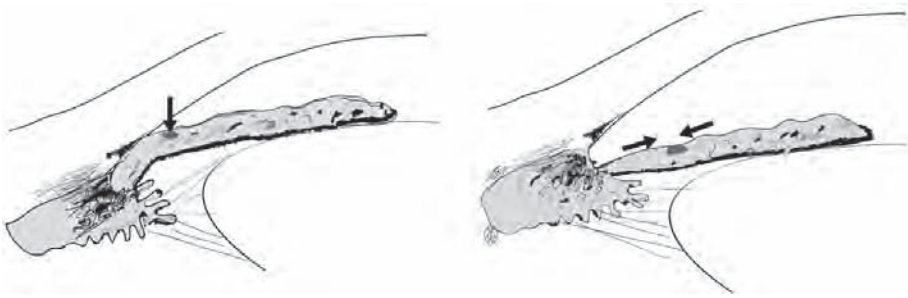

Fig. 1. Schematic diagram illustrating how ALPI contracts the peripheral iris stroma, creating a space between the anterior iris surface and the trabecular meshwork, and thereby opening the angle.

54.9 mmHg and two to four hours post-laser IOP was 18.9 mmHg.[6] Even when extensive PAS are present, the IOP is usually normalized within an hour or two. The effect lasts sufficiently long for the cornea and anterior chamber to clear so that iridotomy can be performed.

ALPI may also be used as primary therapy in eyes with AAC, either with or without preliminary treatment with topical medications.[1,6, 8-12] Immediate ALPI for acute attacks after initial treatment with 4% pilocarpine and 0.5% timolol has been reported successful when given over both 180 degrees[9] and 360 degrees of the peripheral iris.[8]

A more recent randomized controlled trial directly compared ALPI against conventional systemic IOP-lowering medications as the primary treatment for AAC not amenable to immediate laser peripheral iridotomy.[11] Consecutive patients with their first presentation of AAC, with IOP greater than 40 mmHg, were recruited. The AAC eye of each consenting patient received topical pilocarpine (4%) and topical timolol (0.5%). The patients were then randomized into one of two treatment groups. The ALPI group received immediate ALPI under topical anesthesia. The Medical Treatment group was given intravenous acetazolamide, followed by oral acetazolamide, until IOP normalized. Intravenous mannitol would also be administered to the latter group if the presenting IOP was higher than 60 mmHg.

There were no significant differences between the treatment groups in age, duration of attack, and IOP at presentation. The mean IOP in the ALPI-treated group was reduced from 60.8 ± 11.6 mmHg at presentation, to 30.8 ± 9.5 mmHg at 15 minutes, and 20.6 ± 10.1 mmHg at one hour after ALPI. The ALPI-treated group had significantly lower IOP than the medically treated group, at 15 minutes, 30 minutes, and 1 hour after the start of treatment (Fig. 2). The duration of attack did not affect the efficacy of ALPI in reducing IOP in AAC. No serious laser complications occurred.

It was concluded that ALPI was significantly more effective than conventional systemic medications in reducing IOP in AAC not suitable for immediate laser peripheral iridotomy. ALPI was proposed as a safe and more effective alternative to conventional systemic medications as the primary treatment of AAC.[11,13] In the mid-term results, there were no statistically significant differences in mean IOP and requirement for glaucoma drugs between APAC eyes treated with ALPI and systemic

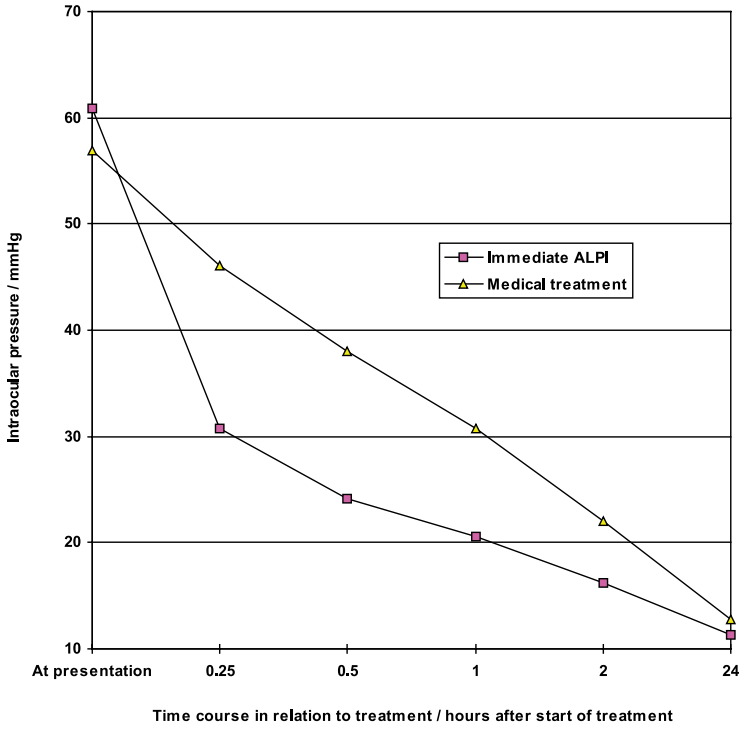

Fig. 2. Randomized controlled trial comparing argon laser peripheral iridoplasty (ALPI) against conventional systemic intraocular pressure (IOP)-lowering medications as first-line treatment of acute primary angle-closure (APAC) – Profiles of mean IOP before and at various time points after commencement of treatment in the two treatment groups.[11]

medications.[14] It should, however, be stressed that since ALPI does not eliminate pupillary block, a laser peripheral iridotomy is still required in AAC eyes.

It is believed that ALPI mechanically pulls open the closed drainage angle, and thereby allowing aqueous to escape through the trabecular meshwork. This hypothesis was supported by ultrasound biomicroscopy study.[8] ALPI may, at least in theory, reduce the chance of PAS formation by reducing the duration of appositional angle-closure. This may potentially help reduce the chance of subsequent progression to chronic angle-closure glaucoma (CACG).

Chronic angle closure (CAC)

Eyes with chronic angle-closure (CAC) and a combination of PAS and appositional closure can respond to ALPI with opening of the appositionally closed portions of the angle. In one study, ALPI was performed on 11 eyes with IOP > 20 mmHg despite maximal medical therapy.[15] All eyes responded with lowering of IOP initially and at six months, seven eyes remained controlled, while four required trabeculectomy. In a large study comparing the long-term clinical course in eyes with CAC with

optic nerve head and visual field damage in patients in New York and Singapore, 31.3% of the New York eyes went on to filtering surgery compared to 53.0% of the Singapore eyes.[16] Seven eyes in the New York group underwent ALPI, after which IOP were controlled and surgery was not required.

If extensive PAS are still present after ALPI, goniosynechialysis (GSL) may be performed. In this procedure, PAS are surgically stripped from the angle wall to restore aqueous access to the trabecular meshwork. GSL is believed to be useful only if the PAS has been present for less than one year.[17] It is effective both alone and in conjunction with other surgical procedures (such as cataract extraction).[18-20] It is also effective when only the inferior 180 degrees of PAS is re-opened.[19-20] In eyes having had acute angle-closure with PAS, combined cataract extraction and goniosynechialysis is more effective than goniosynechialysis alone.[21] Argon or diode laser peripheral iridoplasty can be used postoperatively to further flatten the peripheral iris and prevent synechial reattachment.[19-20]

Plateau iris syndrome

ALPI which compresses the iris root is successful long-term in eyes with plateau iris syndrome (Fig. 3).[22-24] In one series of 23 eyes with a mean follow-up of 79 months, the angle in 20 eyes (87.0%) remained open throughout follow-up after only one treatment.[24] In three eyes, there was gradual re-closure of the angle years later, but they were readily reopened and maintained open by a single repeat treatment. No filtration surgery was necessary in these patients during follow-up.

A combined laser technique, with ALPI and sequential laser peripheral iridotomy in one sitting, has been proposed as a primary treatment for eyes with plateau iris syndrome.[23]

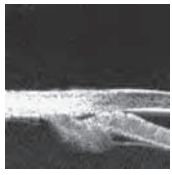

Fig. 3A. Ultrasound biomicroscopy (UBM) image of an eye with plateau iris syndrome after laser peripheral iridotomy.

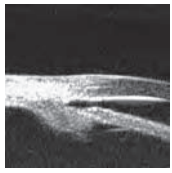

Fig. 3B. Ultrasound biomicroscopy (UBM) image of the same eye with plateau iris syndrome after laser peripheral iridotomy and argon laser peripheral iridoplasty (ALPI) to open up the drainage angle.

Angle closure related to size or position of the lens

Angle-closure caused by an enlarged lens or pressure posterior to the lens is not often responsive to iridotomy, although a component of pupillary block may be present and should be eliminated by iridotomy. These include such types of angle-closure as ciliary block, lens intumescence, anterior subluxation of the lens, or anterior lens displacement secondary to ciliary body edema from panretinal photocoagulation or scleral buckling procedures. In these situations in which the angle remains appositionally closed after laser iridotomy, the apposition can often be partially or entirely eliminated by iridoplasty.[3-4]

ALPI is also effective as a primary treatment to break attacks of acute phacomorphic angle-closure.[1,25-26] In a recent study, ten consecutive patients with acute phacomorphic angle-closure and IOP > 40 mmHg were recruited. Each patient received topical atropine (1%) and timolol (0.5%), and immediate ALPI as initial treatment. After ALPI, the mean IOP was reduced from 56.1 ± 12.5 mmHg to 37.6 ± 7.5 mmHg at 30 minutes, 25.5 ± 8.7 mmHg at 120 minutes, and 13.6 ± 4.2 mmHg at one day. All 10 patients had uncomplicated cataract extraction soon after ALPI. No complications from the laser procedure were encountered.[25]

In acute phacomorphic angle-closure, breaking the attack with ALPI may allow the inflammation and folds in Descemet's to clear, facilitating cataract extraction.

Adjunct to laser trabeculoplasty

If the angle is narrow because of plateau iris configuration or angle-crowding, ALPI can retract the iris away from the trabecular meshwork, widening the area to permit trabeculoplasty burns to be placed.[2,27]

Technique

Pre-treatment measures

The procedure is performed on an outpatient basis under topical anesthesia using an Abraham lens. Prior to treatment, 2% or 4% pilocarpine is applied topically to stretch the iris maximally from the iris root to the pupillary border. Apraclonidine or brimonidine is administered before and after the procedure to prevent a laser-induced IOP rise.

Laser parameters

The argon laser is set to produce contraction burns (500 μm spot size, 0.5 to 0.7 second duration, and, initially, 240 mW power). With the contact lens in place, the beam is aimed at the most peripheral portion of the iris possible (Fig. 4). It is useful to allow a thin crescent of the aiming beam to overlap the sclera at the limbus. The patient may be directed to look in the direction of the beam in order to achieve more peripheral spot placement.

The foot pedal should be pressed for the entire duration of the burn, unless bubble formation and pigment release occur. The contraction effect is immedi-

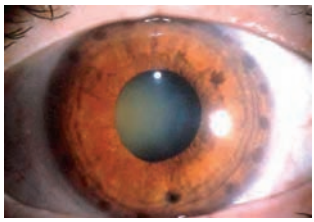

Fig. 4. Slit lamp photograph of an eye with plateau iris syndrome previously treated with argon laser peripheral iridoplasty (ALPI). The dark round laser marks could be clearly seen on the peripheral iris. (Courtesy of Prof. Robert Ritch of New York Eye and Ear Infirmary)

ate and usually accompanied by noticeable deepening of the peripheral anterior chamber at the site of the burn. A lack of visible contraction and deepening of the peripheral anterior chamber at any site is suggestive of too low a power or PAS. If bubble formation occurs or if pigment is released into the anterior chamber, the power should be reduced.

Treatment consists of placing approximately 20 to 24 spots over 360°, leaving approximately two spot-diameters between each spot and avoiding large visible radial vessels if possible. Although rare, iris necrosis may occur if too many spots are placed too closely together.

An extremely shallow anterior chamber and corneal edema, do not preclude peripheral iridoplasty. If necessary, glycerine may help clear the cornea temporarily to facilitate performing ALPI. If the anterior chamber is very shallow, laser applications should be timed enough apart so that heat generated can dissipate.

Other laser settings published for this type of burn, most commonly 200 μm, 0.l or 0.2 second duration and 200 mW power, often provide insufficient contraction and result in bubble formation or pigment liberation into the anterior chamber. When used through the angled mirror of a gonioscopy lens, they are more likely to result in stromal destruction or inadvertent damage to the trabecular meshwork.

When ALPI needs to be repeated because of recurrence of appositional closure at some point after the angle has been initially opened, it is possible to place the contraction burns further peripherally than had been initially possible.

Postoperative treatment

Immediately after the procedure, the patient is given a drop of topical steroid and apraclonidine or brimonidine. Gonioscopy should be performed to assess the effect of the procedure at a subsequent visit. Patients are treated with topical steroids four to six times daily for three to five days. Intraocular pressure is monitored postoperatively and patients treated as necessary if a post-laser IOP rise occurs.

Complications

A mild postoperative iritis is common and responds to topical steroid treatment, seldom lasting more than a few days. The patient may experience transient ocular irritation.

Because iridoplasty is often performed on patients with extremely shallow pe-

ripheral anterior chambers, diffuse corneal endothelial burns may occur. Endothelial burns may be minimized by placing an initial contraction burn more centrally before placing the peripheral burn. This first burn will deepen the anterior chamber peripheral to it, allowing the more peripheral burn to be placed with less adverse consequences. In virtually all cases, the endothelial burns disappear within several days and have not proved to be a major complication.

A transient rise in intraocular pressure can occur as with other anterior segment laser procedures. Pigmented burn marks may develop at the sites of laser applications in some eyes. These are generally of no serious consequences.[12] Iris atrophy may rarely develop,[12] and this can be avoided by using the lowest laser power to achieve iris contraction, and also by leaving untreated spaces between two laser application sites.

Need for re-treatment

The duration of the effect of the iridoplasty is variable. Long-term effectiveness is possible, but patients need to be followed closely for recurrence of the angle-closure, and on occasion, the patients may require re-treatment.

Conclusion

ALPI is a safe and simple out-patient laser procedure that effectively opens up appositionally closed portions of the drainage angle. Since it does not eliminate pupillary block, laser peripheral iridotomy is still indicated if pupillary block is present.

ALPI is now a viable alternative first-line treatment for AAC, in place of systemic IOP-lowering medications. It reduces IOP more rapidly than medications. Ongoing studies will tell whether ALPI can also reduce the rate of conversion to CAC after AAC.

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Trabeculectomy

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Introduction

Population-based prevalence studies have shown primary angle-closure glaucoma (PACG) to be common among Asians.[1,2] Despite the magnitude of the problem, the optimum timing of surgery for PACG is not well established, nor is the long-term efficacy of surgical therapy in controlling intraocular pressure (IOP).[1,3]

For acute PACG, however, a trabeculectomy can be considered if the presence of broad peripheral anterior synechiae (PAS) precludes the control of IOP on maximal tolerated medical therapy, despite a breaking of a relative pupillary block. For chronic PACG patients whose IOP remains elevated after patent laser iridotomy, a trabeculectomy also may be a rational option.[1] Gelber[4] and Playfair[5] have advocated early surgery in certain groups of patients, such as those presenting with severe glaucomatous optic nerve damage and visual field defects, and those showing more than 50% to 75% of angle-closure by PAS on indentation gonioscopy.

Since postoperative complications including flat anterior chamber and malignant glaucoma occur more often in PACG,[6-8] surgical indication should be considered carefully based on each individual case. In addition, more prudent consideration of surgical techniques is needed to prevent such potentially sight-threatening complications.

Surgical technique

Fixation suture

A superior rectus or corneal traction suture allows rotation of the globe inferiorly to bring the superior bulbar conjunctiva into view.

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Preparation of the conjunctival flap

The first procedure is usually performed slightly superonasally or superotemporally to preserve other areas of the eye for further glaucoma surgery. Either a limbus- or fornix-based conjunctival flap is made with non-toothed forceps and blunt scissors. Neither flap is superior to the other in terms of IOP reduction or surgical success rate; however, the character of the bleb is reported to be different in cases with open-angle glaucoma.[9-11] A limbus-based flap seems to produce more a localized and more cystic bleb, and a fornix-based flap generates a more diffuse and flatter one.

In this procedure, an incision to create a limbus-based flap is made 8 mm posterior to the limbus, and is extended parallel to the limbus. Tenon's capsule is next incised to the sclera. While the capsule is elevated from the sclera, the incision is enlarged circumferentially and anteriorly to allow an exposure of 4 to 5 mm of the limbal area. A tenonectomy does not seem to affect the surgical success rate.[12,13]

When a fornix-based conjunctival flap is created, the conjunctiva and Tenon's capsule are cut at the limbus, about 7 to 8 mm circumferentially. Then, blunt dissection under a conjunctival flap is carried out to expose the area for the scleral incision. A short, oblique relaxing incision at one side of the conjunctival flap may be made to improve scleral exposure.

Preparation of the scleral flap

After light cautery of bleeding vessels, the scleral flap with one-half to two-thirds of the scleral thickness, and a 3 to 4 mm length of square- or triangular-shaped flap is made with a sharp blade and toothed forceps. It is important to dissect the flap anteriorly, across the limbus, 1 to 2 mm into the clear cornea to ensure that the sclerostomy is performed in a position anterior to the scleral spur and ciliary body.

Differences in the shape or size of the scleral flap probably have little effect on surgical outcome.[14] Flap thickness may be very important for preventing excess filtration,[15,16] especially in ACG.[6] Hence, the flap should be made at least one-half of the scleral thickness with morphological uniformity.

Intraoperative application of an antimetabolite

Antimetabolites such as mitomycin C (MMC) or 5-fliorouracil (5-FU) are adjunctively used intraoperatively in order to reduce postoperative subconjunctival fibrosis.[17-20] The use of antimetabolites is well-known to be associated with a higher surgical success rate and a higher incidence of postoperative complications. Thus, the risk/benefit ratio should be considered in individual cases.

An application of 0.1 to 0.5 mg/ml solution of MMC or 50 mg/ml solution of 5-FU is made for one to five minutes using a soaked cellulose sponge placed over the episclera and under the scleral flap.[21] The conjunctival flap is draped over the sponge. After the application of antimetabolites, the sponge is removed and the entire area is copiously irrigated with balanced salt solution (BSS).

Paracentesis

Before opening the globe, a paracentesis is performed in the peripheral clear cornea with either a 30- or 26-gauge needle, or with a sharp point blade. In eyes with a shallow anterior chamber, the tip of the needle must be kept parallel to the iris plane in order to avoid iris or lens injury. The paracentesis site also can be used to reform the chamber with BSS at the middle and at the end of surgery.

Excision of an internal block (trabeculectomy)

A block of tissue (0.5 × 2 mm) at the corneoscleral junction is excised. Two radial incisions, 2 mm apart, are made with a sharp blade, starting in the clear cornea and extending 0.5 mm posterior to the initial incision. A blade or Vannas scissors are used to remove a rectangular piece of tissue. Alternatively, an anterior corneal incision parallel to the limbus is first made with a sharp blade, and a Kelly or a Gass punch is then used to excise the tissue. In order to minimize complications such as bleeding, cyclodialysis, inflammation, the trabeculectomy should be performed anterior to the scleral spur. Care should be taken in eyes with broad anterior synechia.

Peripheral iridectomy

The iris is grasped and lifted gently with toothed forceps, and iridectomy is performed with scissors. A broad, peripheral iridectomy that is wider than the sclerostomy helps to avoid iris incarceration in the internal ostium. When the iris tissue is entrapped at the sclerostomy site after iridectomy, irrigation into the site or gentle stroking toward the cornea from the limbus can free the remaining tissue.

Scleral flap closure and assessment of filtration

Initially, the scleral flap is reapproximated to the scleral bed with two interrupted 10-0 nylon sutures placed at both corners in the case of a rectangular flap or with one suture at the top in the case of a triangular flap. Additional sutures can be placed for controlling the outflow. During the suturing of the scleral flap, the anterior chamber is reformed with BSS through the paracentesis track, and the flow around the scleral flap is observed. The adequacy of the outflow can be checked by depressing the bed of the scleral flap gently with forceps. If the flow seems excessive or the anterior chamber shallows, additional sutures can be used. Interrupted suture knots are rotated onto the scleral side to avoid the creation of a conjunctival buttonhole.

Flat anterior chamber and malignant glaucoma occur more often in subjects with PACG as compared to ones with other types of glaucoma.[6-8] To avoid these complications, the scleral flap should be sutured more securely in patients with PACG.[6]

Conjunctival flap closure

A limbus-based conjunctival flap is closed with double or single running sutures created with 10-0 nylon. To avoid creating conjunctival holes surrounding the suture material, a tapered needle is suitable for conjunctival closure. Closure should be watertight to prevent the leaking of wounds.

For a fornix-based flap, two 10-0 nylon sutures or a mattress suture at the edges of the incision can be used to anchor the conjunctiva to the cornea. The sutures are tied tightly, advancing the cut edge of the conjunctiva 2 to 3 mm over the cornea. Here, it is also essential to obtain a tight conjunctival-corneal apposition.

Elevation of the bleb and testing for leaks

BSS is injected through the paracentesis track to deepen the anterior chamber and elevate the bleb. The IOP is simultaneously monitored by a blunt instrument on the cornea, and the wound is tested for leaks. It is essential to ensure that the anterior chamber remains well-formed at the end of surgery in PACG for the prevention of flat chamber and aqueous misdirection.

Postoperative care

Postoperative medications

Topical medications used in the postoperative period include antibiotics, corticosteroids, and cycloplegics. Corticosteroids are used to suppress inflammation[22] and fibrosis, and their use is tapered after six to eight weeks. Cycloplegics should be used to treat PACG, as they maintain the anterior chamber, reduce the risk of aqueous misdirection, and relieve ciliary spasms.[6,8]

Digital massage

Digital ocular compression is applied through the upper lid on either side of the bleb with the eye in down-gaze, in order to elevate the bleb and reduce the IOP in the early postoperative period. However, care should be taken in cases of PACG.

Laser suture lysis

Laser suture lysis is performed when IOP is too high or the filtration bleb is flat. Suture lysis should be performed within the first two to three weeks in cases without the use of MMC, though it may be effective even seven to 21 weeks after surgery in patients treated with MMC.[23] Aggressive, early suture lysis is not recommended in PACG, and postoperative bleb titration should be performed cautiously. Gonioscopy must be performed prior to suture lysis to confirm that there is no tissue or clot occluding the inner sclerostomy site. A suture lysis lens (ex, Hoskins or Ritch lens) or a four-mirror goniolens is positioned over the flap to flatten the conjunctival bleb and obtain a clear view of the nylon suture.[24-26] A power setting

of 150 to 200mW at a duration of 0.1 to 0.2 second and a spot size of 50 um is used to cut the suture. Digital massage may be required to promote aqueous flow after suture lysis.

Postoperative 5-FU injection

In cases prone to early failure such as vascularized and thickened blebs, repeated subconjunctival injections of 5-FU (5 mg in 0.1 ml solution) are recommended during the first two to three weeks.

Early postoperative complications and treatment

Shallow anterior chamber with low IOP

Shallow anterior chamber with low IOP is one of the common complications that occur after trabeculectomy, and may results from a wound leak, ciliochoroidal detachment with reduced aqueous production, or overfiltration. The severity of a shallowing anterior chamber can be graded as follows.[27] Grade 1 is peripheral iris-cornea apposition, Grade 2 is iris sphincter-cornea apposition, and Grade 3 is lens-cornea or vitreous-cornea apposition. Grade 1 and 2 flat chambers usually reform spontaneously with time, responding to moderate interventions such as topical application of 1% atropine. Severe and sustained flat anterior chambers are uncommon. If unrelieved, they may lead to endothelial decompensation, cataract, and formation of synechiae. Balanced salt solution, air, or viscoelastics[28] can be injected into the anterior chamber for reformation.

Wound leak

A wound leak is one of the most common causes of a shallow anterior chamber with hypotony, and may result from conjunctival perforation during surgery or wound dehiscence. Treatment depends on the location of the leak and appearance of the bleb. Aqueous suppression with topical beta-blockers or oral acetazolamide may promote spontaneous healing by temporarily reducing aqueous flow through the fistula. For a small buttonhole with thin, cystic blebs, a large diameter soft contact lens,[29] Simmons shell,[30,31] or symblepharon ring[32] is often capable of sealing the leak mechanically, reforming the anterior chamber, and encouraging the heal of the buttonhole. However, the definitive therapy for an early postsurgical conjunctival wound leak or perforation is suture closure. The conjunctiva is closed using a tapered, noncutting, microvascular needle attached to a polyglactin or 10-0 nylon suture.

Ciliochoroidal detachment

Choroidal detachment often presents as a result of hypotony and leads to a decrease in aqueous humor production (Fig. 1). The incidence of detachment is reported to range from 1.5 and 50.0%, and detachment is more common in eyes with angle-

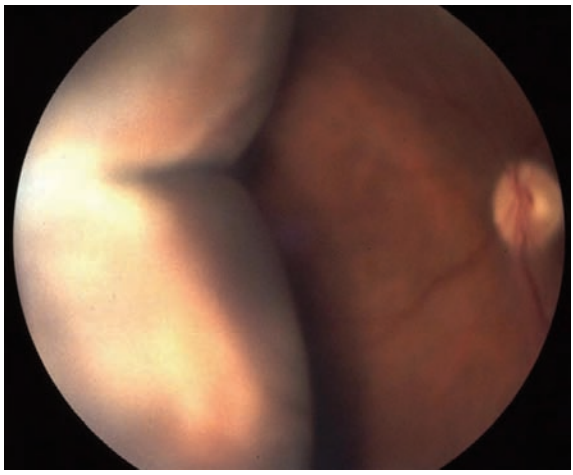

Fig. 1. Choroidal detachment. Fundus photograph showing choroidal detachment in a hypotonous eye.

closure glaucoma and eyes treated with MMC.[33-36] Choroidal detachment can appear as either as low or large-scale detachments that may compromise the visual axis when two detachments are kissing. Choroidal detachments often spontaneously resolve with time, or with atropine and steroid treatment to reduce inflammation.[37] However, suprachoroidal fluid needs to be drained from a sclerostomy site made 4 mm behind the limbus over the pars plana, in cases of kissing choroidal detachments, or in cases with Grade 3 flat anterior chamber.

Overfilteration

Excessive outflow associated with large bleb formation is sometimes observed after trabeculectomy, and may be due to a relatively insufficient resistance to aqueous flow (Fig. 2). This can be prevented by tight initial closure of the scleral flap with the option of sequential suture release or suture lysis. Excessive aqueous flow due to loose scleral flap suturing is mostly managed by observation with topical use of atropine and an additional external tamponade rather than surgical correction. However, earlier surgical interventions are required in eyes with angle-closure glaucoma that predispose the eye to aqueous misdirection syndrome compared to eyes with other types of glaucoma.[7]

Shallow anterior chamber with elevated IOP

Shallowing of the anterior chamber in the presence of an elevated IOP indicates that excessive filtration is not the cause of the shallow anterior chamber. In such cases, the shallow anterior chamber is caused by increased volume or pressure behind the lens-iris diaphragm. This may be caused by aqueous misdirection, pupillary block (rare when an iridectomy is present), or expansion of the choroids or suprachoroidal space by blood or effusion (may be detected ophthalmoscopically).

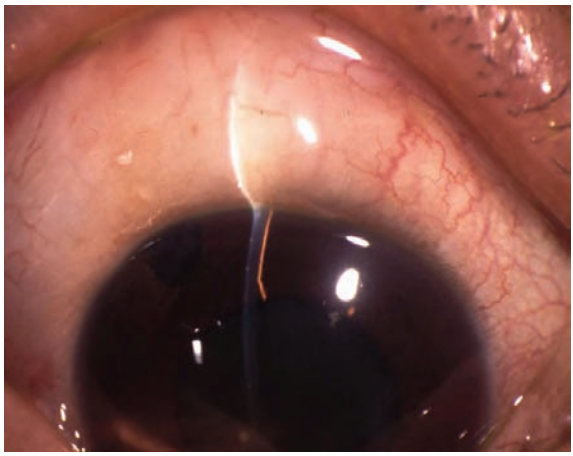

Fig. 2. Overfiltration. A large diffuse bleb nearly encircling the cornea exists in conjunction with shallow anterior chamber.

Aqueous misdirection

Clinically, aqueous misdirection is characterized as the presence of extreme shallowing of the peripheral and central anterior chambers simultaneously, or Glade 3 flat chambers, and elevated IOPs. Risk factors for this condition are pre-existing angle-closure glaucoma, shallow anterior chamber, and pseudoexfoliative syndrome.

The true mechanism of aqueous misdirection is unknown. Some initiating events such as shallowing of the chamber during trabeculectomy are thought to cause misdirection of the aqueous to circulate into or behind a vitreous body.[8] This leads to a cycle of increasing vitreous volume, and the enlarging vitreous body is unable to exchange aqueous across the hyaloid face at the junction of the zonules, ciliary processes, and vitreous face. This progressive vitreous redundancy results in progressive shallowing of anterior chamber and setting up a further cycle of angle-closure glaucoma.

Ultrasound biomicroscopy is useful for checking the posterior chamber structures, the presence of a pupillary block, or supraciliary effusion. Its use is essential to eliminate the possibility of pupillary block. If an iridectomy is not present or patent, one should be created immediately using a laser.

Medical treatment for aqueous misdirection is successful in about 50% of cases.[38,39] Vigorous use of cycloplegics as well as topical steroids and aqueous suppressant or osmotic agents for IOP reduction should be administered. Therapy may include argon laser treatment of visible ciliary processes, or Nd-YAG anterior hyaloidectomy and posterior capsulotomy in aphakic or pseudophakic eyes.[40,41] If these medical and laser treatments are not effective, surgical therapy is required. A pars plana vitrectomy with rupture of the vitreous face is one such approach. Occasionally, a lensectomy must be performed in combination with the vitrectomy in a phakic eye.

Normal anterior chamber depth with elevated IOP

Blockage of internal ostium

This occlusion is usually related to surgical complications such as incarceration of the iris, vitreous, ciliary body, or ciliary processes, or occlusion of the ostium with blood or fibrin. If elevated IOP is believed to be due to fibrin, injection of tissue plasminogen activator may be considered.[42] Argon and Nd-YAG lasers have been reported to open internally-blocked sclerostomy sites successfully.[43]

Encapsulated bleb

An encapsulated bleb, Tennon cyst, or localized cystic bleb develops in approximately 3.6 to 28% of eyes,[44-54] typically during the first eight weeks following surgery. Reported risk factors for encapsulation are uveitis, prolonged preoperative use of topical beta-blockers and parasympathomimetics, prior argon laser trabeculoplasty, prior incisional surgery, history of encapsulated bleb in the contralateral eye, and the use of a limbus-based conjunctival flap.[45-47,49,51,53] Many encapsulated blebs may resolve spontaneously, respond to intensive topical steroid therapy and digital massage, or be controlled with aqueous suppressant. If those therapies do not resolve the problem, needling with 5-FU or surgical revisions can be considered.[44,48,50-52,54]

Late postoperative complications and treatment

Late bleb leaks

The incidence of a late leaking bleb varies from 0 to 3% without antimetabolic agents,[35,55,56] 1.7 to 3.2% with 5-FU,[35,55-57] and 1 to 32% with MMC (Fig. 3).[55,57-59] Late leaking blebs may be accompanied by an increased risk of bleb-related infection and hypotony maculopathy, and are often recalcitrant to therapy. Treatment options include observation with topical antibiotics, use of aqueous suppressants to reduce flow, patching, bandage contact lenses,[29] cyanoacrylate tissue adhesive,[60] fibrin glue,[61] intrableb injection of autologous blood,[62] suture closure, and surgical revision with a sliding conjunctival flap,[63] conjunctival free graft,[64] or amniotic membrane.[65]

Chronic hypotony

The incidence of chronic hypotony (Fig. 4) is higher after trabeculectomy with 5-FU or MMC than trabeculectomy without adjunctive antimetabolites. Risk factors for the development of maculopathy associated with hypotony are young age[66] and myopia.[66,67]

When visual loss is accompanied by maculopathy, subconjunctival injection of blood or surgical revision of the scleral flap should be considered in order to increase IOP.

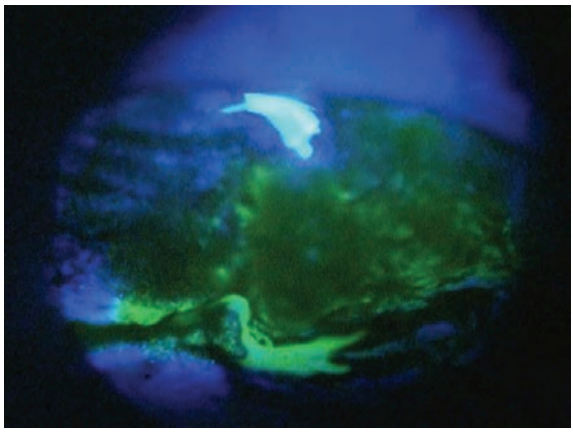

Fig. 3. Leaking bleb and positive Seidel test. Seidel test is performed by instilling 2% fluorescein onto the bleb and subsequent observation under cobalt-blue light. The fluorescein became diluted by aqueous leaking from the bleb.

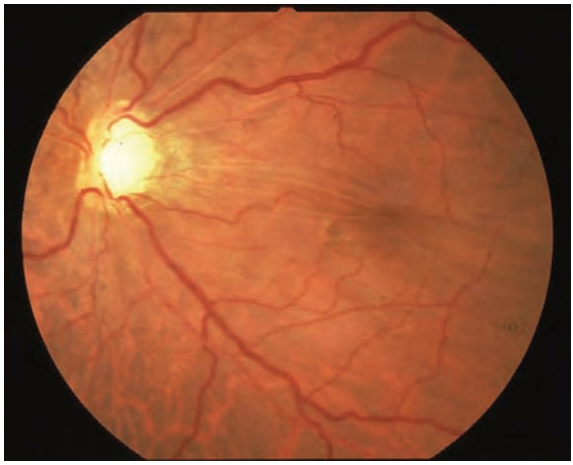

Fig. 4. Chronic hypotony. Retinal folds exist throughout the macula (hypotony maculopathy).

Bleb-related infection

This early postoperative infection results from the entry of bacteria into the eye at the time of surgery. On the other hand, late bleb-related infection can occur months to years after surgery, and is thought to involve the migration of bacteria through the bleb wall as the route of infection (Fig. 5). Clinical diagnosis is based on the sudden onset of pain, conjunctival injection localized to the bleb region, bleb purulence, and associated intraocular inflammation. Reported risk factors are thin-walled blebs, the presence of bleb leakage or oozing, bleb located inferiorly, conjunctivitis, blepharitis, contact lens wear, young age, diabetes mellitus, and a

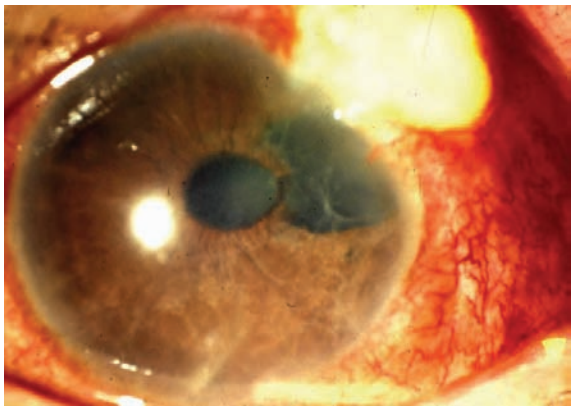

Fig. 5. Bleb-related infection. Exudative discharge can be seen on the bleb with an anterior segment cellular reaction.

compromised immune system.[68-71] Antimetabolites increase the incidence of postoperative bleb-related infection to a level that has been estimated to be as high as 5.7%.[68-71]

When bleb infection occurs without intraocular involvement, intensive topical treatment with wide-spectrum fortified antibiotics should be instituted. For bleb infection with mild anterior segment cellular reaction, intensive topical treatment with fortified antibiotics, periocular injection of antibiotics, and infusion of antibiotics may suffice. However, the patient should be watched carefully for evidence of vitreous involvement, which may occasionally occur. A swab of the conjunctiva over the bleb and anterior chamber tap should be performed for Gram staining and culture sensitivity prior to the initiation of antibiotic therapy. If a hypopyon is present or the vitreous is involved, a vitreous tap should also be performed. In such cases, vitreous aspiration or vitrectomy, and an intravitreal injection of antibiotics are necessary.

Cataract

The reported incidence of cataract progression after trabeculectomy varies from 2 to 30%.[72-75] Risk factors for progression are a flat or shallow anterior chamber after surgery, prolonged hypotony, older age, administration of topical or systemic steroids, preexisting cataract, and use of antifibrotic agents such as MMC and 5-FU.[72-75]

Efficacy of trabeculectomy

Sihota *et al.*[3] underwent trabeculectomy without MMC for PACG patients whose IOP remained higher than 21 mmHg despite a prior iridotomy. In 18 of 24 (75%) eyes, IOP was maintained at lower than 21 mmHg without any medical therapy. The mean IOP was reduced from 25.2 mmHg at baseline to 14.9 mmHg at six years, and no significant difference was found in the mean deviation and corrected

pattern standard deviation between the baseline and six-year values. Wilson[76] investigated the course of conventional trabeculectomy without antimetabolites in eyes with chronic PACG, and found that 80% of 112 eyes had an IOP of < 21 mmHg at the end of a 7-year follow-up. However Akafo *et al*.[77] reported that 45% of 20 eyes with chronic PACG that underwent trabeculectomy without antimetabolites required additional medication to control IOP within a 3.2-year period. Aung *et al*.[78] analyzed the results of trabeculectomy performed for two groups with acute PACG. In the group that responded to medication, IOP decreased to less than 22 mmHg, and trabeculectomy was performed for underlying chronic ACG. In this group, IOP < 21 mmHg was achieved in 21 of 24 patients (87.5%) without the use of medication, and in 24 patients (100%) given medications. In the other group that did not respond to medication, however, success in IOP control was obtained in 18 of 32 patients (56.2%) without medication and 21 of 32 patients (65.6%) with medication. In addition, 31.3% of patients in this group encountered early postoperative complications such as shallow anterior chamber. It was concluded that trabeculectomy may not be the procedure of choice in medically-unresponsive cases of acute PACG. Another study[79] detected postoperative shallow anterior chamber and medically-uncontrolled acute PACG (inflamed eye) as risk factors for surgical failure of trabeculectomy with MMC. In this study, surgical success was obtained in 96.9% of eyes with chronic PACG and in 86.8% of eyes with acute PACG.

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Goniosynechialysis

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Introduction

Angle closure is an anatomic disorder of the eye which is most commonly caused by relative pupillary block. Although iridectomy/iridotomy is considered to be the definitive treatment, up to 52% of patients with primary acute angle closure continue to have elevated intraocular pressure (IOP) requiring glaucoma medications postoperatively (residual angle closure).[1-5] The incidence of residual angle closure is even higher in patients who have had prolonged angle closure prior to the iridectomy.[6,7]

Postoperative IOP control depends on the amount of trabecular meshwork damage and extent of peripheral anterior synechiae (PAS). Proliferation of iris tissue into the trabecular spaces leading to irreversible changes of the meshwork will eventually occur if the PAS remain untreated.

There is a direct but non-linear relationship between IOP and degrees of synechial closure.[8] The IOP is usually elevated when >180° of the angle is closed by the PAS.[9] When > 270° of the angle is closed, medical therapy is usually ineffective and filtering surgery becomes necessary.[9] Nevertheless, filtering surgery has several potentially serious complications which are more common in eyes with angle-closure.[10] Flat anterior chamber and malignant glaucoma occur more frequently.[10] The routine use of antifibrotic agents increases postoperative endophthalmitis and bleb leaks. In addition, filtration is subjected to closure by the healing process and the success rate decreases over time. A far more logical approach is to eliminate the PAS and restore the trabecular function prior to the irreversible ultrastructural changes. *Filtration through the natural pathway should be more physiologic and reliable than the artificial pathway of trabeculectomy.*

Argon laser iridoplasty will open an appositionally closed angle, but will not eliminate PAS. Goniosynechialysis is a surgical procedure designed to strip the synechiae from the angle wall and restore the trabecular outflow. Shaffer first described the procedure by using a cyclodialysis spatula and intraoperative goni-

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oscopy.[11] However, collapsed anterior chambers and uncontrolled intraoperative hemorrhage made the procedure unpopular. Chandler and Simmons[12] proposed anterior chamber deepening as a diagnostic and a therapeutic procedure for the unresolved acute angle-closure. Nevertheless, this procedure does not eliminate extensive or long-standing PAS. Most PAS are strongly established and resist to these gentle efforts.[9] Campbell and Vela[9] described a technique employing a viscoelastic to maintain the anterior chamber and control hemorrhaging, while using an irrigating spatula to separate the PAS (Fig. 1). The procedure was successful in 80% of eyes with minimal complications if the PAS had been present for less than one year. Later studies have confirmed the effectiveness of the procedure in reducing PAS and improving IOP control.[13-21] A study has shown an increase in the tonographic outflow facility following removal of the synechiae.[14] The procedure is effective in removal of the synechiae not only in primary angle-closure but also in secondary angle-closure following vitreoretinal surgery[15] or failed filtering surgeries.[17] Furthermore, the procedure spares the conjunctiva for a future filtering surgery, if needed.

The success of the procedure depends not only on the preoperative duration but also the recurrence of the PAS. Although pupillary block has been eliminated by iridectomy, angle-closure can continue if other non-pupillary block mechanisms coexist and share a role in the pathogenesis. It has been shown that nearly 60% of the patients with a successful surgical iridectomy[22] or 38% with laser iridotomy still have a positive dark room prone provocative test.[23,24] Recurrent attacks and further angle-closure have been reported in both the attacked eyes and the fellow eyes.[5,6,25-28] Factors contributing to the reformation of PAS are early fibrinous postoperative inflammation, plateau iris configuration and the presence of an enlarged or anteriorly situated lens. Cataract formation progresses rapidly following an acute attack.[1] A thickening cataractous lens would crowd the anterior chamber and force the iris back against the trabecular meshwork.

Substantial increases in anterior chamber depth and angle width following cataract extraction with intraocular lens (IOL) implantation have been demonstrated in eyes with angle-closure.[29-31] The narrower the preoperative anterior chamber angle, the greater the postoperative angle widening. Whereas iridolenticular contact was observed in a phakic eye, there was no iris and IOL contact in a pseudophakic one. The iris plane shifted backward, deepening the central anterior chamber by approximately 850 μm. Preoperative biometry performed in a series of 52 eyes of 48 consecutive Thai middle-aged patients who had developed acute angle-closure glaucoma within 6 months showed that average natural lens thickness and central anterior chamber depth were 4.83 mm and 1.8 mm respectively.[32] Since the current IOL (PMMA, silicone, acrylic) thickness in the 20-25 D power ranges from 0.75 mm to 1.42 mm. Replacement of the natural lens with the IOL provided up to 4 mm more axial distance within the anterior chamber, or almost a threefold increase in the central anterior chamber depth. Gaining more space in the anterior segment eliminated angle crowding and appositional closure. In addition, anterior chamber deepening with a viscoelastic during IOL implantation might break recently-formed delicate synechiae.

Several studies have shown that extracapsular cataract extraction (ECCE) with IOL implantation is effective in opening the angle and controlling IOP in refractory angle-closure glaucoma.[33-37] Phacoemulsification is also highly effective in patients with angle-closure glaucoma[38,39] and has several advantages over ECCE. The pro-

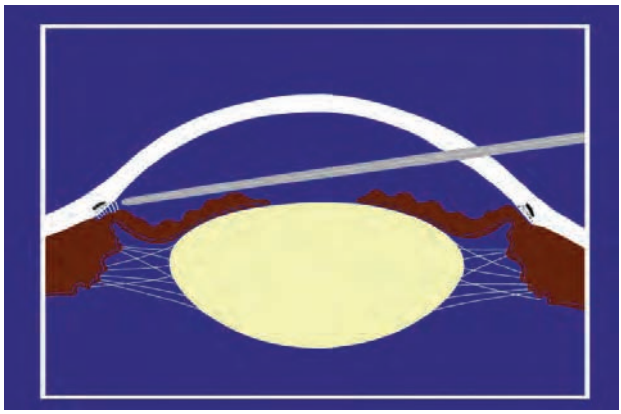

Fig. 1. Goniosynechialysis. A blunt-tipped spatula is inserted into the anterior chamber filled with a viscoelastic. The synechiae are precisely stripped from the angle wall at the point of adhesion by pushing the spatula posteriorly.

cedure offers a higher success rate in removing of the lens with less inflammation and fewer complications. In addition, the temporal clear corneal approach spares the superior conjunctiva for a possible filtering surgery. However, up to 32% of the patients still had persistent PAS and required long-term treatment with glaucoma medications after lens removal and IOL implantation.[23,39]

We performed phacoemulsification and IOL implantation in 39 eyes of 37 patients who developed primary acute angle-closure within 4 months and had persistent IOP elevation following the laser treatment. At six weeks postoperatively, 22 (56.4%) had IOP < 21mmHg without medications. Thirteen of the 17 eyes with IOP > 21 mmHg and PAS >180° underwent successive GSL. Postoperatively, 10 eyes had controlled IOP without medications. This suggests that although phacoemulsification and IOL implantation is effective in reducing IOP and PAS in patients with residual angle-closure, GSL further improves the success by eliminating the need for glaucoma medications. Only appositional closure or recently-formed PAS can be separated during the lens removal but not the firmly established synechiae.

GSL becomes more effective when performed after lens removal. An increase in the anterior chamber space provides an ample room to perform the procedure and decreases the chance of synechial reformation. Combined phacoemulsification and GSL (phaco-GSL) has been shown to be safe and highly effective in controlling the IOP and decreasing PAS in > 90% of 52 eyes that developed acute angle-closure within six months and had persistent IOP elevation following the laser treatment.[32, 40, 41] Postoperative IOP was reduced to the low to mid-teens regardless of the preoperative level. Recurrence of the PAS, although uncommon, might occur during the first three months. The success of phaco-GSL have been stable since the third postoperative month for up to fourteen years, providing a long-lasting or even permanent cure.

Indications

GSL is best for patients who have had a previously normal trabecular meshwork that has recently developed PAS on the basis of acute or chronic angle-closure, surgical procedures such as cataract extraction and penetrating keratoplasty, or trauma. Patients with acute angle-closure should have uncontrolled pressure and persistent synechial closure following successful laser iridotomy and peripheral iridoplasty. The extent of PAS should be >180°and correlates with the IOP level. If not, an open-angle mechanism may coexist and makes the prognosis unfavorable. The shorter the duration of synechial closure, the better the prognosis. However, a postoperative fibrinous anterior chamber reaction commonly occurs if the operation is performed during the first four weeks after the acute attack. The optimal timing for the operation is suggested at week six after the acute attack when the eye becomes quiet.[32]

Contraindications

GSL is contraindicated in patients who are likely to have anatomic changes of the trabecular meshwork from long-standing PAS. Patients with congenital angle anomalies and secondary angle-closure following uveitis or membranous pulling from neovascularization, iridocorneal endothelial syndrome or posterior polymorphous dystrophy are poor candidates.

Preoperative evaluation and treatment

The extent of PAS must be evaluated and correlated with the level of IOP. The duration of the PAS must be determined. Glaucomatous cupping should suggest long-standing PAS from previous subclinical attacks despite a history of a recent acute attack. Ultrasonic biometry performed by immersion technique gives a more accurate measurement than the conventional method. Biometry is not only important for IOL power calculation but also for operative planning. Eyes with an extremely narrow anterior chamber depth < 1.8 mm or asymmetrical anterior chamber depth > 0.2 mm may have subclinical lens dislocation. A capsular tension ring, an IOL with suture loops for sclera fixation or anterior vitreous tapping may be necessary.

The eye should be treated with frequent steroids until quiet to prevent postoperative fibrinous reaction. Pilocarpine is useful for a responsive pupil but not a paralytic one. Intravenous mannitol may be considered in patients with very high pressure.

Surgical technique

A clear view of the angle structures is essential in performing GSL. A blind procedure not only induces iatrogenic injury to the trabecular meshwork but also the nearby ocular structures, which may result in uncontrollable intraoperative hemorrhage.

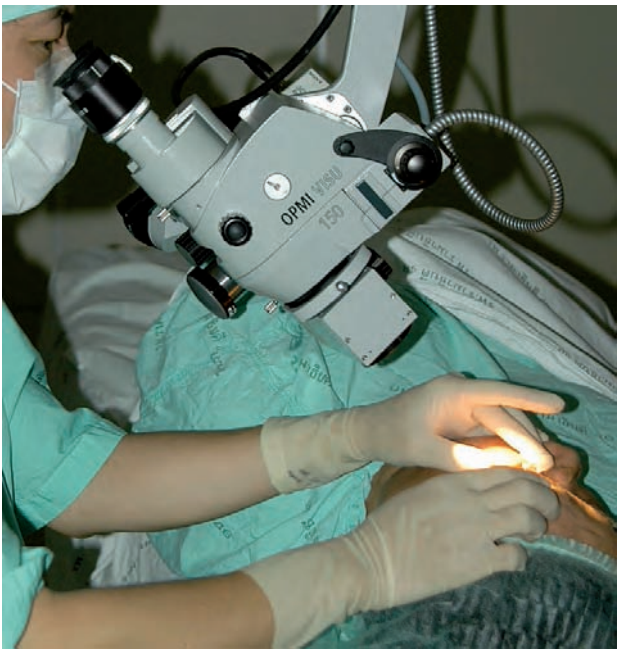

Fig. 2. Rotating the patient head and tilting the operating microscope allows a comfortable surgical approach. (The photograph was taken in a nonsterile manner for an illustration purpose.)

GSL can be performed with a surgical loupe equipped with a headlight for illumination. This technique provides convenient unrestricted range of surgical view. However, an operating microscope provides a much clearer view. The microscope should be easily tilted. The microscope equipped with straight eyepieces provides a direct visual axis view to which a beginning surgeon may find more accustomed than the angled one.

GSL can be performed either under topical, intraocular, peribulbar or retrobulbar anesthesia. Patients should be draped so that there is no restriction in changing head position. The head will be rotated to the left or right > 45° to allow the surgical view during the operation (Fig. 2). If head rotation is limited, the microscope must be tilted horizontally making surgical approach cumbersome. A large nose makes the nasal approach harder than the temporal one. If the surgery is performed under topical anesthesia, ocular movement away from the microscope will further assist the surgical approach.

Procedure

Corneal traction sutures may be used to mobilize and rotate the eye. However, these are unnecessary if the operation is performed through at least three corneal paracentesis tracks evenly spaced 120° apart. Three beveled paracentesis tracks directed to the opposite angle are made with a 15° sharp blade at 3-, 7- and 11-o'clock positions in the right eye and at 2-, 5- and 9-o'clock positions in the left.

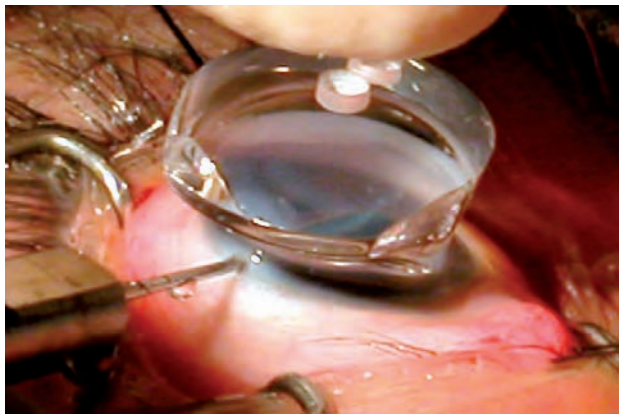

Fig. 3. GSL was performed under direct visualization through a Barkan lens. A blunt-tipped Swan knife was introduced into the anterior chamber and advanced toward the opposite angle.

An anterior deepening procedure is performed by depressing the posterior lip of a paracentesis track, allowing egress of the aqueous from the anterior chamber followed by depressing the limbus with a rounded muscle hook to facilitate aqueous flow from the posterior chamber into the anterior chamber. When the aqueous is completely released from both chambers, a viscoelastic is injected into the anterior chamber to maximally deepen the anterior chamber and raise IOP. Since the posterior chamber is empty, the iris will be stretched and bowed posteriorly (Fig. 1).

When combined with phacoemulsification, GSL should be performed after lens removal and IOL implantation. The phacoemulsification can be performed either through a temporal clear corneal or scleral incision. If performed through the scleral incision, complete hemostasis is necessary to avoid a blood layer between the goniolens and cornea surface that will significantly obscure the surgical view. Following IOL implantation, the viscoelastic is removed and acetylcholine chloride, 1:100 (Miochol-E, Novartis Ophthalmics, Inc., Duluth, GA) injected into the AC to constrict the pupil. However, the miotic is unnecessary in an eye with a paralyzed pupil.

Performing phacoemulsification in an eye with a shallow anterior chamber requires surgical skill. Inadvertent corneal damage or lens dislocation may occur. In addition, a vitreous tap is occasionally required to decompress the eye.

GSL will proceed only if the presence of PAS is confirmed by direct gonioscopy with a Barkan, Koeppe or Swan-Jacob goniolens. The handle of the latter may be more comfortable to manipulate. A pediatric goniolens fits into Asian eyes better than a larger child or adult goniolens. Following anterior chamber deepening with a viscoelastic, a blunt-tipped spatula or Swan knife is introduced into the anterior chamber and advanced toward the opposite angle (Fig. 3). The knife tip is then pressed against the most peripheral iris next to the point of angle adhesion and pressed posteriorly until the trabecular meshwork is exposed. Horizontal sweeping of the knife or excessive force that can cause hemorrhage or cyclodialysis is avoided. The procedure is repeated in adjacent areas through the three corneal paracentesis tracks until the entire angle is opened. Limited hemorrhage might occur but usually localizes in the viscoelastic and does not disperse to obscure the

surgical field. At the end of the procedure, the entire viscoelastic is removed and a large air bubble is injected to deepen the anterior chamber. Intraocular injection of acetylcholine chloride, 1:100 (Miochol-E, Novartis Ophthalmics, Inc., Duluth, GA) may be used to constrict the pupil and tighten the peripheral iris away from the angle if the iris sphincter is still reactive. Alternatively, surgical pupilloplasty can be performed to constrict the atonic dilated pupil. Intracameral tissue plasminogen activator may be considered if the procedure has to be performed in eyes with a very recent uncontrolled acute attack. Recent modification of the procedure includes intraoperative visualization with a double-mirror indirect gonioscopy lens,[42] a dental mirror[43] or intraocular fiber optic, scleral indentation[44] and separation of the PAS by pulling with iris microforceps.

Complications

Postoperative complications include a fibrinous aqueous reaction, transient IOP elevation, limited hyphema and photophobia from the paralytic mydriasis following the acute attack. A precise surgical technique, complete removal of the viscoelastic, and frequent steroids should prevent these mild complications. Surgical pupilloplasty or creating an artificial pupil may help alleviate the photophobia. The latter is achieved by performing a small 4 mm diameter central circular capsulorrhexis and leaving the lens epithelium beneath the capsular remnant intact. Late postoperative opacification of the anterior capsule remnant results in a second smaller pupil (Fig. 4).

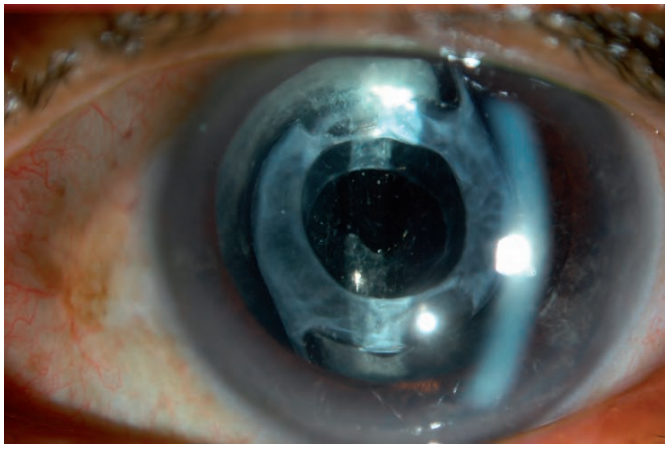

Fig. 4. Postoperative opacification of the unpolished anterior capsular remnant with a small capsulorrhexis-opening creates an artificial second pupil, behind the mydriatic natural pupil. The third pupil can also be created by performing an Nd:YAG laser posterior capsulotomy.

Postoperative management

Patients are treated with frequent topical steroids and antiglaucoma medications which will be slowly tapered within a month. Occasional aqueous release through the paracentesis tracks at the slit-lamp may be necessary if an uncontrolled IOP rise occurs on the first postoperative day. Gonioscopy typically reveals irregular pigmentation on the newly exposed trabecular meshwork and the angle wall (Fig. 5). Angle recession or a cyclodialysis cleft is an undesirable finding. Anterior chamber imaging by ultrasound biomicroscopy (Fig. 6) or optical coherence tomography (Fig. 7) should also reveal separation of the PAS and reopening of the angle when the procedure is successfully performed.

A B

Fig. 5. PAS following an acute attack (A). Postoperative gonioscopy disclosed opening of the angle with irregular pigmentation on the newly exposed trabecular meshwork and the angle wall (B).

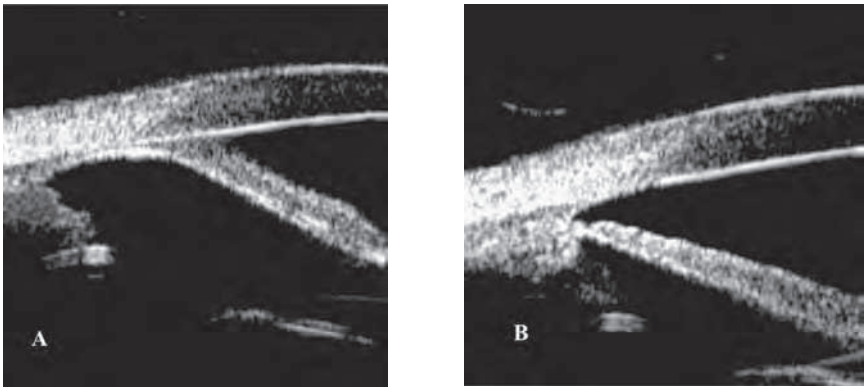

Fig. 6. Ultrasound biomicroscopy demonstrated preoperative PAS (A) and postoperative separation of the synechiae and widening of the anterior chamber angle (B).

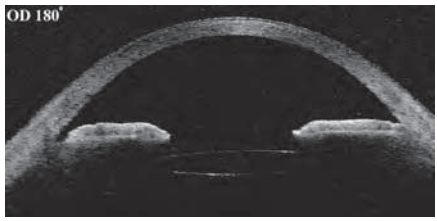

Fig. 7. Anterior segment optical coherence tomography scanned at 180° of the right eye following phaco-GSL revealed reopening of the temporal anterior chamber angle, but a remaining closure of the nasal angle.

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Phacoemulsification in patients with preexisting primary angle-closure glaucoma

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Introduction

The coexistence of angle-closure glaucoma (ACG) and a visually significant cataract is commonly encountered. The treatment of choice for ACG is surgical iridectomy or laser iridotomy. After iridotomy, it is difficult to determine the cause of an asymptomatic progressive VF defect or elevated intraocular pressure (IOP). Some studies[1,2] using UBM showed that most eyes with post-iridotomy residual angle closure had characteristics similar to plateau iris, including an anteriorly placed ciliary process and a narrow ciliary sulcus. Other studies with UBM have revealed that multiple mechanism ACG, due primarily to coexistence of pupillary blocking and plateau iris, is more common (54.8% in Chinese patients[3]) in ACG, residual angle closure would result in poor control of IOP even after complete dissolution of pupillary blocking by iridotomy. And an appositionally closed angle with previous iridotomy may result in recurrent acute angle closure or progression to the chronic ACG. In Asian eyes, the rate of progression from AACG to CACG can be as high as 58%.[4] Therefore, lens extraction may have a beneficial effect in these ACG eyes. Cataract operation is difficult with a miotic pupil, posterior synechia, PAS, shallow anterior chamber and pre-existing glaucomatous optic nerve damage. Risk and complications are correspondingly greater with cataract surgery in glaucomatous eyes than in non-glaucomatous eyes. As with any surgery, it is important to discuss the risks and benefits of cataract surgery alone for co-existing cataract and ACG.

Indication of cataract surgery

We do not consider that a cataract procedure alone can reliably control the pressure, but there often is merit to staging these procedures. The advantages of cataract surgery alone are: restoring vision promptly, single procedure, technically easiest,

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short surgery time, reducing operative and post-op complications related to the wound, facilities in post-op assessment of optic nerve and visual field, opportunity for glaucoma operation later if needed, improving IOP control, reducing glaucoma medications. Decreasing the number of medications needed for glaucoma control improves the patient's quality of life, encourages compliance, and reduces expenditures.

Disadvantages of cataract surgery alone include the early post-op IOP rise, especially in two to eight hours post-op. Etiology may be TM collapse in area of incision, pigment or cortical debris, breakdown of BAB, altered prostaglandin metabolism, toxic damage to TM, viscoelastic effect. The other disadvantage is reduced long-term IOP control, compared to combined surgery. We cannot depend on beneficial effect of cataract surgery for IOP control-variable: most eyes have long-term 1-3 mmHg decrease.[5-7]

Indications of cataract surgery alone are: the patient is a glaucoma suspect, the pressure is stable or reasonably well-controlled, the patient may be on one or two glaucoma medications and has no need for systemic carbonic anhydrase inhibitors (CAIs), the patient has had previous laser iridectomy or laser trabeculoplasty and the pressure is well controlled, the patient has had a previous trabeculectomy and has functioning filtering blebs, there is no significant glaucomatous visual field loss or cupping.

Mechanism of IOP lowering by cataract surgery

Today, phacoemulsification technique using small sutureless clear corneal incisions and in-the-bag implantation of foldable posterior chamber intraocular lenses (IOLs) eliminates the need for sutures and reduces the duration of operations significantly. Some studies[8-9] report that phacoemulsification in glaucomatous eyes improve glaucoma control by reducing IOP, or the number of required glaucoma medications, or even both. Although the relationship between cause and effect has often been observed, the nature by how cataract surgery influences IOP is not fully understood. Possible mechanisms include hyposecretion of aqueous humor, decreased resistance to aqueous humor outflow, and biochemical or BAB alteration. In patients with glaucoma, phacoemulsification can cause less damage to an already compromised outflow facility. Theoretically, the high fluid flow rate generated by phacoemulsification in a relatively closed space may wash out glycosaminoglican deposition in the trabecular meshwork (TM). In addition, it may cause mechanical effect to the TM, inducing cell division and renewed phagocytosis of meshwork debris. Based on these assumptions, IOP would be expected to be lower after phacoemulsification cataract extraction. Mathalone *et al.*[10] demonstrate that the possible mechanism by which phacoemulsification improves IOP control may be associated with decreased resistance to aqueous outflow, it may result from increased uveoscleral rather than trabecular outflow. The endogenous prostaglandin F^2 released postoperatively is thought to enhance uveoscleral outflow. Other possible mechanisms include the decrease in secretion of aqueous humor, promoted by increased traction on the ciliary body via the zonular fibers as a result of postoperative shrinkage of the lens capsule or of biomechanical BAB alterations after surgery.

Surgical approach

Preoperative preparation

It is often necessary for patients to discontinue certain medications prior to undergoing surgery.

Oral anticoagulants such as aspirin, warfarin and persantine should be discontinued, if possible. Effective anticoagulation can lead to hyphema from iris manipulation or even suprachoroidal hemorrhage from a precipitous drop in IOP. These medicines should not be discontinued if discontinuation poses a significant risk to the general health of the patient.

Aqueous suppressants should be continued until the day of surgery. This is especially true for patients with advanced glaucomatous optic neuropathy.

If the patient's history reveals prolonged use of miotics for glaucoma management, these agents should be stopped at one week interval before surgery and can be managed with alternative drugs. Miotics cause a breakdown in the blood-aqueous barrier (BAB) and promote inflammation.[11,12] Discontinuing miotics prior to intraocular surgery may facilitate pupillary dilation and decrease the amount of postoperative inflammation. In addition, the prolonged stimulation of the ciliary body and pupillary sphincter induced by miotics can be counterproductive when attempting to manage a shallow anterior chamber or malignant glaucoma. Inflammatory pupillary membranes, posterior synechiae, and pseudoexfoliation will be evidenced and surgical plans for the pupil can be considered. In preparation for surgery, pupil dilation is accomplished with three topical agents, a cycloplegic, a mydriatic, and a nonsteroidal anti-inflammatory drug (NSAID).

Epinephrine agents should be discontinued because of their effects on conjunctival vasculature.

We prescribe broad spectrum topical antibiotics for several days prior to intraocular surgery. We also use tobramycin as a preoperative wash.

Anesthesia

Retrobulbar, peribulbar, subconjunctival, or topical anesthesia may be considered for cataract surgery. Some clinicians believe that retrobulbar and peribulbar anesthesia should be avoided, if possible, because of its many associated complications. Now, we usually use topical or sub-Tenon's anesthesia. Because topical or sub-Tenon's anesthesia has little associated risk and has been shown to be efficacious and can be used in most of the patients who are able to cooperate.

Phacoemulsification in acute ACG

The benefits and risks of early phacoemulsification in ACG eyes and the best timing for such interventions should be evaluated. It would be undesirable to perform phacoemulsification if the eye were congested, the cornea were edematous, the anterior chamber were shallow, and the pupil were unable to be well dilated. When surgeries were performed in these eyes, the risks of developing complications would be higher. Pars plana vitreous tap can be considered before starting the phaco procedure in eyes with shallow anterior chamber and uncontrolled IOP. This

will bring down the IOP as well as deepen the anterior chamber.[13] The same vitreous tap procedure has been used for phaco with a crowded angle.[14] If the anterior chamber is too shallow, we can use a low-molecular weight viscoelastic (Viscoat) to protect the corneal endothelium from injury. In this way, cataract surgery may become safer and easier. The patient can also be highly sensitized to pain, probably as a result of recent inflammation. Excessive and exaggerated postoperative anterior chamber inflammation can occur, and intraoperative subconjunctival steroid injection would then be helpful.

After phacoemulsification,[15-18] IOP is reduced substantially and satisfactory IOP control is obtained in eyes with poorly controlled PACG. A quantitative evaluation of angle configuration using UBM revealed that the anterior chamber was 1.37 times deeper and the angle 1.57 times wider after cataract surgery.[19] A quantitative study of angle configuration using UBM, revealed that lens extraction has a more potent effect than iridotomy on deepening of the anterior chamber and widening of the angle.[20,21] Lens extraction is effective in resolving residual angle closure. Morphologic analysis using UBM revealed that the angle of plateau iris syndrome eyes opened after lens extraction, but that iridociliary apposition persisted. Lens extraction has the ability to lower IOP and would widen the angle even without structural alteration of plateau iris, because the lens plays a central role in the pathogenesis of PACG by means of its anatomic peculiarities, such as its increased thickness, relative anterior positioning and progression of its thickness.[22,23]

Small pupil management

We often find some small pupils in patients with PACG and coexistent cataract (Fig. 1). The main causes usually are: inflammation, long-term using of miotics, difficult dilation in the older patients, excessive iris manipulation leads to intraoperative miosis, poor pre-op dilation regimen, Intraoperative Floppy Iris Syndrome (IFIS). Our goals in management of the miotic pupils are to achieve an adequate pupil size (4-5 mm) and to preserve pupil reactivity and a normal pupil contour (Fig. 2). It is important that the pupil be large enough for our comfort level. A small pupil can impair a surgeon's visualization, which can make it difficult to see the lens capsule for a proper capsulorrhexis. Attempting to emulsify a cataract through an undilated pupil and shallowed anterior chamber can result in iris sphincter tear or trauma, bleeding, ruptured capsule, lost nucleus, and breach of the vitreous cavity.

Most of small pupils are result from posterior adhesions. So, release of posterior adhesions between the iris and the anterior lens capsule will result in an adequate pupil diameter for cataract surgery. Generally, synechiolysis can be achieved under viscoelastic protection with a blunted pinhead or spatula passed through the incision. In case of marked peripupillary membranes, we can strip them at the same time. A cohesive viscoelastic injected to the pupillary space will create a surgically adequate pupil following the procedures. If we could not acquire a pupil large enough, we also use other techniques.

Procedures that act directly on the sphincter will be required. Pupil stretching can be performed by placing two iris hooks through the wound and directing force both inferiorly and superiorly to physically open the pupil. The easiest method to achieve a desirable pupil is to stretch the pupil bimanually with two iris hooks through the wound to stretch the pupil sphincter inferiorly and superiorly. The same procedure is then performed nasally and temporally. Pupil stretch should

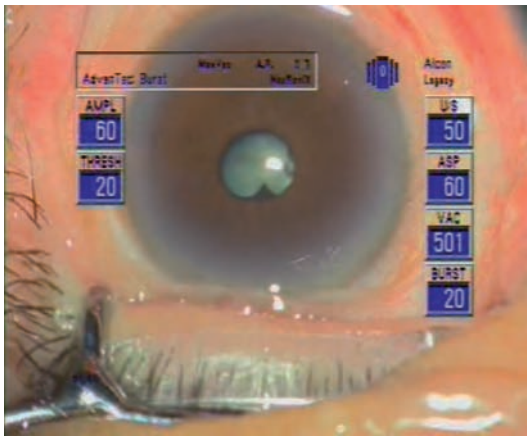

Fig. 1. Small pupil results from posterior adhesions in patient with PACG and coexistent cataract.

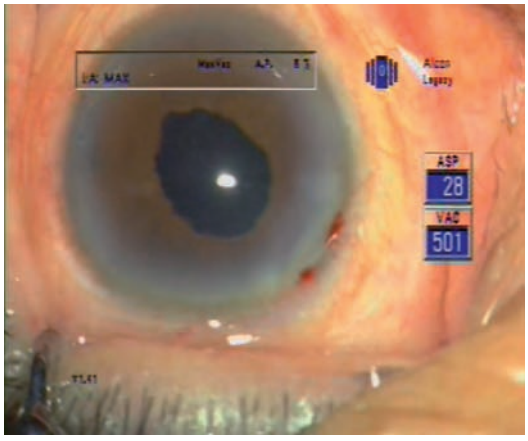

Fig. 2. Achieving phacoemulsification by an adequate pupil size (4-5 mm) and preserving the pupil contour as soon as possible.

be performed under viscoelastic to maintain a deep anterior chamber. The two instruments should be used steadily, slowly, simultaneously in order to ensure the tears are minimized. A stretch in one meridian may be adequate for most cases; occasionally, it is necessary to stretch in multiple meridians.

Another method to enhance the effect of the pupil stretch is to make a series of mini sphincterotomies with Vanass scissors.[24] If only very small incisions are made in the sphincter tissue, the pupil will function still and will be aesthetically appealing after surgery.

Iris hooks (Grieshaber, Schaffhausen, Switzerland) have also been used during cataract surgery.[25] The hooks are positioned parallel to the iris plane through small, short, peripheral paracenteses. Four small retractors are placed through the paracenteses at the 10, 2, 4, and 8 o'clock positions. The hooks should be used to create

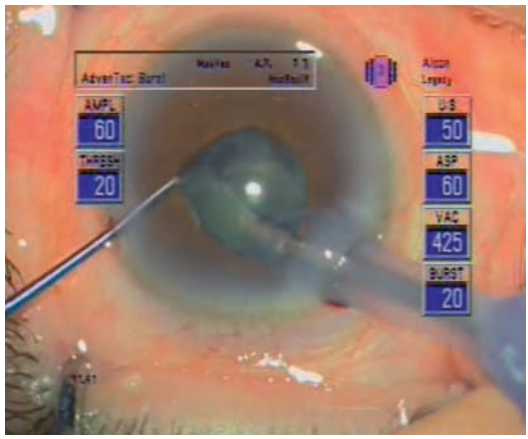

Fig. 3. Using a hook to move the iris and facilitate exposure for phacoemulsification and I/A.

an adequate size pupil rather than a very large pupil to prevent the occurrence of an atonic pupil postoperatively. Gradual enlargement of the pupil is preferred over rapid, sudden tugging.

The ring expanders has been designed to enlarge the miotic pupil without damaging the sphincter. These expanders are made of solid PMMA, silicone, or expansible hydrogel material. They can create the largest diameter pupil with the least tendency for sphincter tears.

If the pupil is not large enough, we can use second instrument (*e.g.*, a hook) to move the iris and facilitate exposure for capsulorhexis and phacoemulsification (Fig. 3). Cataract extraction then is performed in the usual fashion

Managing shallow anterior chamber during cataract surgery

Every attempt should be made to avoid excessive shallowing of the anterior chamber during surgery. Shallowing of the anterior chamber can lead to endothelial damage during the surgery. We advocate to use dispersive and cohesive viscoelastic agents simultaneously during surgery. First place dispersive viscoelastic agents, and then place cohesive viscoelastic agents just over lens. Dispersive viscoelastic agents are pushed up to coat the endothelium. When we perform CCC and insert IOL, cohesive viscoelastic agents maintain the anterior chamber space and bag. As soon as the phaco starts, the cohesive is aspirated and dispersive coating remains to protect the corneal endothelium. If the anterior chamber is too shallow, we can perform a puncture through pars plana beforehand. We can pump a little water from the anterior vitreous cavity. This procedure will bring down the IOP, as well as deepen the anterior chamber.

Managing hyphema during cataract surgery

Intraoperative anterior chamber hemorrhage most commonly occurs at the time of dealing with the miotic pupil. Bleeding is best treated with observation, as

most iris root/ciliary body bleeding spontaneously stops within minutes. Persistent bleeding may be treated with cohesive viscoelastic tamponade. It is unnecessary to vigorously irrigate the anterior chamber to remove small amounts of blood as most hyphemas clear spontaneously without adverse sequelae.

Postoperative pressure spikes

Various studies have shown that the peak post-op IOP is usually within four to eight hours after cataract surgery. Therefore, when patients are seen postoperatively, the IOP measured on the first post-op day is probably lower than it was earlier. The significance of this is that in eyes with pre-existing glaucoma, with concomitant optic nerve damage, even transient post-op IOP increases can cause significant vision loss. We are convinced that, the higher the molecular weight and viscosity of the viscoelastic, the greater the likelihood of having a significant post-op rise in the IOP. So, we can use a low-molecular weight viscoelastic. We thoroughly remove all the viscoelastic at the end of the procedure. In case of posterior capsular tear, removal of the viscoelastic can sometimes cause vitreous to enter the anterior chamber, possibly resulting in IOL dislocation, extension of the capsular tear, pupillary distortion and/or difficulty in post-operative IOP control. When the opening is a small, we use a bimanual technique for removing vitreous and viscoelastic. We use a separate irrigator through the sideport incision and a vitrector tip through the main incision. If any vitreous enters the anterior chamber, we cut it cleanly without further hydratation and traction on the vitreous. We occasionally get a very high IOP on the first post-op day. The incision is handy to easily release a slight amount of aqueous at the slit lamp to quickly lower the IOP, make the patient comfortable and administer medical therapy to control the IOP.

Post-operative medications

Cataract surgery is usually performed under topical anesthesia, a patch and shield are usually placed over the eye for the first postoperative night. Because of the miotic pupil and ACG, an antibiotic/steroid ointment may be placed on the eye prior to the patch and shield. The eye is examined on the first postoperative day.

All patients who undergo intraocular surgery are placed on a regimen of topical antibiotics and anti-inflammatory medication. However, a larger number of eyes with glaucoma will be steroid-responders than eyes without glaucoma. We still tend to use topical steroid drops post-op in these eyes, as we believe control of the inflammation is more important. Topical steroids are used to decrease inflammation and then may be tapered accordingly. Topical steroids are used six times per day for two weeks and then three to four times per day for an additional two weeks. An antibiotic drop (tobramycin) is used for one week. In the eyes on chronic miotics and/or in which we stretch the pupil, we use a topical non-steroidal anti-inflammatory drug (NSAID) drop along with the topical steroids. Topical NSAIDs will also prevent postop CME. Topical mydriatic is instilled once per day for two to four weeks if necessary. If the IOP is not in a safe range after we check it the next day, we also start to use some anti-glaucoma medications. It is important to remember that patients require frequent follow-up visits during the early postoperative period and must be monitored closely for IOP increases.

Conclusions

If a patient has a cataract and well-controlled or stable glaucoma, we might consider surgically removing the cataract and treating the glaucoma with pressure-lowering medications or laser treatments. Cataract surgery resulted in not only complete dissolution of lens volume and pupillary block, but also attenuation of the anterior positioning of the ciliary processes, all of which contributed to postoperative widening of the angle in eyes with primary angle closure. Cataract surgery alone will sometimes lower the pressure in the eye.

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Combined surgery

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Introduction

With the aging of the population and the increased risk of cataract development in patients with glaucoma in recent decades, the incidence of coexisting glaucoma and cataract is also on the rise. Besides these two relevant factors, antiglaucomatous medications and glaucoma surgery significantly accelerate the development of cataracts. One study has shown that antiglaucomatous medications may play a role in the progression of nuclear cataracts.[1] In addition, glaucoma surgery significantly increases the risk for the development of cataracts, reaching 78% in patients with poor medical control of intraocular pressure (IOP).[2,3] For these reasons, the combined presence of glaucoma and cataract is a frequently observed condition.

Patients with coexisting cataract and glaucoma have their own physiopathologic characteristics. (1) Both cataract and glaucoma can cause a drop in visual acuity. On the one hand, observation of ocular fundus and examination of the visual field cannot be made, because of the blockage of an opaque lens, and the extent of visual function damage caused by glaucoma cannot be evaluated. On the other hand, the prognosis of visual function after surgery cannot be estimated correctly. (2) In patients with glaucoma, the number of endothelial cells decreases during acute attack and chronic conditions.[4-6] Complicated intraocular surgical manipulation can result in a further drop in the number of endothelial cells.[7] This can explain the higher rate of corneal edema occurring after surgery. (3) In patients with segmental atrophy iris and iris posterior synechia, the size and shape of pupil are abnormal and blood-aqueous barrier may be destroyed. Manipulation in the anterior chamber and management of the pupil can exacerbate the inflammatory reaction and result in failure of a functional filtering bleb. All of these characteristics make dually-affected eyes different from those with simple cataract or simple glaucoma. Therefore, combined surgery should be focused on and customized to each patient.

Recovery of visual acuity and control of intraocular pressure are the ultimate aims for the treatment of this type of disease. In order to reach these aims, many

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kinds of clinical strategies can be chosen. Besides combined phacoemulsification with goniosynechialysis, several surgical options are possible: (1) cataract surgery first and glaucoma surgery as a second phase; (2) glaucoma surgery and postponement of the cataract surgery; (3) combined cataract and glaucoma surgeries. Among these strategies, some controversies exist. For example, some studies have shown that a stable IOP control can be acquired by staged cataract and glaucoma surgery.[8,9] However, other studies have suggested that as a result of minimally invasive phacoemulsification, IOP can be effectively lowered when combined procedures are performed, and some advanced techniques in trabeculectomy have been developed and improved in recent years.[10,11] There is still a question of whether staged or combined procedures yield better results. Many more observations and studies are needed in the future to clear up these controversies. Regardless, each clinical strategy decision must still be customized to every patient because each strategy has its own characteristics. Besides the disease features, the subjective desires of the patient and the skills of the surgeon are conditions that must be considered. The combined surgeries that are commonly used in clinical work will be described in this chapter.

Combined phacoemulsification with intraocular lens implantation and goniosynechialysis

In angle-closure glaucoma, blockage of the trabecular meshwork by the iris is a pathogenic factor that results in the elevation of IOP; IOP is usually elevated when more than 180°of the anterior chamber angle is closed by peripheral anterior synechiae (PAS).[12] To counteract the pathogenic mechanism that causes IOP to rise, goniosynechialysis, which was recommended by Shaffer in 1957[13] for use with direct intraoperative gonioscopy to determine the extent of synechial closure during primary peripheral iridectomy, was introduced and bas evolved over the past three decades. Goniosynechialysis is a surgical procedure that is designed to strip PAS from the anterior chamber angle wall by mechanical power, open the anterior angle, and restore trabecular function in eyes with a closed anterior chamber angle.[12] With simple angle-closure glaucoma, Nd:YAG laser peripheral iridotomy and Argon laser peripheral iridoplasty should be performed prior to goniosynechialysis to widen the angle in order to avoid postoperative reformation of PAS due to a shallow anterior chamber and inflammatory reaction.[12] However, in angle-closure glaucoma with cataract, the probability of PAS reformation drops significantly, because the lens-iris diaphragm moves posteriorly, the anterior chamber deepens, and the angle widens after lens extraction and intraocular lens (IOL) implantation.[14,15] Many studies have shown that phacoemulsification used together with goniosynechialysis is an effective treatment option for angle-closure glaucoma when angle-closure is the unique factor leading to the elevation of IOP.[16,17]

Indications

Previous studies have shown that goniosynechialysis is successful in approximately 80% of eyes with angle-closure glaucoma if the PAS have been present for less than one year.[12] For eyes with acute or chronic angle-closure glaucoma with cataract,

the procedure is effective when PAS have existed for six months to one year.[12] However, for secondary glaucoma with cataract, the question of whether combined phacoemulsification with goniosynechialysis should be undertaken is a subject of controversy. The state of the function of the trabecular meshwork after surgery is the key issue. For secondary glaucoma with irreversible trabecular structural changes, such as neovascular glaucoma and glaucoma secondary to uveitis, the IOP cannot be lowered even if the trabecular meshwork is exposed completely. As a result the procedure is forbidden.[18] Some notes regarding the choice of the procedure need to be specified:

1. The success rate of the procedure is related not only with the duration of PAS, but also with the mechanisms underlying synechial closure. PAS may recur if the mechanism is still present.

2. Irreversible damage to the trabecular meshwork occurs in areas of persistent PAS with proliferation of iris tissue into the intertrabecular spaces, which obstructs aqueous outflow.[18] Even if a trabecular meshwork with irreversible damage is exposed completely, the IOP cannot be lowered.

Opportunity

If the operation is performed during the first four weeks after the acute attack, a severe fibrinoid anterior chamber reaction is likely to occur, and the effect will be attenuated. Therefore, the best timing for the operation appears to be six weeks after the attack.[18] In the case of chronic glaucoma with cataract, the earlier the operation is performed, the better the outcome.

Procedure

1. Some procedures in standard clear-cornea phacoemulsification with IOL implantation, including the infusion of viscoelastic into the anterior chamber, the energy output by phacoemulsification, and the mechanical effect of irrigation and aspiration, can strip PAS from the anterior angle wall and expose the trabecular meshwork. In a sense, phacoemulsification can be viewed as a combined surgery.

2. After standard phacoemulsification with IOL implantation, a viscoelastic agent is injected at an angle to separate the synechial tissue indirectly, and in the course of goniosynechialysis, the surgical instruments are not in direct contact with the synechial tissue. After completing separation, the viscoelastic agent is replaced with a balanced salt solution with an automated irrigation/aspiration system. This method is popular at present, because of its simplicity and efficacy.

3. If the closed angle cannot be opened with a viscoelastic agent, another method can be used as follows: after standard phacoemulsification with IOL implantation, goniosynechialysis is performed with a Barkan operating goniolens in the anterior chamber filled with viscoelastic agent. A blunt cyclodialysis spatula is inserted into a chosen paracentesis track and advanced toward the opposite angle under direct visualization. The spatula tip is then pressed against the most peripheral edge of the iris next to the points of angle adhesion and pressed posteriorly until the trabecular meshwork is exposed. The procedure is repeated in adjacent areas using the other paracentesis tracks until the entire angle is open. The viscoelastic agent is then evacuated and replaced with balanced salt solution.[12]

Complications

Besides the corresponding complications of phacoemulsification with IOL implantation, hyphema is the most common complication and is often caused by horizontal sweeping of the spatula tip or excessive force. If hemorrhage occurs, an additional viscoelastic agent is injected into the anterior chamber to raise IOP. The bleeding usually localizes as a droplet and cannot disperse to obscure the surgical field.[18] An inadvertent cyclodialysis cleft is another major complication. Damages to other intraocular tissues can be avoided with careful intraoperative manipulation.[13] Postoperative uncontrolled IOP may result from irreversible damage of the trabecular meshwork and recurrence of PAS.[18]

Staged cataract and glaucoma surgery

Some studies have stated that because of the better IOP-lowering effect of trabeculectomy alone compared with combined surgery,[19,20] it has been recommended that two procedures be separated in cases with low target IOP. The term 'staged procedure' refers to the filtering surgery, which is performed initially and is followed by cataract surgery after four to six months, at which point the functional filtering bleb has formed and IOP has approached stability. Staged surgery has some advantages over combined surgery: (1) the relatively lower need for intraoperative manipulation in each procedure is helpful for the formation of a functional filtering bleb;[21,22] (2) the IOP-lowering amplitude, which can cause the final IOP to approach target IOP following cataract surgery, can be designed during the first procedure. Because many factors can be controlled by surgeons and many techniques such as the duration of antimetabolite treatment can be chosen, the strategy can be used to effectively lower IOP. However, some disadvantages exist, as two surgeries must be performed and four to six months needed to restore visual acuity. The key issue in choosing the strategy is how to keep the IOP lowered after cataract surgery.

Indication

Some patients have both angle-closure glaucoma and cataract, and their IOPs cannot be controlled with maximumly level of medication and the use of a laser. Patients with cataracts after glaucoma surgery can be viewed as a distinct group of people for which staged surgery is needed.

Procedure

The first stage – glaucoma surgery

Trabeculectomy is a common surgery. Many clinical studies demonstrate that cataract surgery, including phacoemulsification and extracapsular cataract extraction (ECCE), can affect the filtering bleb and raise IOP.[8,9,23,24] In order to reach target IOP after the second stage procedure, an IOP level lower than the target IOP must be acquired before cataract surgery and after trabeculectomy. Some aspects should receive particular attention in this stage:

1. The method by which to obtain a better filtering flow at the first stage; the target IOP should be reached when the second stage is finished.

(A) Use of antimetabolite: As is commonly known, antimetabolite is the most important factor affecting long-term IOP control.[25,26] There is not yet consensus on some important issues, such as which antimetabolite to use on whom and when, for how long and in what concentration it should be used. In order to obtain an IOP level lower than the target IOP, the concentration and duration of antimetabolite treatment must be customized according to glaucomatous type, the age of the patient, the thickness of Tenon's fascia and conjunctiva, previous surgery and uveitis. Mitomycin C (MMC) was originally applied at higher doses and longer duration (*e.g.*, 0.5 mg/ml applied for 5 minutes).[27] Others have reported efficacy at lower doses and shorter duration (*e.g.*, 0. 25 mg/ml applied for 2 minutes).[28-30] In the Tongren Eye Center of the Tongren Hospital, we apply 0.4mg/ml MMC for one to three minutes to acquire a satisfactory IOP. 5-FU is used at a typical dose (5 mg/ml) and the surgical site is soaked for five minutes. Subsequent subconjunctival injections may be given later.[31] An antimetabolite-soaked sponge is placed under the conjunctival flap and scleral flap before entering the anterior chamber. After removal of the antimetabolite, the area is irrigated copiously with balanced saline solution. Both the encapsulated filtering bleb leading to uncontrolled IOP and a thin-walled filtering bleb resulting in hypotony and endophthalmitis can be avoided by appropriate use of antimetabolite.

(B) Factors of the scleral flap: Regardless of the shape of the scleral flap (triangular, rectangular, or square), a definite association between the shape of the scleral flap with IOP has not been observed. However, the size and thickness of the scleral flap are strongly associated with IOP. A smaller scleral flap can result in a lower IOP. A scleral flap with a size of 2 × 2.5 mm is created in our institution, and a satisfactory IOP is achieved. A thin scleral flap can increase the filtering flow, and a relatively low IOP can be obtained. In our institution, we create a scleral flap with a scleral thickness of 1/3 -1/2, and an IOP slightly lower than target pressure is acquired.

(C) Opportunities to remove the releasable sutures: The time at which to remove the releasable sutures is decided by the IOP, the status of the filtering bleb and on the age of the patients,as well as other factors. For young patients, especially with a deep anterior chamber and with a tendency towards scarring of the filtering bleb, removal of releasable sutures should be performed as early as possible to ensure formation of a functional filtering bleb even if IOP is not high. IOP is not the only standard used to determine the appropriate time at which to remove the releasable sutures. Laser suture lysis should be considered if IOP cannot be controlled by the removal of releasable sutures.

2. Choice of incision site: The principle used for choosing the incision site of cataract surgery is to find a proper location far away from the incision site of the filtering bleb. With clear-cornea phacoemulsification becoming more popular in recent years, the choice of an incision site for trabeculectomy has broadened. In our institution, we often make a superior conjunctival flap and perform phacoemulsification at the superotemporal clear cornea. If, for some reason, ECCE is needed, a superonasal conjunctival flap for trabeculectomy and a temporal cataract incision should be made.

The second stage – cataract surgery

Cataract surgery is performed at four to six months after glaucoma surgery when the functional filtering bleb and IOP approach stability (Fig. 1). This process is different from simple cataract extraction, and restoration of visual acuity and control of IOP are essential following the operation. Because many operations and acute attacks have often occurred previously in these patients, many complicated ocular appearances can be observe. Therefore, surgery should be customized to every patient. Below are some issues should be considered and corresponding ways to solve these problems. These issues reflect our experience and comprehension gath-

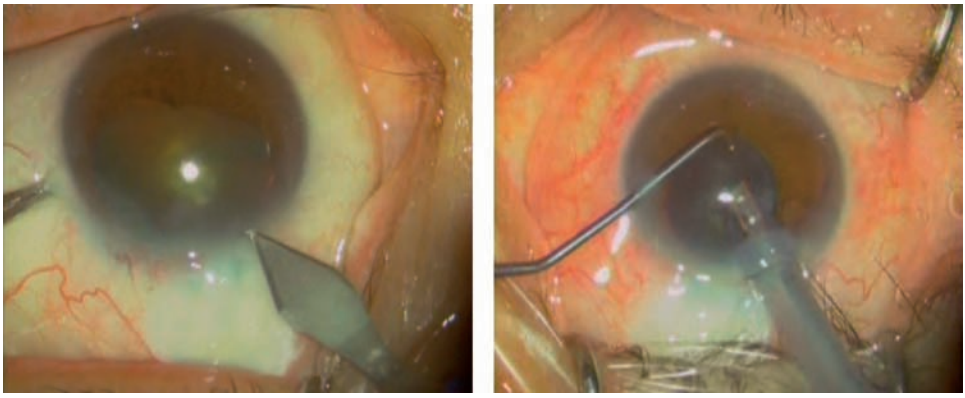

Fig. 1. Phacoemulsification cataract extraction with IOL implantation is performed at a superotemporal clear cornea at 4-6 months after glaucoma surgery when the functional filtering bleb and IOP approach stability.

ered from clinical work.

(1) The choice between phacoemulsification and ECCE: Many studies have shown that damage caused to ocular tissues by phacoemulsification without complications is less than that caused by ECCE.[32-34] In the period of more than 30 years in which surgeons have performed phacoemulsification which requires flawless surgical skills and precise machine functions, the process has approached the state of the art. Minimally invasive phacoemulsification procedures, which have been developed in recent years, can cause damage to ocular tissues and breakdown of the blood-aqueous barrier, which may decrease to the minimum level.[35] We think phacoemulsification should be chosen, unless the amount of corneal endothelium is too low to keep the cornea clear following phacoemulsification. In that case, ECCE should be chosen.[36,37]

(2) Protective measures of corneal endothelium: Corneal endothelium has been lost to a certain extent in patients that have suffered acute attack and long-term chronic angle-closure glaucoma. Therefore, the means by which to protect corneal endothelium from loss is an important issue that cannot be neglected. Some measures can be taken: (a) Phacoemulsification parameters can be set with low energy output and high vacuum. A pulse or burst phacoemulsification mode can also be chosen. Minimally invasive phacoemulsification including a bimanual technique

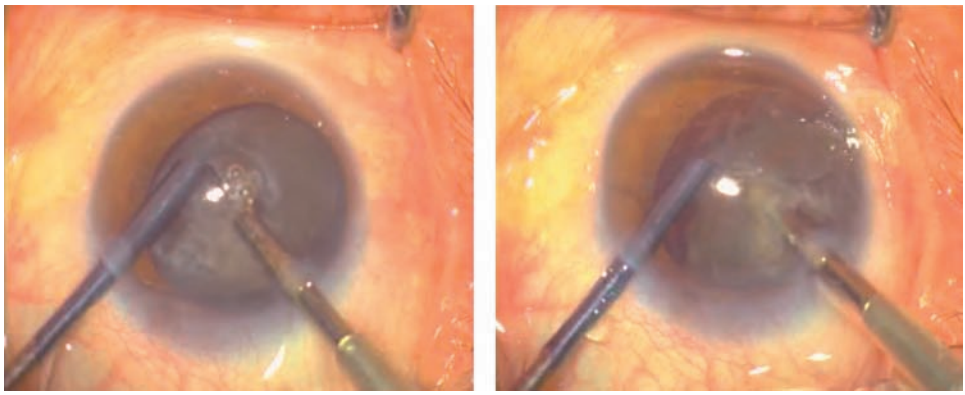

Fig. 2. Minimally invasive phacoemulsification is performed using the bimanual cataract technique with a 1.4 mm clear cornea incision.

and cold phacoemulsification can cause a further loss of corneal endothelium (Fig. 2).[35] The so-called 'cold phaco', namely the micropulse system, can reduce the total energy used and lead to less tissue trauma and less endothelial cell loss. Previous studies have shown that the rate of endothelial cell loss is 8-10% when traditional phacoemulsification is used, and the rate of cellular loss is lower when minimally invasive cataract surgery is applied.[38,39] Tsuneoka *et al*. analyzed 637 eyes using the bimanual cataract technique, with a 1.4 mm clear cornea incision, and obtained a mean endothelial cell loss rate of 7.8% with different nuclear hardnesses.[40] (b) With the large, firm nucleus, ECCE should be chosen over phacoemulsification, because it causes less damage to the corneal endothelium.[37] (c) Viscoelastic agents with various features should be used reasonably; one such procedure is the soft shell technique.[41]

(3) Protective measures for the blood-aqueous barrier: The extent of destruction of the blood-aqueous barrier affects the formation of a functional filtering bleb. Some measures can be taken to reduce the destruction: (a) Phacoemulsification can be adopted instead of ECCE, and minimally invasive phacoemulsification can cause damage to the barrier to drop to a minimal level.[42,35] (b) If iris posterior synechia exists and the pupil is big enough, continuous circular capsulotomy (CCC) should be completed directly and no iridolysis will be necessary. (c) Anti-inflammatory therapy should be administered before and after the operation.

(4) Opportunity for IOL implantation: (a) If there is slight damage to the blood-aqueous barrier and less postoperative inflammatory reaction, IOL can be implanted into a capsular bag immediately following lens extraction. Thus, the second surgery can be avoided and visual acuity can be improved at the same time. The optimal IOL is a heparin surface-modified IOL that can decrease the postoperative reaction.[43] (b) With the obvious breakdown of the blood-aqueous barrier and inflammatory reaction, implantation of IOL can be postponed as the inflammatory reaction diminishes. (c) Implantation of IOL cannot be considered when patients have a crowded anterior segment and have a tendency for malignant glaucoma.

(5) Surgical management of an abnormal pupil: (a) When patients show segmental atrophy of the iris, a dilated pupil, and iris posterior synechia, iridolysis is not needed, and CCC with a diameter of 5.0-5.5 mm can be performed directly

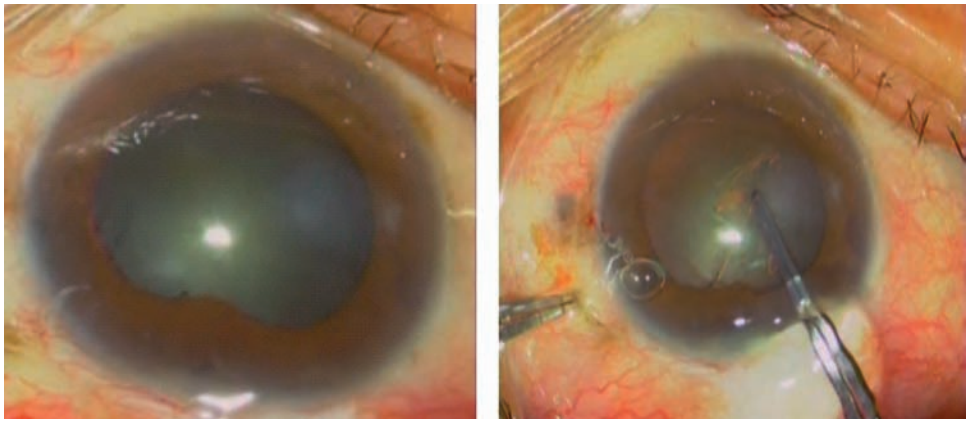

Fig. 3. The pupil is big enough and shows iris posterior synechia. CCC without posterior synechiolysis can decrease the breakdown of the blood-aqueous barrier as much as possible.

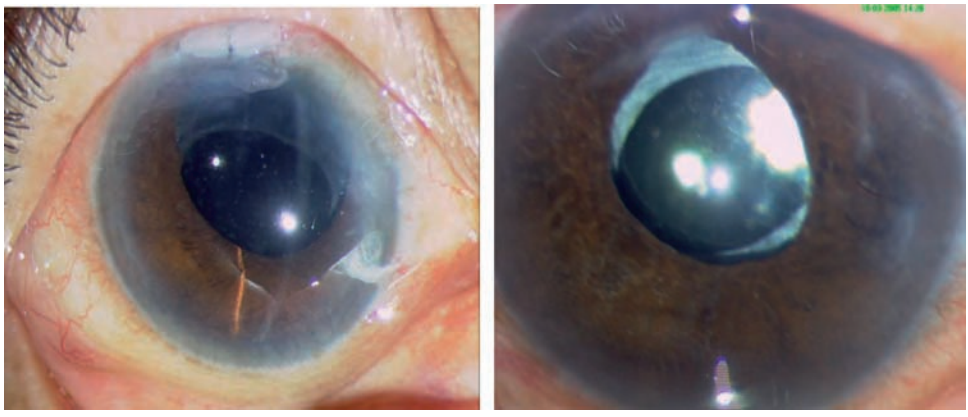

Fig. 4. CCC with a diameter of 5.0mm was performed on the eye with a segmented atrophy iris and dilated pupil. The residual anterior capsular membrane becomes opaque and forms a new artificial pupil' to block the entry of excessive amounts of light.

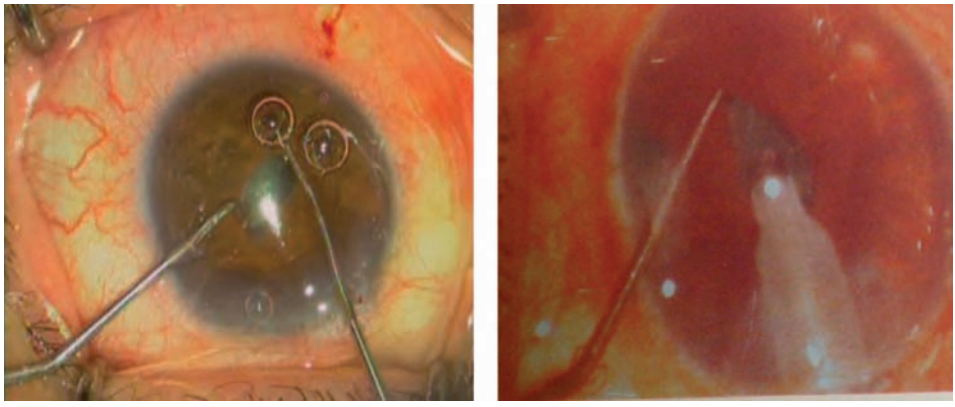

Fig. 5. When a pupil is small and shows posterior synechia, iridolysis can be performed with a blunt tip or a chopper, and phacoemulsification can be completed with the assistance of a chopper.

(Fig. 3). The residual anterior capsular membrane will become opaque and can be looked as a new 'iris' to block the entry of excessive amounts of light. This new artificial 'pupil' can attenuate symptoms such as glare and phengophobia (Fig. 4). (b) A small pupil with posterior synechia is incapable of reacting to mydriatics because of the long-term use of miotics. The use of miotics should be stopped prior to surgery, and iridolysis can be performed with a blunt tip on a syringe filled with viscoelastic agent or a chopper (Fig. 5). If the pupil is dilated, CCC can be performed directly. Otherwise, CCC can be performed by an experienced surgeon without visualization. A flexible iris hook can gently stretch and retain the iris for maximum visibility during the procedure.[44]

(6) Management of advanced glaucoma with cataract: The viscoelastic agent should be carefully extracted from the anterior chamber to alleviate the threat of visual acuity loss by transitory raised IOP.

Complications

(1) The first stage: Complications are the same as those of trabeculectomy. The use of antimetabolites should be emphasized. If used excessively, a thin-walled filtering bleb can form followed by hypotony, choroidal detachment, and macular edema, and these can cause a severe outcome. Additionally, if used insufficiently, vascularization of the filtering bleb can raise IOP.

(2) The second stage: Complications are the same as those of cataract surgery. When compared to a simple cataract, the incidence of corneal decompensation is higher. For patients with advanced glaucoma, a postoperative transitory increase in IOP can lead to a loss of visual acuity.

Combined cataract and glaucoma surgery

Through combined cataract and glaucoma surgery, visual acuity can be improved and IOP can be reduced simultaneously. One study by Friedman *et al*. specified the long-term benefit of combined surgery with respect to IOP after two years of follow-up, with a mean reduction of 8 mmHg in patients with phacoemulsification cataract extraction and 6-8 mmHg in patients with ECCE.[45,46] Compared with staged surgery, combined surgery has some advantages: 1. the IOP-lowering effect and improvement of visual acuity can be obtained using only one procedure; 2. the effect of transitory raised IOP on visual acuity loss can be avoided in staged surgery; 3. quality of life can be improved because the visual acuity of the patient increases immediately after surgery. At the same time, the cost of hospitalization can also be reduced. However, the probability that a functional filtering bleb will form after combined surgery is relatively low as result of complicated intraocular manipulation. Numerous studies show that compared with combined surgery, the IOP reduction rate and the progressive follow-up results are better when trabeculectomy is performed alone.[19,47,48] The means by which to maintain efficient filtration and promote a potential functional filtering bleb are the most important challenges of combined surgery.

The success rate of combined surgery has recently been improved significantly, and this improvement is ascribed to two factors, phacoemulsification techniques and use of antimetabolites.[33-39]

Today's rapidly advancing phacoemulsification techniques, including small incisions and foldable lenses implanted in the bag, facilitate safer and more efficient combined surgery. Although no randomized, controlled trials assessed the use of cataract surgery by nuclear expression or by phacoemulsification during combined surgery, evidence-based studies by Jampel and Friedman have indicated that these procedures, can result in lower long-term IOP, and six of nine observational studies reported a greater IOP reduction in eyes undergoing phacoemulsification as opposed to nuclear expression.[45,46] In the six observational studies with one to two years of follow-up, the mean reduction of IOP in the phacoemusification groups was 5.3-8.6 mmHg, and that in ECCE groups was 2.5-6.5 mmHg.[49-54] In summary, IOP is lowered more (1-2 mmHg) when phacoemulsification rather than ECCE is used in combined cataract and glaucoma surgery.[45,46] The use of antimetabolites, which inhibit tissue proliferation, is the decisive factor for long-term control of IOP. Two randomized, controlled trials have been conducted to evaluate the effect of MMC in combined cataract and glaucoma surgery. Investigators used 0.5 mg/ml MMC of varying duration in the MMC groups. Results showed that the MMC groups had greater mean IOP lowering (mean, 7.7 mmHg and 5.8 mmHg versus 3.1 mmHg and 2.9 mmHg), required fewer medications (mean, 0.6 versus 1.4/eye, 0 of 14 eyes versus 5 of 15 eyes) and larger filtering blebs one year after surgery.[55,56] A preponderance of evidence has suggested that the use of MMC in combined cataract and glaucoma surgery provides a small benefit (2-4 mmHg)[45,46]

Besides the use of phacoemulsification and antimetabolites, the releasable suture technique and laser suture lysis can improve the success rate and reduce complications of combined surgery.[57,58] Evidence-based studies have demonstrated that athough there is a lack of sufficient evidence, the overall outcome of combined surgery seems to be similar for staged and combined procedures within the limited database. Therefore, indication for combined surgery is broadening.[45,46]

Indications

A number of conditions cannot be controlled by medication and laser therapy, and require significant improvement of visual acuity. Patients with these types of conditions include: patients with uncontrolled IOP and coexisting cataract with blurred vision; patients with progressive and advanced glaucoma and cataract; patients with poor compliance to medication.

Procedure

Phacoemulsification cataract extraction with IOL implantation combined with trabeculectomy

Many studies have shown that the long-term IOP is lower in eyes undergoing phacoemulsification rather than ECCE when combined with trabeculectomy.[45,46] Among many surgical combinations phacoemulsification cataract extraction is the optimum choice because it causes less trauma to ocular tissues and has less of an effect on the functional filtering bleb.[49-54] Two kinds of incision site can be chosen in combined surgery. One is a one-site procedure, and the other is a two-site procedure. One-site surgery is performed with a scleral tunnel for phacoemulsification

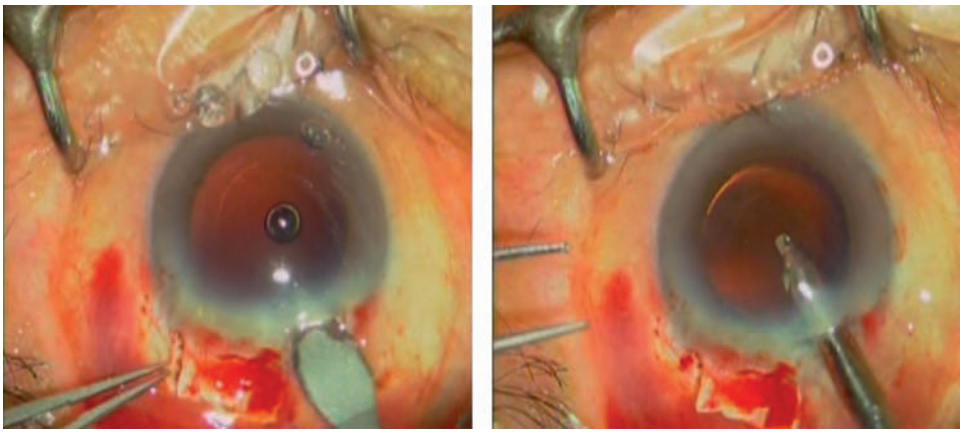

Fig. 6. Phacoemulsification cataract extraction with IOL implantation is performed with a temporal clear cornea incision immediately after the conjunctival flap and scleral flap are created at the 12-o'clock position. Mitomycin C must be applied before corneal incision is performed.

and a scleral flap on which both sides of the scleral tunnel are cut radially for trabeculectomy. Two-site surgery is performed with a limbus-based conjunctival flap for the trabeculectomy in the superior quadrant and a temporal clear cornea incision for phacoemulsification. Three randomized, controlled trials have evaluated the effect of one-site and two-site combined cataract and glaucoma surgery. Study results demonstrated a similar, slightly greater reduction of IOP using the one-site procedure (mean, 15.1, 11.0, 6.6 mmHg in the two-site operation versus 12.7, 7.1, 5.2 mmHg in the one-site operation). No statistical analysis of the difference in the magnitude of the IOP reduction was provided.[59-61] Some studies have suggested that two-site surgery results in slightly lower (1-2 mmHg) IOP than one-site surgery.[45,46]

(1) Two-site surgical procedure:

Standard trabeculectomy is performed with a limbus-based conjunctival flap and a rectangle-shaped partial-thickness scleral flap at the 12-o'clock position. A mitomycin C-soaked sponge (0.4mg/ml) is applied under the conjunctival and scleral flap. The duration of mitomycin C is customized according to the age of the patient and the thickness of the conjunctiva and Tenon's fascia. The sponge is removed and the area is irrigated copiously with balanced saline solution when soaking is completed. Attention is then turned to the cataract procedure. Standard phacoemulsification cataract extraction with IOL implantation is performed with a temporal clear cornea incision (Fig. 6). After miosis, trabeculectomy and peripheral iridectomy are completed under the scleral flap. The scleral flap is closed with two 10-0 sutures at the posterior angles of the scleral flap and one suture between the two posterior angles. Two releasable sutures are made at both edges of the scleral flap. Tenon's fascia is closed with interrupted sutures, and the conjunctiva is closed in a running fashion.

(2) One-site surgical procedure:

A corneo-scleral limbus-based conjunctival flap is dissected at the 12-o'clock position. A piece of sponge soaked in 0.4 mg/ml mitomycin C is applied to the

scleral surface adjacent to the corneo-scleral limbus, and the conjunctival flap and the Tenon's fascia layer are draped over the sponge. After about two minutes, the sponge is removed and the area is irrigated copiously with balanced saline solution. A 4-mm scleral groove of approximately 1/3 the scleral thickness is created 3 mm posterior to the corneoscleral limbus,and a scleral tunnel is dissected into the clear cornea. An incision through the scleral tunnel into the anterior chamber is made with a 3.2-mm keratome blade. Standard phacoemulsification cataract extraction with IOL implantation is then performed. After miosis, both sides of the scleral tunnel are cut radially with Vannas scissors to create a scleral flap after which a trabeculectomy and a peripheral iridectomy are performed. The scleral flap is closed with interrupted 10-0 nylon sutures. Two releasable sutures are made at both edges of scleral flap. Tenon's fascial and conjunctival closure are performed in the same fashion as for the two-site procedure.

ECCE with IOL implantation combined trabeculectomy

Patients have a corneal endothelium density that closes the threshold and may cause cornea decompensation to occur. Patients have lenses with large, firm nucli, and severe damage of ocular tissues may result from the excessive energy created by phacoemulsification.

A limbus-based conjunctival flap and rectangle-shaped partial-thickness scleral flap are made at the 12-o'clock position. A groove-shaped incision, 10 mm length is extended from both sides of the scleral flap. The incision for ECCE is created at the limbus at the 12-o'clock position under the scleral flap. Can-opener anterior capsulotomy and hydrodissection are performed through the incision. The incision is then enlarged bilaterally along the groove-shaped incision and each suture is prepared at a point 2 mm from both edges of the scleral flap. Standard extracapsular extraction with nucleus expression followed by aspiration of cortical soft lens matter is then performed. After IOL implantation, ligation of prepared sutures on both sides of the scleral flap is performed. Trabeculectomy and peripheral iridectomy are then completed under the scleral flap. The scleral flap is closed with two 10-0 sutures at the posterior angles of the scleral flap and one suture between the two

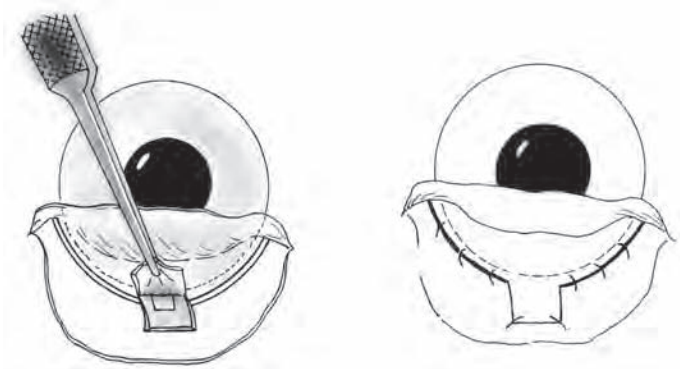

Fig. 7. A conjunctival flap, scleral flap, and limbal incision are created from both sides of the scleral flap. The limbal incision at both sides of the scleral flap is sutured after ECCE and IOL implantation. Trabeculectomy and peripheral iridectomy are then completed under the scleral flap. The scleral flap is closed with two 10-0 sutures at the posterior angles of the scleral flap.

posterior angles. Two releasable sutures are placed at both edges of the scleral flap. Tenon's fascia and conjunctiva are then sutured separately (Fig. 7).

Postoperative management

Postoperative management is very important not only for phacoemulsification cataract extraction with IOL implantation, but also for ECCE with IOL implantation combined with trabeculectomy. Correct postoperative management is a key factor to ensure that the functional filtering bleb forms. Because of the complicated procedures, severe postoperative inflammatory reaction, and low success rate of the functional filtering bleb, some aspects should be noted:

(1) Postoperative IOP control at an early stage: If the IOP is high at an early postoperative stage, transitory raised IOP caused by viscoelastic agents should be considered. If the increase of IOP is because the scleral flap is closed too tight to allow the filtering flow, pressure on an adjacent area of the filtering bleb under a microscope can cause the scleral flap to split, thereby increasing the filtering flow and lowering the IOP. If the IOP shows another rapid increase, releasable sutures should be removed unless the scleral inner incision is blocked. Releasable sutures should be removed one at a time in order to avoid hypotony and shallow anterior chamber. It should be emphasized that raised IOP is not the only standard used to determine the removal of releasable sutures. For young patients, especially those with deep anterior chamber and with a tendency towards scarring of the filtering bleb, removal of releasable sutures should be performed as early as possible to ensure formation of a functional filtering bleb even if IOP is not high. Laser suture lysis should be considered if the IOP cannot be controlled with the removal of releasable sutures. Postoperative hypotony and shallow anterior chamber can be prevented if the scleral flap is closed tightly and releasable sutures are used during surgery.

(2) Postoperative anti-inflammatory enhancement: Control of the postoperative inflammatory reaction will be helpful for the formation of a functional filtering bleb. The use of glucocorticoid eye drops will be stopped when the inflammatory reaction within the adjacent filtering bleb disappears. Cycloplegica will be added if hypotony, shallow anterior chamber, and obvious inflammatory reaction appear.

Complications

Complications are the same as those of trabeculectomy, cataract surgery, IOL implantation, and use of antimetabolites. Compared with simple trabeculectomy and cataract surgery, it has its own characteristics:

(1) The severe postoperative inflammatory reaction is the most important cause leading to failure of a filtering bleb and uncontrolled IOP.

(2) Use of antimetabolites should be carefully planned and monitored because many incisions are made during the surgery. A thin-walled filtering bleb can form, and healing of cataract incisions will be delayed if they are used in excess.

(3) If there is obvious exudation in the anterior chamber and a tendency towards pupil block, mydriasis and anti-inflammatory therapies at an early stage may prevent malignant glaucoma.

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Paracentesis

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Introduction

Treatment for primary angle closure glaucoma (PACG) includes regimes targeting the acute phase of the disease (nowadays often referred to as acute primary angle closure – APAC), post-acute phase of the disease, and also established chronic phase of the disease (conventionally referred to as chronic angle closure glaucoma – CACG).

The treatment for APAC has conventionally been the use of both topical and systemic intraocular pressure (IOP)-lowering medications. As soon as IOP is controlled and sufficient corneal clarity is re-established (post-acute phase of PACG), laser peripheral iridotomy has been the next step in treatment, with the aim of preventing recurrence of the acute disease, and also to prevent progression to the CACG.

This conventional management algorithm for PACG has many limitations, and it is because of these limitations that a series of surgical trials has been undertaken in recent years, with the hope of moving one step closer to the ideal treatment algorithm for PACG.

Intraocular pressure control in APAC – Limitations of conventional systemic medications

The initial treatment for APAC aims at rapidly reducing IOP, so as to relieve excruciating symptoms and prevent further irreversible ocular tissue damage,[1] before the definitive treatment of laser peripheral iridotomy can be safely performed. The initial treatment may involve one or more of the following IOP-lowering drugs: 1) topical ß-blocker, *e.g.*, timolol; 2) topical miotic agent, *e.g.*, pilocarpine; 3) systemic

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(oral/intravenous) carbonic anhydrase inhibitor, *e.g.*, acetazolamide; 3) oral hyperosmotic agent, *e.g.*, glycerol; 4) intravenous hyperosmotic agent, *e.g.*, mannitol. Topical steroids may also be used to control inflammation before surgery.

These treatments may fail to reduce IOP in a significant proportion of APAC patients. Even when they are effective, they may take hours, or even days, to reduce IOP to a safe and symptom-free level (authors' unpublished data). The longer the IOP is raised, the more irreversible damage there is to the optic nerve head, iris, lens, and drainage pathways. Patients may suffer prolonged periods of excruciating symptoms. Furthermore, the systemic drugs may cause systemic side effects, such as paraesthesiae, drowsiness, confusion, loss of appetite, polydipsia and polyuria. More serious systemic side effects may also occur with carbonic anhydrase inhibitors, such as metabolic acidosis and electrolyte disturbance,[2,3] respiratory failure,[4] Stevens-Johnson Syndrome,[5] and blood dyscrasias.[6] Systemic hyperosmotic agents can cause metabolic disturbance such as acidosis, pulmonary oedema and congestive heart failure, acute renal failure, and even intracranial hemorrhage and anaphylactic reaction.[7,8] For these reasons, current medical regimens to control IOP in APAC patients are not ideal.

Immediate anterior chamber paracentesis – safe and effective adjunct to systemic medications?

In situations where laser iridoplasty is not possible, immediate paracentesis has been proposed as an alternative procedure to rapidly lower the IOP in APAC.[9] The unique advantage of immediate anterior chamber paracentesis lies in the rapidity of IOP control (Fig. 1) and almost instantaneous relief of the severe symptoms.[9] Rapid IOP control limits the extent of ocular tissue damage from high IOP. For a sustained pressure reduction, it appears that conventional medications are still necessary when paracentesis has been performed.[9] Furthermore, laser iridotomy is also necessary after paracentesis, to eliminate pupil block. Since paracentesis reduces IOP and clears corneal edema so rapidly, it may allow laser peripheral iridotomy to be performed earlier than is conventionally possible.

The performance of anterior chamber paracentesis in an eye with APAC poses unique technical difficulties, as compared to paracentesis in a post-cataract extraction eye. First of all, the patient is in severe pain and may be photophobic. The patient may not co-operate fully at the slit lamp, and eyelid speculum is often, if not always, required for a safe procedure. The patient may be nauseated, or even vomiting. The patient may thus not be able to stay entirely still on the chin rest at the slit lamp. An APAC eye has a shallow anterior chamber, and thus the risk of iris and/or lens damage from the paracentesis slit knife is present. In our experience, the additional discomfort arising from the paracentesis is minimal compared to what APAC causes. The time required for the procedure is also very short, usually taking few seconds only. We had encountered no difficulties in finishing the procedures. One of the practical tips is to enter the anterior chamber with only a very short section of the fine tip of the slit knife, and thereby limiting the risk of lens / iris damage. A slight twist of the slit knife after entering the anterior chamber often helps to further open up the small slit wound, allowing aqueous to come out easily. Furthermore, as this is an intra-ocular procedure, it is important that aseptic techniques are practiced.

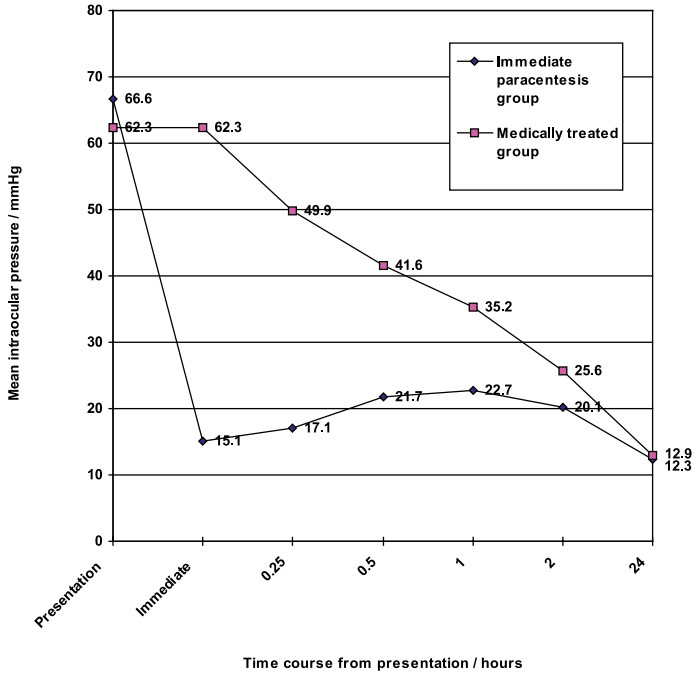

Fig. 1. The profile of mean intraocular pressure (IOP) in acute primary angle closure (APAC) eyes treated with immediate anterior chamber paracentesis and systemic medications, compared to that in APAC eyes treated with systemic medications in conventional fashion.[10]

Immediate ALPI can lower IOP and relieve symptoms in APAC almost as rapidly, but the argon laser may not be readily available in most emergency settings. Furthermore, immediate laser iridoplasty also requires round-the-clock availability of such expertise, which may pose logistical difficulties. On the contrary, the instrument necessary for immediate anterior chamber paracentesis is minimal, and can be made readily available in any emergency setting. Furthermore, it is envisaged that after proper training, on-call ophthalmology residents may also be competent enough to perform an effective and safe paracentesis.

The role and benefits of paracentesis in the management of APAC are yet to be more clearly defined by prospective randomized clinical trials.

Treatment of post-acute PACG

Once IOP has been controlled in APAC, the target of the next step in treatment is to prevent recurrence of the acute attack, and to avoid progression to CACG. The ideal treatment for APAC should, on the one hand, eliminate any pupillary block to prevent future attacks, and on the other, should widen the angle and eliminate

ay residual appositional closure as much as possible to prevent progression to CACG.

Traditionally, the treatment of choice has been laser peripheral iridotomy. The efficacy of laser peripheral iridotomy in preventing recurrence of acute angle closure in oriental eyes has not been well studied. Its ability to prevent progression to CACG has, however, been shown to be limited. In one study, 58.1% of APAC eyes treated with conventional medical regimes followed by laser peripheral iridotomy progressed to CACG after a mean follow up of 50.3 months.[10] An alternative treatment that can do better than this has to be found.

Conclusions

Systemic IOP-lowering medications and laser peripheral iridotomy have, for decades, been the unchallenged treatment of choice in APAC. In the light of recently available data, especially those from studies on oriental eyes, it has become increasingly clear that these treatment modalities are still far from ideal.

Argon laser peripheral iridoplasty (ALPI) has recently been established as a superior first-line treatment for APAC, replacing systemic medications altogether. Immediate anterior chamber paracentesis has the potential to be an effective adjunct to systemic medications in APAC in situations when ALPI is not possible.

Hopefully, with each research study, we are one step closer to establishing the ideal treatment algorithm for PACG.

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