Primary Angle-Closure Glaucoma in Cape People of Mixed Ethnic Background with Special Emphasis on Chronic Angle-Closure Glaucoma

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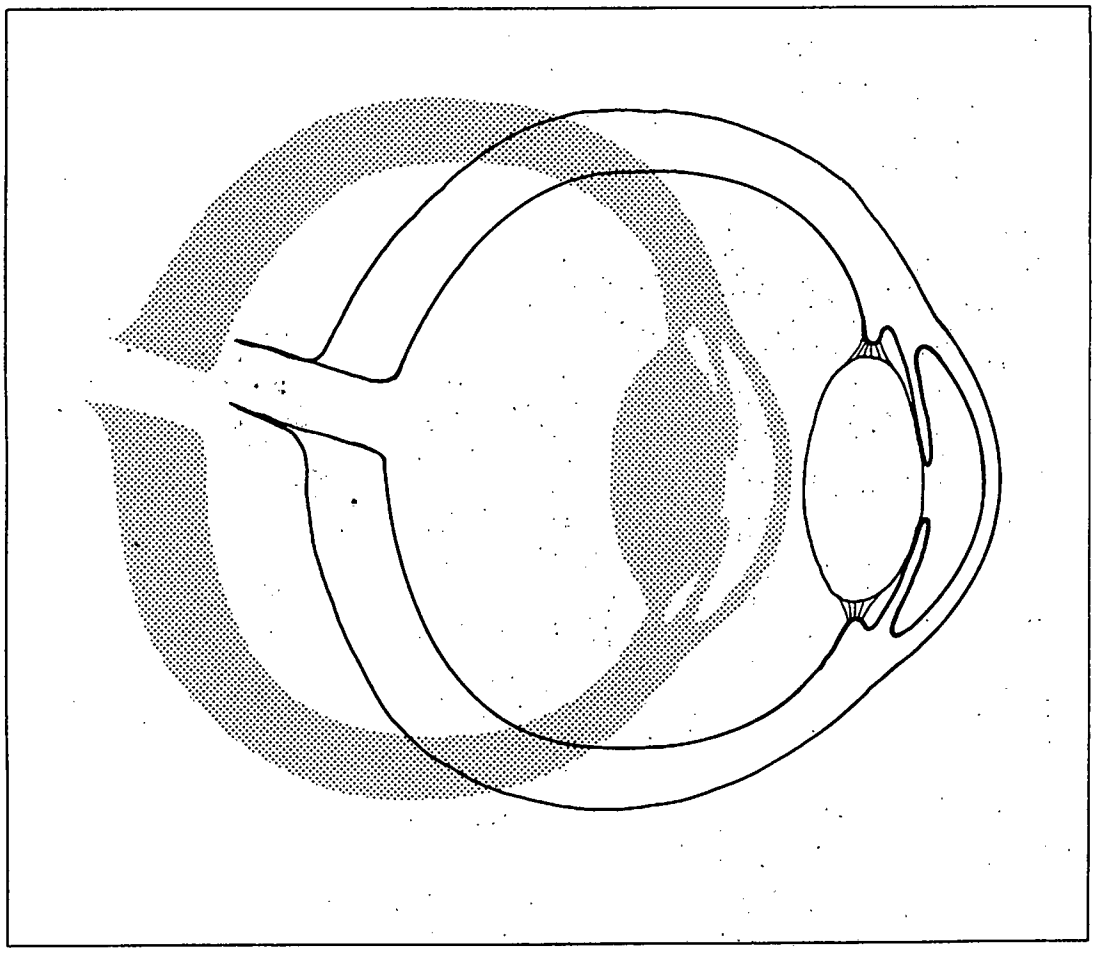

A Thesis Submitted to the Faculty of Medicine
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DEDICATION

This thesis is dedicated to my wife Susie,

to my children, Mark and Nicola

and to my parents, Frank and Jean Salmon.

Contents

Abstract

Primary angle-closure glaucoma is more common than primary open-angle glaucoma in Southeast Asia. The disease is not well understood in these people and little research has been undertaken in this field. This thesis presents the results of a series of studies undertaken between 1986 and 1992 in Cape Town, South Africa, on patients with primary angle-closure glaucoma.

"Cape coloured" people of mixed Southeast Asian, indigenous African and European ethnic background were studied. Primary angle-closure glaucoma is more common in this ethnic group than it is in whites or blacks. This predisposition may reflect an Oriental genetic influence on their ocular structures. The disease has a high prevalence rate in these people, as demonstrated by the findings of a population-based survey undertaken in the village of Mamre, situated 56km from Cape Town. An age-related trend towards hypermetropia was found. The prevalence of Shaffer grade 1 angles in this village was 9%, and of primary angle-closure glaucoma 2.3%; this prevalence increased with age in both sexes. Women were affected four times more than men and the sex difference persisted across all age groups. The prevalence of chronic angle-closure glaucoma was 2% and of chronic open-angle glaucoma 1.5%.

These patients have a shorter eye and a shallower anterior chamber than normal individuals. An anterior lens position and not a large lens is the main reason for their crowded ocular anterior segments. Plateau iris syndrome may play an important role in the pathogenesis of chronic angle-closure glaucoma in this ethnic group.

"Coloured" patients with primary angle-closure glaucoma are more likely to present with chronic symptoms and signs than with acute glaucoma. The disease causes significant ocular damage and visual loss before patients become aware of their disability.

The risks of Nd-YAG laser iridotomy are small and the long-term intraocular pressure levels after prophylactic iridotomy are good. However, those eyes with a plateau iris configuration tend to develop elevated intraocular pressure with time. In patients with chronic angle-closure glaucoma the need for trabeculectomy in addition to iridotomy cannot be predicted on presentation. The current practice of laser iridotomy followed, if necessary, by medical therapy and trabeculectomy, is thus an effective approach to the management of chronic angle-closure glaucoma. In those patients requiring drainage surgery, trabeculectomy is an efficient method of controlling the intraocular pressure.

Primary angle-closure glaucoma, and especially chronic angle-closure glaucoma, is a significant cause of visual loss in Cape people of mixed ethnic background. If the disease is diagnosed early the treatment is simple, safe and effective. Efforts should be made to identify individuals at risk and to heighten awareness of the condition amongst health-care workers and ophthalmic practitioners. There is sufficient evidence to suggest that the conclusions of this work may be relevant to the people of Southeast Asia.

List of Illustrations

List of Tables

Preface

I commenced work as a specialist in the Department of Ophthalmology at Groote Schuur Hospital, Cape Town on the 1st December, 1985 and assumed responsibility for the glaucoma clinic at the same time. On the 14th December, 1985 I examined a patient with iridoschisis associated with chronic angle-closure glaucoma. It was because of my subsequent study of iridoschisis that I became aware of the problem of primary angle-closure glaucoma in the people of mixed ethnic background (the so-called "coloureds") who live in the Western Cape. The study of this form of glaucoma has been my overriding academic interest for seven years.

This thesis concerns the "coloured" patients with primary angle-closure glaucoma who presented at Groote Schuur Hospital from 1986 to 1991. A prevalence study was undertaken in the village of Mamre in 1992. The object of the thesis is to present my findings and in particular to examine the entity of chronic angle-closure glaucoma. The health and economic consequences of this form of glaucoma are significant because 10.5% of the South African population have a similar ethnic background to the people described in this thesis. In addition, chronic angle-closure glaucoma appears to be more common than chronic open-angle glaucoma in Orientals, although few studies have been undertaken in these people. Many of the conclusions of this thesis may be relevant to the populations of Southeast Asia; a geographic area where approximately 450 million people live.

This thesis was made possible with the help and support of many people. In particular I wish to thank:

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Dr. Richard Maske who continuously advised me and who reviewed parts of the thesis; Dr. Trevor Carmichael who provided valuable input and constant support; Dr. Sedick Isaacs, Miss Sonya Swanevelder and Dr Theuns Kotze who assisted with the statistical analysis; Dr. Andre Mermoud, my glaucoma fellow from Switzerland whose assistance with the prevalence study and whose help in the glaucoma clinic in 1992 was invaluable; Mrs Meg Donald who helped with the gathering of data; Mrs Rita List who took the anterior segment photographs; and the staff of the Department of Medical Graphics for the art-work.

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The following journal articles have arisen from this thesis:

- The association of iridoschisis and primary angle-closure glaucoma.
JF Salmon and ADN Murray. *Eye* 1992; **6** : 267-272.

- The presenting features of primary angle-closure glaucoma in patients of mixed ethnic background. JF Salmon. *South Afr Med J*; 1993.

- The prevalence of primary angle-closure glaucoma and open-angle glaucoma in Mamre, Western Cape, South Africa. John F Salmon, Andre Mermoud, Andrew Ivey, Sonya Swanevelder, Margaret Hoffman. *Arch Ophthalmol* 1993.

- Long-term intraocular pressure control after Nd-YAG laser iridotomy in chronic angle-closure glaucoma. JF Salmon. *Journal of Glaucoma* 1993.

- The role of trabeculectomy in the treatment of advanced chronic angle-closure glaucoma. JF Salmon. *Journal of Glaucoma* 1993.

- The role of ethnicity in the frequency of primary angle-closure glaucoma. JF Salmon, R Martell. *South Afr Med J* 1993.

The following Congress presentations have arisen from the thesis:

- Primary angle-closure glaucoma. Ophthalmological Society of South Africa, Bloemfontein, March 1991.

- The association of iridoschisis and primary angle-closure glaucoma. College of Ophthalmology, Glasgow, May 1991.

- The prevalence of primary angle-closure glaucoma in Mamre, Western Cape. Ophthalmological Society of South Africa, Cape Town, February 1993.

- The mechanism of angle occlusion in chronic angle-closure glaucoma. Ophthalmological Society of South Africa, Cape Town, February 1993.

1.0 Introduction
Primary Angle-Closure Glaucoma.

1.1 Nomenclature and Definitions

Over the years many definitions of "glaucoma" have been suggested. The lack of a standard definition occurs in part because the word "glaucoma" does not refer to a single disease entity but rather a group of diseases that differ in their clinical presentation, pathophysiology and treatment. The classification system that has proven to be the most useful was introduced by Barkan in 1938 and divides the acquired glaucomas into open-angle forms and angle-closure forms.[1]

In open-angle glaucoma there is increased resistance to aqueous humour outflow through the trabecular meshwork - Schlemm's canal - episcleral venous system. In angle-closure glaucoma there is increased resistance to the outflow because the peripheral iris covers the trabecular meshwork preventing the aqueous humour from reaching the outflow channels. Each type is subdivided into primary and secondary forms.

Primary open-angle glaucoma is generally bilateral, although not necessarily symmetrical, and is characterised in at least one eye by either or both of the following: (i) changes in the appearance of the disc or nerve fibre layer (for example: size of the cup, thinning or notching of the disc rim, progressive change, disc haemorrhage and nerve fibre layer defects); and (ii) the presence of abnormalities in the visual field (for example: an arcuate defect, nasal step, paracentral scotoma and general depression) in the absence of other causes or explanation for a field defect.[2] The diagnosis can be made when the intraocular pressure is normal, although most patients have an intraocular pressure of more than 21 mmHg. The onset occurs in adulthood, the angles are open and there is an absence of other secondary causes of open-angle glaucoma.

The definition of primary angle-closure glaucoma differs from that of primary open-angle glaucoma. This form of glaucoma is generally bilateral, although not necessarily symmetrical and is characterised in at least one eye by partial or total closure of the angle with the iris root.[3] The appearance of the optic disc and the visual field may be normal. The onset occurs in adulthood and there is an absence of other secondary causes of angle occlusion (for example: lens intumescence, lens subluxation, iris neovascularisation, ocular inflammation and trauma). Two forms of primary angle-closure glaucoma are recognised; these are based on the mechanism of angle closure: pupillary block and plateau iris.

In the pupillary block form of primary angle-closure glaucoma, the initiating event is believed to be a functional block between the pupillary portion of the iris and the anterior lens surface, which is associated with mid-dilation of the pupil.[4] This functional block causes a build-up of aqueous in the posterior chamber, leading to a forward shift of the peripheral iris and closure of the anterior chamber angle. Three forms of pupillary block glaucoma may be distinguished on the basis of symptoms and clinical findings: acute angle-closure glaucoma, subacute angle-closure glaucoma and chronic angle-closure glaucoma.

In acute angle-closure glaucoma the symptoms are sudden and severe and patients present with pain, blurred vision and a red eye. During an acute attack the angle is usually totally closed by the iris root and the intraocular pressure is significantly elevated.

In subacute angle-closure glaucoma the symptoms are either mild or absent. Typical intermittent symptoms of headache, eye pain or haloes are experienced when angle closure occurs. Patients usually have normal intraocular pressure. Repeated subacute episodes may occur before an acute attack ensues or before peripheral anterior synechiae, with chronic intraocular pressure elevation, develops. This condition is also referred to as "intermittent" angle-closure glaucoma.

In chronic angle-closure glaucoma no symptoms are experienced until late in the course of the disease, when visual loss occurs. Portions of the anterior chamber are permanently closed by peripheral anterior synechiae and the intraocular pressure is chronically elevated. The term "creeping" angle-closure glaucoma has been used to describe this condition. In this thesis raised intraocular pressure is considered to be more than 21 mmHg. Although this is an arbitrary cut-off point, it is useful for comparison purposes and is in keeping with the criteria accepted by other authors.[5-7] Those patients with normal intraocular pressure (<22 mmHg), a partially closed angle and glaucomatous optic neuropathy with a corresponding glaucomatous visual field are also classified as having chronic angle-closure glaucoma.

In practice, a combination of these clinical types is often seen.[8] A patient presenting with an acute or subacute attack may have a deeply excavated disc in one or both eyes due to long-standing chronic angle-closure glaucoma. Similarly, a patient with chronic angle-closure glaucoma may also be suffering from asymptomatic subacute episodes of angle closure. For this reason many studies refer to only two categories of primary angle-closure glaucoma: acute and chronic, the latter including some subacute cases.

In plateau iris, an anterior position of the ciliary processes results in an abnormal configuration of the peripheral iris.[9] This leads to occlusion of the trabecular meshwork by peripheral iris.

Primary open-angle glaucoma has been comprehensively studied in the West. Much has been learnt about the epidemiology, clinical features and treatment of this condition.[2] Primary angle-closure glaucoma, however, is a relatively uncommon condition in the West and much less is known about the disease. Primary angle-closure glaucoma appears to be significantly more common than primary open-angle glaucoma in Orientals and has been called "the most common form of glaucoma in the world."[10] In view of this statement, it is surprising how few papers have been published on the subject of chronic angle-closure glaucoma.

The so-called "coloureds", who live in the Western Cape, South Africa, have strong historical links with the East, which can be traced back to the 17th century when the Cape was governed by the Dutch East India Company. The ancestors of these people were mainly Southeast Asians (from Indonesia and Malaysia) introduced by the Company to work at the Cape, and indigenous Africans (Khoi-khoi or "Hottentots" and San or "Bushmen") with a subsequent admixture of East Africans (from Madagascar and Mozambique) and Europeans.[11] They form an anthropologically distinct population, the relative recent origin of which is the result of early gene mixing at the Cape.[12] This thesis is a study of primary angle-closure glaucoma in the "coloured" people, with particular emphasis on chronic angle-closure glaucoma.

1.2 Historical Review

In this thesis, a detailed discussion of the relevant literature is found in each chapter. The purpose of this review is therefore to provide an historical overview of the subject of primary angle-closure glaucoma. The book by Hyams, published in 1990, is particularly useful and provides a comprehensive and detailed review of angle-closure glaucoma.[8] The book by Louw and Lim, published in 1989, is essentially a colour atlas combined with a summary of Louw's earlier studies, and is less useful.[13]

The early history of angle-closure glaucoma has been well documented by Louw and Duke-Elder.[14,15] Three early references to this condition are worth noting. In the Hippocratic aphorisms, one of the two descriptions of blindness may refer to angle-closure glaucoma "when headaches develop in cases of ophthalmia and accompany it for a long time there is a risk of blindness." The 13th century Syrian, Salah Yusuf Hannah, described a condition that he called "migraine of the eye" that resembles modern descriptions of acute angle-closure glaucoma. Richard Banister, a British oculist, published a clear description of end-stage or absolute glaucoma, which included the observation that the eye was hard on palpation.

The term "acute glaucoma" was first used by Lawrence in 1829 in describing ocular inflammation.[15] Glaucomatous cupping was noted after the development of the ophthalmoscope by von Helmholtz in 1851[15] Further understanding came with the studies of aqueous humour circulation in animal and human eyes by Leber,

Weber and Knies[15] However, the association between shallow anterior chambers and acute attacks of angle-closure glaucoma only became clear in the late 19th century. Smith supported the theory of glaucoma being caused by obstruction to outflow of intraocular fluid, resulting from obliteration of the angle of the anterior chamber by the root of the iris.[14] It was during this time that von Graefe proposed iridectomy as a treatment for glaucoma.[16] Although he performed the operation on thousands of glaucoma patients, obtaining the most beneficial results, he never could explain why the iridectomy was effective.

In 1920 Curren introduced the concept of physiological obstruction of the flow of aqueous humour through the pupil from the chamber to the anterior chamber.[17] Raeder proposed the first anatomical classification in 1924 and distinguished between "shallow chamber glaucoma" and "deep chamber glaucoma."[15] In 1931, Curren reported peripheral iridotomy to be successful in eyes with shallow chambers, but not in eyes with normal depths.[17] With the development of the gonioscope by Saltzmann, Koeppe and Troncoso the mechanism of angle closure was confirmed.[18-20] The modern gonioscopic classification was originally suggested by Barkan in 1938 and elaborated by Sugar in 1941.[1,21] Chandler further advanced the understanding of the anatomical relationships underlying the physiological changes involved in pupillary block.[22]

In 1969 van Herick reported a method of estimating the width of the angle of the anterior chamber.[23] The system of angle grading which is used almost universally today was introduced by Shaffer and records the angle in degrees of arc subtended by the inner surface of the trabecular meshwork and the anterior surface of the iris, at about one third of the distance from its periphery[24] (Figure 1.1).

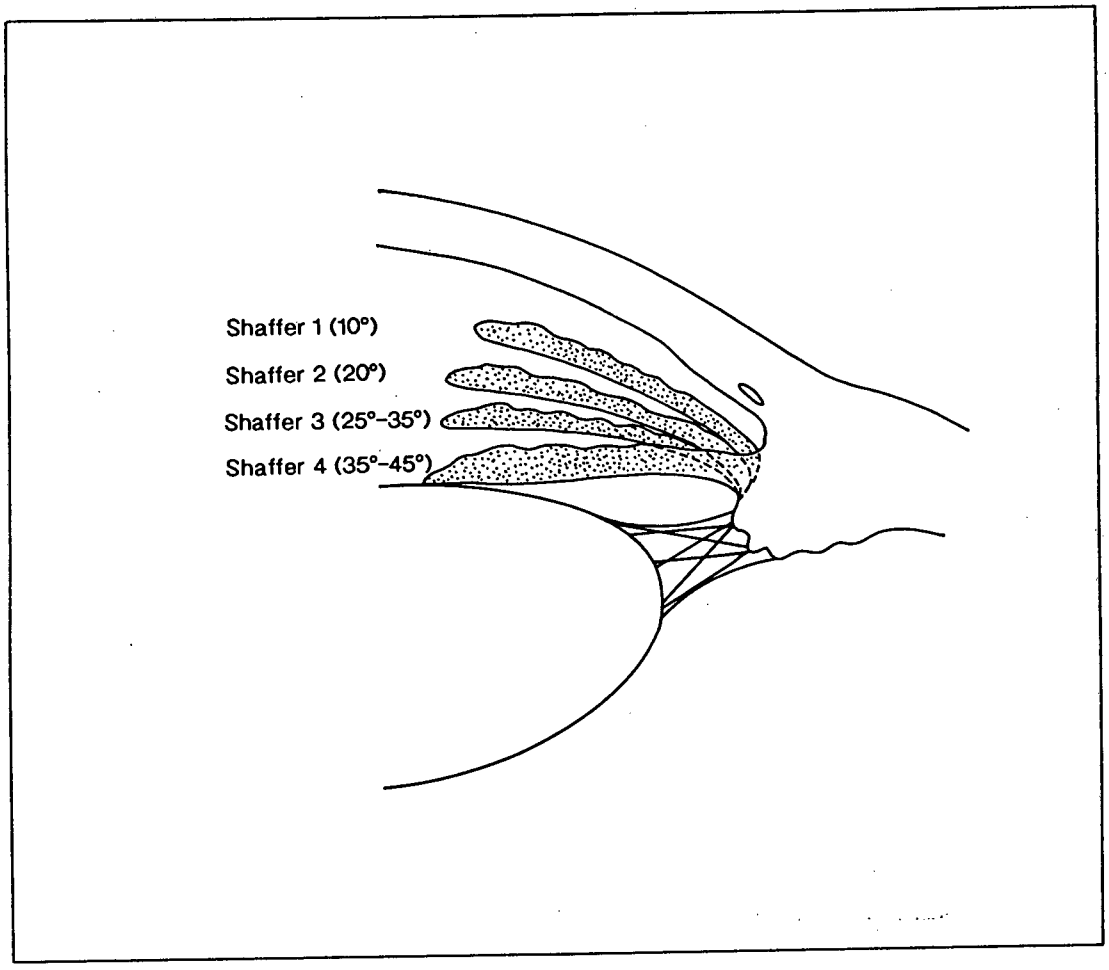

Figure 1.1 Shaffer's gonioscopic classification of the anterior chamber angle, based on the angular width of the angle recess.

In practice, the examiner grades the angle either by a rough estimation of the number of degrees of arc or according to the visibility of the various angle structures. This makes Shaffer's system of grading similar to that suggested earlier by Scheie, except that the grades are numbered in the opposite direction[25] (Figure 1.2). Spaeth subsequently proposed a more precise system that recorded the geometric angle, the configuration of the iris root and the insertion of the iris into the ciliary body.[26] In 1960 Gorin introduced the concept of "shortening of the angle" and in 1964 Lowe described "creeping angle closure".[27,28] In a series of studies Lowe investigated and described the biometry of eyes with primary angle-closure glaucoma.[29]

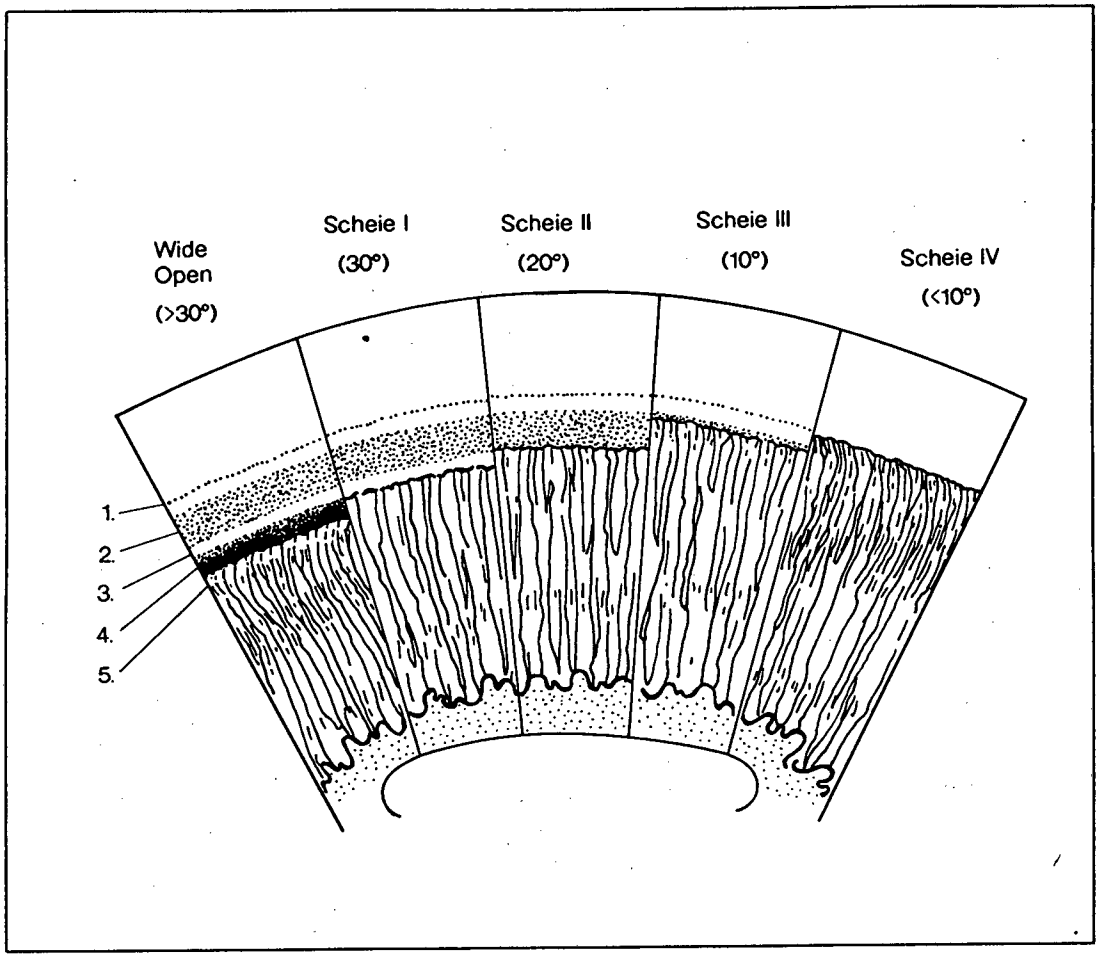

Figure 1.2 Scheie's gonioscopic classification of the anterior chamber angle, based on the extent of visible angle structures: 1. Schwalbe's line; 2. trabecular meshwork; 3. scleral spur; 4. ciliary body band; 5. root of the iris.

A literature review of the epidemiology of primary angle-closure glaucoma is found in Chapters 2 and 3. The relevant literature concerning the aetiology, mechanisms and clinical features of primary angle-closure glaucoma is reviewed in detail in Chapters 4-7. The development of the laser has revolutionised the surgical treatment of angle-closure glaucoma and the literature relating to the therapy of chronic angle-closure glaucoma is reviewed in Chapters 8-10.

1.3 Aims and Organisation of the Thesis

The aim of this thesis is to examine fully the disease of primary angle-closure glaucoma in the people of mixed ethnic background who live in the Cape Peninsula, South Africa. It comprises a series of clinical studies, each addressing an aspect of the disease. Particular attention has been paid to chronic angle-closure glaucoma and its management. The patients described were studied at Groote Schuur Hospital, Cape Town, between 1986 and 1991 and a prevalence study was undertaken in the village of Mamre, situated 56km from Cape Town, in 1992.

The following aspects are considered and each is covered in one chapter: the role of ethnicity in the frequency of primary angle-closure glaucoma (a hospital-based prevalence survey); the prevalence of this disease in Mamre (a village in the Western Cape where the inhabitants have a similar ethnic background to those studied at Groote Schuur Hospital); the aetiology of the disease (specifically examining the dimensions of eyes with chronic angle-closure glaucoma); the pathogenesis of the condition (a study of the mechanism of angle occlusion in chronic angle-closure glaucoma); the presenting features of primary angle-closure glaucoma in these people; the association of this disease with iridoschisis and iris atrophy; the role of prophylactic laser iridotomy in the prevention of chronic angle-closure glaucoma in eyes at risk; and the therapy of chronic angle-closure glaucoma (the role of Nd-YAG laser iridotomy and trabeculectomy in the treatment of this form of glaucoma).

1. **The role of ethnicity in the frequency of primary angle-closure glaucoma.** It has been previously established that primary angle-closure glaucoma is significantly more common than primary open-angle glaucoma in Asia, whereas in Africa and

Europe the situation is reversed. In order to study the role of ethnic background in the frequency of primary angle-closure glaucoma in Cape Town and in particular in people of mixed ethnic background, all patients with primary glaucoma who attended the glaucoma clinic at Groote Schuur Hospital during a 30-month period were reviewed. Primary angle-closure glaucoma was diagnosed in 17% (11/63) of whites, 13% (11/85) of blacks and 46.7% (114/244) of "coloureds" with primary glaucoma; a difference that is statistically highly significant ($P<0.001$). The HLA antigen frequencies in 97 "coloured" patients with primary angle-closure glaucoma were similar to those found in a control group of individuals with a similar ethnic background. This study highlights the fact that Cape people of mixed ethnic background are more predisposed to primary angle-closure glaucoma than are whites or blacks. Because of their strong historical and genetic ties to Southeast Asia, this greater propensity to primary angle-closure glaucoma might be explained by an Oriental genetic influence on the structures of the eye, rather than by an African or European genetic influence.

2. **The prevalence of primary angle-closure glaucoma in Mamre, Western Cape.** To determine the prevalence of primary angle-closure glaucoma in Cape people of mixed ethnic background, a population-based prevalence survey of individuals aged 40 years or older residing in Mamre, a village near Cape Town, was undertaken. Of a total of 1194 people, 987 (82.7%) were examined. Primary angle-closure glaucoma was diagnosed in individuals with previous acute or intermittent symptoms of angle closure and in individuals with an "occludable" angle and an intraocular pressure greater than 21 mmHg or a glaucomatous visual field. An age-related trend towards hypermetropia was found; this was greatest in women over the age of 50 years. Gonioscopy identified Shaffer grade 1 angles in 9% (89/987). The prevalence of primary angle-closure glaucoma was 2.3% (23/987) and increased with age in both sexes. Women were affected more than four times as often as men and the sex difference persisted across all age groups. Twenty

people had chronic angle-closure glaucoma and three had subacute angle-closure glaucoma. In comparison, the prevalence of primary open-angle glaucoma was 1.5% (15/987). Primary glaucoma was the leading cause of bilateral blindness in the community, with a prevalence rate of 0.5% (5/983). This survey identifies primary angle-closure glaucoma, and chronic angle-closure glaucoma in particular, as a significant public health problem in the Western Cape Province. Because of the ethnic background of the people studied, these findings may also apply to the populations of Southeast Asia.

3. **The dimensions of eyes with chronic angle-closure glaucoma.** The aetiology of the disease can be understood by studying the relationships between the different structures in the eyes of patients with chronic angle-closure glaucoma. To determine the ocular measurements in people of mixed ethnic background with chronic angle-closure glaucoma, contact A-scan ultrasonography and keratometry was performed on 46 patients with this diagnosis. The measurements were compared with those found in 23 matched individuals with normal eyes. The correlation between the measurements found in the right and left eyes of both groups was statistically highly significant ($P=0.0001$) and thus only the right eye measurements are reported. Although the mean axial length was less (22.43 mm v. 23.17 mm, $P=0.0001$), the mean anterior chamber depth shallower (2.48 mm v. 2.80 mm, $P=0.0002$) and the mean "relative lens position" more anterior in eyes with chronic angle-closure glaucoma compared with normal, the mean lens thickness in both groups was the same (4.73 mm). These measurements are significantly different from those reported in other ethnic groups. Contrary to what has been found in Western studies, an anterior position of the lens, without significant enlargement of the lens, is mainly responsible for the crowded anterior segment in our patients with chronic angle-closure glaucoma.

4. **The mechanism of angle occlusion in chronic angle-closure glaucoma.** It has been previously established that Asian and African patients with primary angle-closure glaucoma commonly present with an asymptomatic gradual chronic closure of the angle. The aim of this study was to establish whether mechanisms other than pupillary block play a role in the pathogenesis of chronic angle-closure glaucoma. In order to study the mechanism of angle occlusion, 33 patients of mixed ethnic background with chronic angle-closure glaucoma underwent a series of provocative tests. The responses were recorded in those eyes in which the pupillary block mechanism had been eliminated by means of a laser iridotomy. Two groups were defined: 25 eyes of 16 patients were designated as having a steep iris (a subtended angle of 10° - 20°) and 26 eyes of 17 patients as having a plateau iris. Of the 25 eyes with a steep iris plane, 1 (4%) demonstrated a rise of intraocular pressure of 8 mmHg or more to light and dark prone provocative testing. In comparison, of 26 eyes with a plateau iris, 17 (65%) and 20 (77%) were positive to these tests respectively, a difference that is statistically significant (corrected $P<0.001$). These results suggest that plateau iris syndrome may play an important role in the pathogenesis of chronic angle-closure glaucoma in this ethnic group.

5. **The presenting features of primary angle-closure glaucoma and the recognition of an asymptomatic presentation of chronic angle-closure glaucoma.** To examine the presenting features and effect of primary angle-closure glaucoma on people of mixed ethnic background, all "coloured" patients who presented at Groote Schuur Hospital with this diagnosis during a 5-year period were studied. Of the 92 patients, 33 (36%) presented with acute angle-closure glaucoma and 59 (64%) with chronic angle-closure glaucoma. The level of intraocular pressure on presentation correlated well with the number of quadrants of angle closure (correlation coefficient: $r = 0.73$; $P<0.001$). When individual eyes were assessed, a mean cup : disc ratio of $\geq$ 0.8 was present in 35% (65/184) and glaucomatous

visual field loss was present in 56.5% (104/184). Total uniocular blindness secondary to chronic angle-closure glaucoma was found in 16 patients (17%). This study indicates that "coloured" patients with primary angle-closure glaucoma are more likely to present with chronic symptoms and signs and that the disease may result in devastating ocular damage and visual loss. Similar findings have been reported in Asians and in Africans with primary angle-closure glaucoma. In patients of mixed ethnic background with signs of primary glaucoma, chronic angle closure should be excluded by careful gonioscopic evaluation of the drainage structures of the eye.

6. **The association of iridoschisis and primary angle-closure glaucoma:** "Iridoschisis" is the term used to describe a localised cleavage of the iris stroma into two layers. The anterior leaf of iris disintegrates into fibrils which float freely in the anterior chamber. Twelve patients with iridoschisis in one or both eyes were studied to determine the clinical features of the condition and to examine the relationship of iridoschisis to primary angle-closure glaucoma. A spectrum of iris pathology, from subtle intrastromal atrophy to extensive splitting of the anterior layer of iris with fibrillar disintegration, was found in the affected and fellow eyes. Gonioscopy revealed partial or complete chronic angle closure, particularly involving the superior angle, in all patients. Seven had glaucomatous disc damage and 5 had normal discs. The mean axial length and anterior chamber depth measurements in patients with iridoschisis were similar to those found in matched patients with chronic angle-closure glaucoma, but significantly less than the measurements found in matched normals ($P<0.001$). This study suggests that iridoschisis is an unusual manifestation of iris stromal atrophy and results from intermittent or acute elevation of intraocular pressure. Primary angle-closure glaucoma should be excluded in patients who present with iridoschisis.

7. **The role of prophylactic Nd-YAG laser iridotomy in the prevention of chronic angle-closure glaucoma.** The performance of a prophylactic peripheral iridectomy to prevent pupillary block in the fellow eye of patients with acute glaucoma is accepted practice. However, the benefit of prophylactic iridotomy in asymptomatic individuals considered to be at risk of developing primary angle-closure glaucoma or in the fellow eye of patients with unilateral chronic angle-closure glaucoma is not as clearly defined. To examine the results and risks of Nd-YAG laser iridotomy performed prophylactically in the asymptomatic fellow eye of patients with chronic angle-closure glaucoma in one eye, 17 consecutive patients treated in this manner were studied. A small haemorrhage occurred at the iridotomy site in 7 eyes (41%) and a mild transient iritis was noted in all eyes. The intraocular pressure rose above 10 mmHg in 3 eyes and above 20 mmHg in 2 eyes (29.4%) despite pre-treatment with oral acetazolamide, but returned to normal within 24 hours in each case. After a mean follow-up of 33 months, the intraocular pressure remained below 21 mmHg in 12 eyes (70.6%). In 5 eyes the intraocular pressure rose above 21 mmHg with time. Four of these 5 eyes had a plateau iris and in one, progressive chronic angle closure occurred despite the presence of a patent iridotomy. This study suggests that the risks of Nd-YAG laser iridotomy are small enough to justify this form of therapy in eyes considered to be at risk of developing primary angle-closure glaucoma. Although long-term follow-up is required before a definitive conclusion can be reached, it appears that progressive angle closure may be prevented with laser iridotomy in eyes with a steep iris plane at risk of developing pupillary block. Particular attention should be paid to excluding the presence of a plateau iris in people of mixed ethnic background, since these patients require careful follow-up and additional dilute topical pilocarpine therapy on a daily basis to prevent angle occlusion secondary to plateau iris syndrome.

8. **Long-term intraocular pressure control after Nd-YAG laser iridotomy in chronic angle-closure glaucoma.** To evaluate the long-term results of Nd-YAG laser iridotomy, a study was undertaken of 52 consecutive patients (78 eyes) with chronic angle-closure glaucoma who had undergone Nd-YAG laser iridotomy. After a mean follow-up of 22 months the intraocular pressure was less than 22 mmHg without additional treatment in 7 eyes (9%) and with glaucoma medication in 40 eyes (51.3%). At the last follow-up visit, the intraocular pressure was between 22 mmHg and 24 mmHg on an average of two medications in 8 eyes (10.2%). Trabeculectomy was required in 23 eyes (29.5%). Those eyes with an intraocular pressure on presentation of more than 35 mmHg, or with three or more quadrants of angle closure or with a cup : disc ratio of more than 0.6, were more likely to undergo trabeculectomy. However, linear discriminant analysis of the ocular findings on presentation revealed that those eyes which underwent trabeculectomy could only have been predicted in 78% and that 36% of eyes considered to be at risk, which were subsequently controlled with or without glaucoma medication, would have undergone unnecessary trabeculectomy (prediction accuracy: 57%). This study confirms that the current practice of Nd-YAG laser iridotomy, followed if necessary by medical therapy and trabeculectomy, is effective in the management of chronic angle-closure glaucoma. However, careful long-term monitoring of intraocular pressure control and visual field performance is required in patients with advanced disease.

9. **The role of trabeculectomy in the treatment of advanced chronic angle-closure glaucoma.** To examine the results and complications of trabeculectomy performed for advanced angle-closure glaucoma, a retrospective study was undertaken of 39 patients (46 eyes) with chronic angle-closure glaucoma

who had undergone trabeculectomy during a 5-year period. The main indication for trabeculectomy was an inability to control the intraocular pressure on glaucoma medication. Surgery was not complicated by visual loss or malignant glaucoma. The intraocular pressure was successfully reduced to below 21 mmHg in 30 eyes (66.7%) without medication and in a further 11 eyes (24.4%) with additional topical glaucoma medication after a mean follow-up period of 19 months. A second trabeculectomy was required in 4 patients (mean period: 35.8 months later) and a cataract extraction with intraocular lens implantation was required in 9 patients (mean period: 23.9 months later). These results indicate that although trabeculectomy is effective and relatively safe in the management of advanced chronic angle-closure glaucoma, at least one-third of patients will require a second operation within 3 years.

1.4 References

1. Barkan O. Glaucoma: classification, causes and surgical control. *Am J Ophthalmol* 1938; **21** : 1099-1113.
2. American Academy of Ophthalmology. *Primary Open-Angle Glaucoma. Preferred Practice Pattern.* San Francisco: AAO, 1992.
3. Barkan O. Narrow-angle glaucoma: Pupillary block and the narrow-angle mechanism. *Am J Ophthalmol 1954;* **37** : 332-350.
4. Mapstone R. Mechanics of pupil block. *Br J Ophthalmol* 1968; **52** : 19-25.
5. Drance SM. Angle-closure glaucoma among Canadian Eskimos. *Can J Ophthalmol* 1973; **8** : 252-254.
6. Leighton DA, Phillips CI, Tsukahara S. Profile of presenting states of eyes in angle-closure glaucoma. *Br J Ophthalmol* 1971; **55** : 577-584.
7. Pollack IP. Chronic angle-closure glaucoma. Diagnosis and treatment in patients with angles that appear open. *Arch Ophthalmol* 1971; **85** : 676-689.
8. Hyams S. *Angle-Closure Glaucoma. A Comprehensive Review of Primary and Secondary Angle-Closure Glaucoma.* 1st ed. Amsterdam: Kugler and Ghedini, 1990.
9. Pavlin CJ, Ritch R, Foster FS. Ultrasound biomicroscopy in plateau iris syndrome. *Am J Ophthalmol* 1992; **113** : 390-395.
10. Congdon N, Wang F, Tielsch JM. Issues in the epidemiology and population-based screening of primary angle-closure glaucoma. *Surv Ophthalmol* 1992; **36** : 411-423.
11. Marais JS. *The Cape Coloured People. 1652-1937* 1st ed. Johannesburg, Witwatersrand University Press, 1957; 1-31.

12. Botha MC. Blood group gene frequencies: an indication of the genetic constitution of population samples in Cape Town. *S Afr Med J* 1972; **46**: suppl, 1-27.

13. Lowe RF, Lim ASM. *Primary Angle-Closure Glaucoma* 1st ed. Singapore: PG Publishing, 1989.

14. Lowe RF. Primary angle-closure glaucoma: a short history. *Trans Ophthalmol Soc Aust* 1965; **24** : 80-88.

15. Duke Elder S. *System of Ophthalmology. Diseases of the Lens and Vitreous; Glaucoma and Hypotony*. Vol. 11. St Louis; CV Mosby. 1969; 379-388.

16. von Graefe A. Iridectomy in glaucoma: a study of the glaucomatous process. (A shortened version of the original work which appeared in *Arch f Augenheilk* 1857; **3** : 108, abstracted and translated into English by Adler FH). *Arch Ophthalmol* 1929; **1** : 71-86.

17. Curren EJ. Peripheral iridotomy in acute and chronic glaucoma: some results after ten years duration: anatomical classification of glaucoma. *Trans Ophthalmol Soc UK* 1931; **51** : 520-538.

18. Salzmann M. Die Ophthalmoskopie der Kammerbucht *Z Augenheilk*, 1914; **31** : 1-19.

19. Koeppe A. Das stereo-mikroskopische Bild des lebenden Kammerwinkels an der Nernstspaltlampe beim Glaukom. *Klin Monatsbl Augenheilk* 1920; **65** : 389-391.

20. Troncoso MU. Gonioscopy and its clinical applications. *Am J Ophthalmol* 1925; **8** : 433-449.

21. Sugar HS. Newer conceptions in the classification of the glaucomas. *Am J Ophthalmol* 1949; **32** : 425-433.

22. Chandler PA. Narrow-angle glaucoma. *Arch Ophthalmol* 1952; **47** : 695-700.

23. van Herick W, Shaffer RN, Schwartz A. Estimation of width of angle of anterior chamber, incidence and significance of the narrow angle. *Am J Ophthalmol* 1969; **68** : 626-629.

24. Shaffer RN. Gonioscopy In: Symposium on Glaucoma. *Transactions of the New Orleans Academy of Ophthalmology* St Louis: CV Mosby, 1975; 210-220.

25. Scheie HG. Width and pigmentation of the angle of the anterior chamber: a system of grading by gonioscopy. *Arch Ophthalmol* 1957; **58** : 510-512.

26. Spaeth GL. The normal development of the human anterior chamber angle: a new system of descriptive grading. *Trans Ophthalmol Soc UK* 1971; **91** : 709-739.

27. Gorin G. Shortening of the angle of the anterior chamber in angle-closure glaucoma. *Am J Ophthalmol* 1960; **49** : 141-146.

28. Louw RF. Primary creeping angle-closure glaucoma. *Br J Ophthalmol* 1964; **48** : 544-550.

29. Louw RF. Aetiology of the anatomical basis for primary angle-closure glaucoma. *Br J Ophthalmol* 1970; **54** : 161-169.

2.0 The Role of Ethnicity in the Frequency of Primary Angle-Closure Glaucoma.

2.1 Introduction

In Western Europe and North America primary angle-closure glaucoma is significantly less common than chronic open-angle glaucoma.[1-3] The situation is reversed in East and Southeast Asia however, where primary angle-closure glaucoma has been reported to be more common than primary open-angle glaucoma[3-10] (Figure 2.1). It is interesting to note that the ethnic group with the highest prevalence of primary angle-closure glaucoma are the Eskimos, who are a mongoloid people thought to be related to the people of East Asia.[3, 11-13]

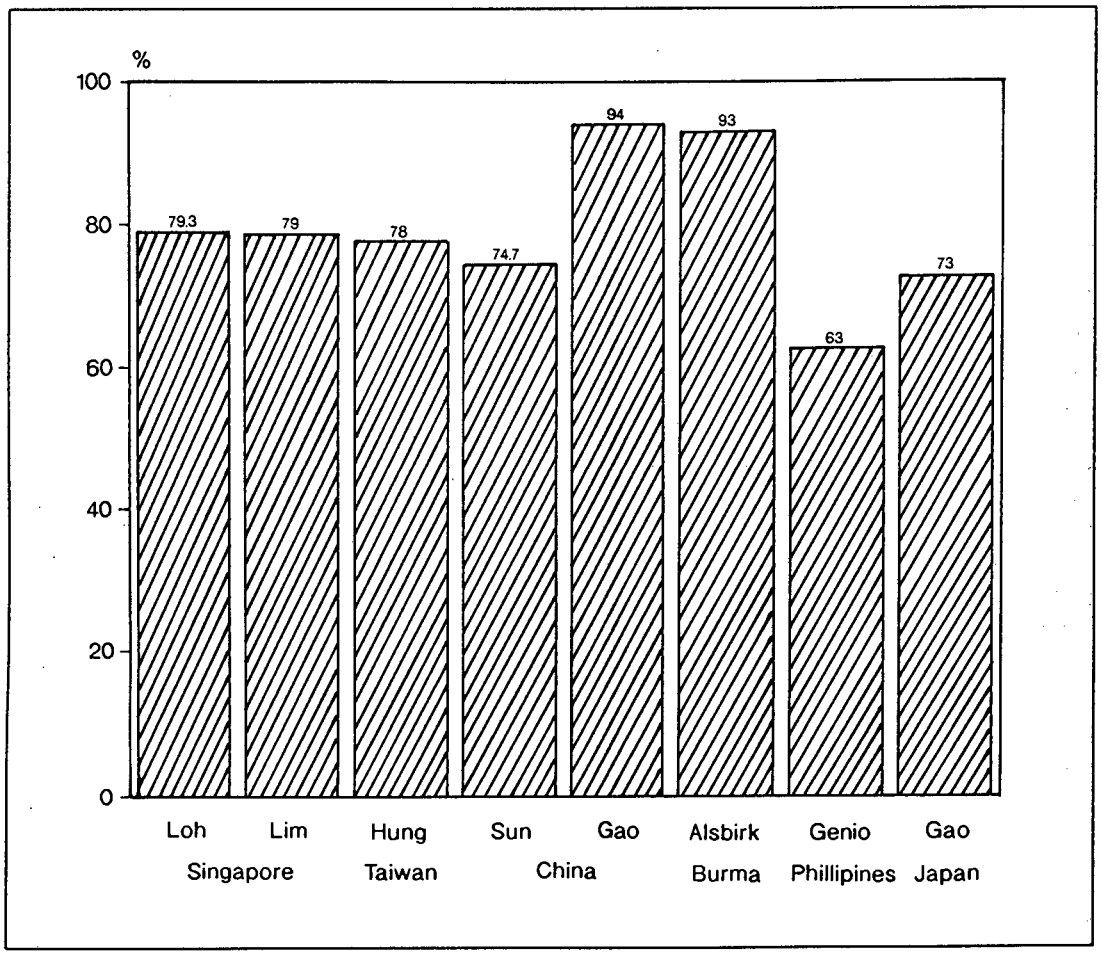

Figure 2.1
Estimates of the relative frequency of primary angle-closure glaucoma among cases of primary glaucoma in Asia, from hospital-based case series.

In the Western Cape, South Africa, the so-called "coloured" people of mixed ancestry have strong genetic links with the East which can be traced back to the 17th century when the Cape was governed by the Dutch East India Company.[14] Their ancestors were mainly Southeast Asians (from Indonesia and Malaysia) and indigenous Africans (Khoi-khoi and San) and to a lesser extent East Africans (from Madagascar and Mozambique), West Africans and Europeans. They form an anthropologically distinct population, whose relatively recent origin is the result of early gene mixing at the Cape.[15]

To determine whether the Southeast Asian ancestry in this ethnic group results in a greater prevalence of primary angle-closure than that found in whites or blacks in Cape Town, all patients with primary glaucoma who attended the glaucoma clinic at Groote Schuur Hospital during a 30-month period were reviewed (Figure 2.2). The ratio of primary angle-closure glaucoma to primary open-angle glaucoma was determined in three ethnic groups: whites, blacks and "coloureds". In addition, the frequencies of the histocompatibility antigens were evaluated in 97 "coloured" patients of mixed ancestry with primary angle-closure glaucoma.

Figure 2.2
Groote Schuur Hospital, Cape Town.

2.2 Patients and Methods

All patients with primary glaucoma who attended the glaucoma clinic at Groote Schuur Hospital between July 1988 and December 1990 were reviewed. Of the 392 patients, 243 (62%) were "coloureds", 86 (22%) were blacks and 63 (16%) were whites.

The diagnosis of primary angle-closure glaucoma was made if the intraocular pressure was > 21 mmHg in the presence of a partially or totally occluded angle in at least one eye and was made irrespective of the optic nerve appearance. Most patients had chronic angle-closure glaucoma.[16] Secondary causes of angle closure such as iris neovascularisation, lens intumescence and subluxation, trauma and uveitis were specifically excluded. Primary open-angle glaucoma was diagnosed if

an open angle was found on gonioscopy in a patient with glaucomatous disc cupping and a corresponding visual field loss.

Histocompatibility antigens were determined in 97 patients of mixed ethnic background with primary angle-closure glaucoma. HLA-A, -B, and -C typing was performed by the NIH complement-dependent microdroplet lymphocyte toxicity technique.[17] B cells, separated from peripheral blood by the nylon-wool method, were used for HLA-DR and -DQ typing performed by the technique agreed upon for the Seventh International Histocompatibility Workshop.[18, 19] Local antisera as well as sera obtained by exchange with other laboratories were used. A control group was drawn from people with the same ethnic background and consisted of 3716 individuals for the comparison of the HLA class I antigen frequencies and 549 individuals for the comparison of HLA class II antigen frequencies. Frequencies were compared between patients and controls at 16 A-locus, 29 B-locus, 8 C-locus, 10 DR-locus and 3 DQ-locus HLA antigens, using the Chi-square test for proportions with Yates' correction. The P-values were multiplied by the number of comparisons made, as there was no prior reason to suspect any significant differences would be found. A corrected P-value of <0.05 was considered statistically significant. The Chi-square test was used to compare the frequency of primary angle-closure glaucoma in the three ethnic groups.

2.3 Results

Primary open-angle glaucoma was almost twice as common as primary angle-closure glaucoma in this clinic. When the ethnic background of the patients was evaluated, it was found that 11 of 63 (17.5%) whites, 11 of 85 (12.9%) blacks and 114 of 244 (46.7%) "coloureds" had primary angle-closure glaucoma (Figure 2.3). The prevalence of primary angle-closure glaucoma in this glaucoma clinic was significantly greater in "coloureds" than in whites or blacks ($P<0.001$).

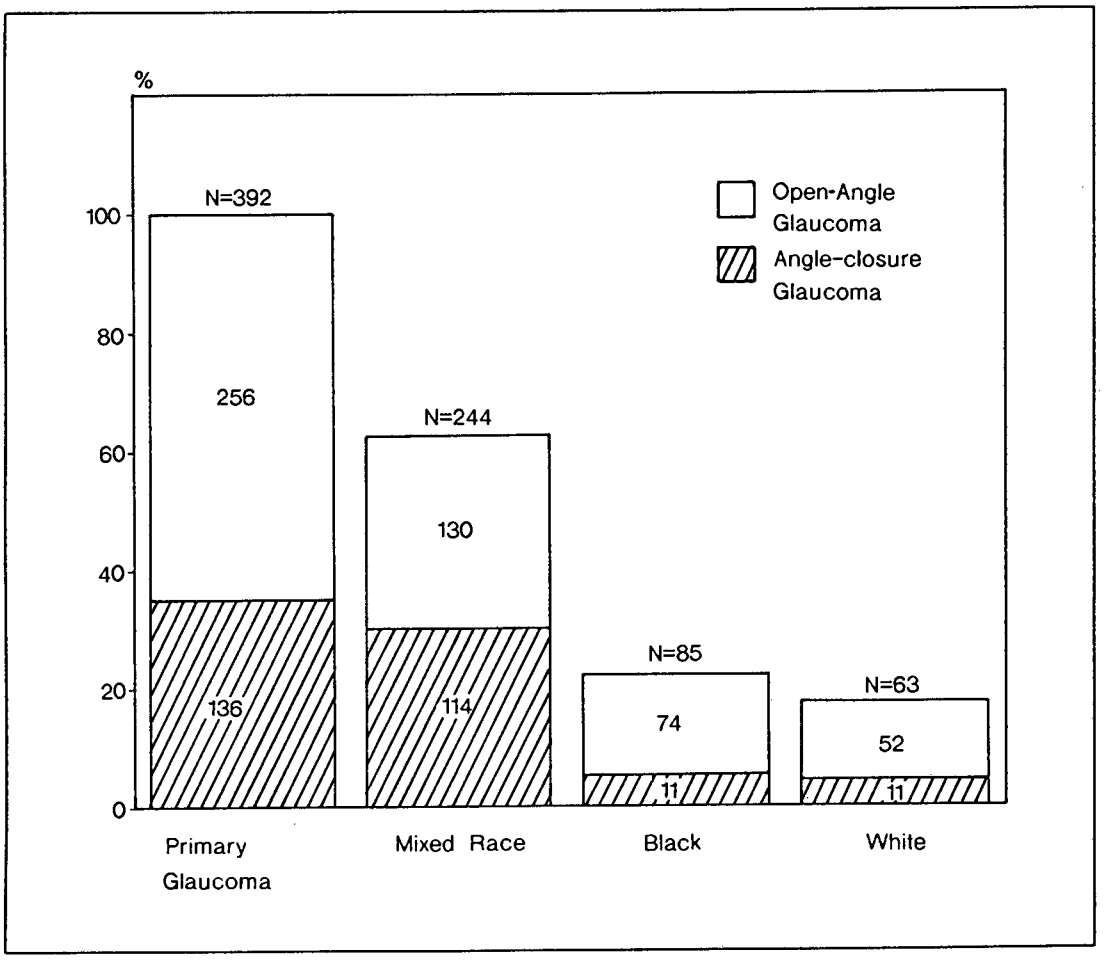

Figure 2.3 Frequency of primary angle-closure glaucoma in three ethnic groups at the glaucoma clinic Groote Schuur Hospital.

When HLA frequencies in patients and controls were compared, no statistically significant differences were noted between the groups (Table 2.1).

TABLE 2.1
HLA PHENOTYPE FREQUENCY IN PATIENTS OF MIXED ANCESTRY WITH PRIMARY ANGLE-CLOSURE GLAUCOMA (PACG) AND CONTROLS.

ANTIGEN	PACG		CONTROLS		YATES	P-VALUE
	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE		
A1	21	76	610	3106	1.5154	0.200<P<0.300
A2	24	73	1160	2556	1.5607	0.200<P<0.300
A3	14	83	552	3164	0.0009	0.950<P<0.980
A10	20	77	559	3157	1.8695	0.100<P<0.200
A11	17	80	469	3247	1.6276	0.200<P<0.300
A23	4	93	427	3289	4.4093	0.020<P<0.050
A24	23	74	701	3015	1.1459	0.200<P<0.300
A28	16	81	586	3130	0.0027	0.950<P<0.980
A29	5	92	326	3390	1.1382	0.200<P<0.300
A30	16	81	679	3037	0.0989	0.700<P<0.800
A31	2	95	84	3632	0.0467	0.800<P<0.900
A32	1	96	220	3496	3.2922	0.050<P<0.100
A33	7	90	242	3474	0.0048	0.900<P<0.950
A36	2	95	32	3684	0.4830	0.300<P<0.500
A43	7	90	207	3509	0.2227	0.500<P<0.700
A74	1	96	140	3576	1.2939	0.200<P<0.300
B7	14	83	756	2960	1.6995	0.100<P<0.200
B8	8	89	350	3366	0.0459	0.800<P<0.900
B13	3	94	147	3569	0.0280	0.800<P<0.900
B14	10	87	255	3461	1.2449	0.200<P<0.300
B15	16	81	440	3276	1.5280	0.200<P<0.300
B18	12	85	367	3349	0.4082	0.500<P<0.700

TABLE 2.1 continued. . . .

HLA PHENOTYPE FREQUENCY IN PATIENTS OF MIXED ANCESTRY WITH PRIMARY ANGLE-CLOSURE GLAUCOMA (PACG) AND CONTROLS.

ANTIGEN	PACG		CONTROLS		YATES	P-VALUE
	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE		
B22	2	95	42	2456	0.0134	0.900<P<0.950
B27	6	91	172	3544	0.2245	0.500<P<0.700
B35	16	81	425	3291	1.8958	0.100<P<0.200
B37	2	95	64	3652	0.0199	0.800<P<0.900
B38	2	95	91	3625	0.0080	0.900<P<0.950
B39	3	94	143	3573	0.0132	0.900<P<0.950
B41	3	94	161	3555	0.1161	0.700<P<0.800
B42	3	94	231	3485	1.1050	0.200<P<0.300
B44	14	83	627	3089	0.2469	0.500<P<0.700
B45	4	93	198	3518	0.0861	0.700<P<0.800
B46	0	97	4	2494	0.8538	0.300<P<0.500
B47	4	93	79	3637	0.9580	0.300<P<0.500
B48	0	97	3	2495	1.3938	0.200<P<0.300
B49	0	97	70	3646	0.9631	0.300<P<0.500
B50	3	94	22	3694	5.6437	0.010<P<0.020
B51	7	90	182	3534	0.6429	0.300<P<0.500
B52	10	87	148	3568	7.9999	0.001<P<0.010
B53	3	94	96	3620	0.0001	0.990<P<1.000
B57	12	85	313	3403	1.4175	0.200<P<0.300
B58	6	91	614	3102	6.6797	0.001<P<0.010
B60	3	94	166	3550	0.1596	0.500<P<0.700
B61	7	90	178	3538	0.7374	0.300<P<0.500

TABLE 2.1 continued. . . .

HLA PHENOTYPE FREQUENCY IN PATIENTS OF MIXED ANCESTRY WITH PRIMARY ANGLE-CLOSURE GLAUCOMA (PACG) AND CONTROLS.

ANTIGEN	PACG		CONTROLS		YATES	P-VALUE
	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE		
B70	8	89	580	3136	3.3830	0.050<P<0.100
C1	3	94	125	3591	0.0194	0.800<P<0.900
C2	8	89	609	3107	4.0389	0.020<P<0.050
C3	11	86	586	3130	1.0892	0.200<P<0.300
C4	33	64	866	2850	5.4447	0.010<P<0.020
C5	2	95	141	3575	0.3795	0.500<P<0.700
C6	33	64	1162	2554	0.2168	0.500<P<0.700
C7	40	57	1536	2180	0.0072	0.900<P<0.950
C8	10	87	259	3457	1.1389	0.200<P<0.300
DR1	13	80	61	488	0.3908	0.500<P<0.700
DR2	39	54	189	360	1.6440	0.100<P<0.200
DR3	16	77	114	435	0.4234	0.500<P<0.700
DR4	21	72	117	432	0.0193	0.800<P<0.900
DR5	28	65	158	391	0.0189	0.800<P<0.900
DR6	22	71	113	436	0.2861	0.500<P<0.700
DR7	20	73	138	411	0.3864	0.500<P<0.700
DR8	6	87	29	520	0.0451	0.800<P<0.900
DR9	5	88	10	539	2.9842	0.050<P<0.100
DR10	3	90	9	540	0.3977	0.500<P<0.700
DQ1	71	22	363	186	3.3430	0.050<P<0.100
DQ2	28	65	149	400	0.2178	0.500<P<0.700
DQ3	50	43	240	309	2.8487	0.050<P<0.100

2.4 Discussion

Previous studies have shown that the prevalence of primary angle-closure glaucoma is influenced by the ethnic background of the population studied[1,2,11-13,20-24] (Table 2.2). In the East, primary angle-closure glaucoma is significantly more common than primary open-angle glaucoma.[3] In the glaucoma clinic at Groote Schuur Hospital, I had the opportunity to compare the relative frequency of this form of glaucoma in three distinct ethnic groups, and in particular was able to determine the relationship between primary angle-closure glaucoma and primary open-angle glaucoma in people of mixed ethnic background, the so-called "coloureds".

TABLE 2.2
PREVALENCE OF PRIMARY ANGLE-CLOSURE GLAUCOMA IN INDIVIDUALS OVER THE AGE OF 40 YEARS IN DIFFERENT ETHNIC GROUPS FROM POPULATION-BASED STUDIES*.

COUNTRY		AUTHOR	PREVALENCE
Wales		Hollows (1)	0.1%
Sweden		Bengtsson (2)	0.1%
Israel		Hyams (20)	0.5%
Greenland	- Eskimo	Clemmesen (11)	5.0%
Canada	- Eskimo	Drance (12)	2.9%
Alaska	- Eskimo	Arkell (13)	2.7%
China		Hu (21)	1.3%
Japan		Shiose (22)	0.3%
South Africa	- Tswana	David (23)	1.0%
	- Pondo	Bartholomew (24)	0.25%

*Figures for America, Continental Europe and Southeast Asia are not available.
The number in parenthesis refers to the number of the reference.

A diagnosis of primary angle-closure glaucoma was made in 11 of 63 (17%) white patients and in 11 of 85 (13%) black patients with primary glaucoma. Although selection bias may play a role in this study, these figures correlate well with those found in Johannesburg in 1973, when it was reported that 35 of 196 (17%) blacks and 60 of 300 (20%) whites with primary glaucoma attending the glaucoma clinic, had primary angle-closure glaucoma.[25] These percentages are significantly less than the 46.7% (114 of 244) found in "coloureds" in this study.

The fact that "coloured" people are more likely to have primary angle-closure glaucoma than blacks or whites was noted in a 1964 study of the types of glaucoma treated in a clinic at Groote Schuur Hospital.[26] Although the criteria for the diagnosis of primary angle-closure glaucoma is not recorded and no comment is made on ethnic differences in the frequency of primary angle-closure glaucoma in this early paper, it can be calculated from the associated table that 61% of "coloureds" (68/112), 23.5% of whites (23/98) and 19.5% of blacks (8/41) with primary glaucoma had primary angle-closure glaucoma.[26] This fact was not recognised by Mann in her book "Culture, Race, Climate and Eye Disease" published in 1966 and was not included in a recent major review on the epidemiology of primary angle-closure glaucoma.[3,27]

This study shows no differences in the histocompatibility antigen profile of patients with primary angle-closure glaucoma and controls. This indicates a lack of association between primary angle-closure glaucoma and histocompatibility antigens and supports the findings of Ritch (20 patients) and Gieser (35 patients) in the United States.[28,29] It also confirms that the "coloured" patients in this study are

significantly different genetically to white and black South Africans and that the sample of patients is representative of the ethnic background from which they were drawn.[15]

It can be concluded that Cape people of mixed ethnic background are significantly more predisposed to primary angle-closure glaucoma than whites or blacks. Because of their strong historical and genetic ties to Southeast Asia, the increased risk of primary angle-closure glaucoma in these people might be explained on the basis of an Oriental genetic influence on the ocular structure of these patients, rather than an African or European genetic influence.

2.5 References

1. Hollows FC and Graham PA. Intraocular pressure, glaucoma and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966; **50** : 570-586.
2. Bengtsson B. The prevalence of glaucoma. *Br J Ophthalmol* 1981; **65** : 46-49.
3. Congdon N, Wang F, Tielsch JM. Issues in the epidemiology and population-based screening of primary angle-closure glaucoma. *Surv Ophthalmol* 1992; **36** : 411-423.
4. Loh PCK. The problem of glaucoma in Singapore. *Singapore Med J* 1968; **9** : 76-80.
5. Lim ASM. PACG in Singapore. *Aust J Ophthalmol* 1979; **7** : 23-30.
6. Hung PT. Aetiology and mechanism of PACG. *Asian Pac J Ophthalmol* 1990; **2** ; 82-84.
7. Sun SJ, Guan JX, Hu RH, Wang XY. A statistical and family-history-based analysis of primary glaucoma. *Chin J Ophthalmol* 1985; **21** : 32-34.
8. Gao PW, Kubota, T, Sujino K *et al.* A statistical comparison of glaucoma in the Third Affiliated Hospital of China Medical College and Kyushu University (Japan). *Acta Soc Ophthalmol Jpn* 1989; **93** : 458-465.
9. Alsbirk PH. Prevention and control of visual impairment and blindness (with special reference to glaucoma) in Burma. *World Health Organization, Consultant Report, SE Asia Region/Ophthalmol* 1984; **78** (5).
10. Genio CA, Gavino BC. Glaucoma profile at the Phillipines General Hospital. *Phillipines J Ophthalmol* 1983; **15** : 1-2.

11. Clemmesen V, Alsbirk PH. Primary angle closure glaucoma in Greenland. *Acta Ophthalmol* 1971; **49** : 47-58.

12. Drance SM. Angle closure glaucoma among Canadian Eskimos. *Arctic Ophthalmol Symposium* 1973; **8** : 252-255.

13. Arkell SM, Lightman DA, Sommer A, Taylor HR, Korshin OM, Tielsch JM. The prevalence of glaucoma among Eskimos of Northwest Alaska. *Arch Ophthalmol* 1987; **105** : 482-485.

14. Marais JS. *The Cape Coloured People. 1652-1937* 1st ed. Johannesburg, Witwatersrand University Press; 1957; 1-31.

15. Botha MC. Blood group gene frequencies. An indication of the genetic constitution of population samples in Cape Town. *S Afr Med J* 1972; **46** (supp), 1-27.

16. Salmon JF. The presenting features of primary angle-closure glaucoma in patients of mixed ethnic background. In press. *S Afr Med J*

17. Terasaki PI, McClelland J, Park MS, McCurdy B. Microdroplet lymphocyte cytotoxicity test. In: Ray JG, Hare DB, Petersen PD, Kayhoe DE (eds) : *Manual of Tissue Typing Techniques* Bethesda, NIH, 1974.

18. Danilovs JA, Ayoub G, Terasaki PI. B lymphocyte isolation by thrombin-nylon wool. In: Terasaki PI (ed) : *Histocompatibility Testing 1980* Los Angeles, UCLA Press, 1980; p 287.

19. Bodmer JG, Pickbourne P, Richards S. Joint report 1a serology. In: Bodmer WF, Batchelor JR, Bodmer JG, Festenstein H, Morris PJ (eds) : *Histocompatibility Testing 1977* Copenhagen, Munksgaard, 1977; p. 35.

20. Hyams SW, Keroub C, Pokotilo E. The computer in clinical research. Prevalence of glaucoma. *Doc Ophthalmol* 1977; **43** : 17-21.

21. Hu Z, Zhao ZL, Dong FT. An epidemiological investigation of glaucoma in Beijing and Shun-yi County. *Chin J Ophthalmol* 1989; **25** : 115-118.

22. Shiose Y, Kitazawa Y, Tsukuhara S *et al.* Epidemiology of glaucoma in Japan : a nationwide survey. *Jpn J Ophthalmol* 1991; **35** 133-155.

23. David R, Stone D. The prevalence of glaucoma in a homogenous African population. In: David R, Ticho V (eds) : *Recent Advances in Glaucoma.* Elsevier Science Publishers BV 1984; pp 145-153.

24. Bartholomew RS. Glaucoma in a South African black population. A population study on the Pondo tribe of South Africa. *S Afr Arch Ophthalmol* 1976; **3** : 135-150.

25. Luntz MH. Primary angle-closure glaucoma in urbanised South African Caucasoid and Negroid communities. *Br J Ophthalmol* 1973; **57** : 445-456.

26. Sacks S. The glaucomas at the Cape. *S Afr Med J* 1964; **38** : 594-595.

27. Mann I. *Culture, Race, Climate and Eye Disease* Springfield, Charles C Thomas Publisher 1966; p 540.

28. Ritch R, Podos SM, Henley W, Moss A, Southren AL, Fotino M. Lack of association of histocompatibility antigens with primary open-angle glaucoma. *Arch Ophthalmol* 1978; **96** : 2204-2206.

29. Gieser DK, Wilensky JT. HLA Antigens and acute angle-closure glaucoma. *Am J Ophthalmol* 1979; **88** : 232-235.

3.0 The Prevalence of Primary Angle-closure Glaucoma in Mamre, Western Cape, South Africa.

3.1 Introduction

Primary angle-closure glaucoma has been reported to be significantly more common than primary open-angle glaucoma in Eastern races.[1] This finding is mainly based on the results of hospital or glaucoma clinic case series.[2,3] Such studies are subject to the criticism that primary angle-closure glaucoma is more likely to cause symptoms such as pain or haloes that will prompt a patient to seek medical attention and that hospital-based studies may thus tend to overestimate the relative importance of primary angle-closure glaucoma.[1] Two population-based prevalence studies have been performed in Asia and prevalence rates of 0.3% (Japan) and 1.3% (China) have been reported.[4-6] Neither used gonioscopic evaluation of the anterior chamber angle to screen an entire community. In addition, the prevalence of primary open-angle glaucoma may have been under-represented because of the greater technical challenge of diagnosing this disease.[1] To my knowledge, there are no glaucoma prevalence rates available for the countries of Southeast Asia.

The "coloured" people form an anthropologically distinct population whose relatively recent origin is the result of early gene mixing at the Cape.[7] Their ancestors were Southeast Asians, Southern and Western Africans and Western Europeans.[7, 8] Based on glaucoma clinic statistics, chronic angle-closure glaucoma has been shown to be more common in Cape patients of mixed ancestry than in whites or blacks[9] (Chapter 2). The presenting features and characteristics of the disease appear to be similar to those described in Southeast Asia.[10]

To determine the prevalence of primary angle-closure glaucoma and the ratio of angle-closure glaucoma to open-angle glaucoma in this ethnic group, the inhabitants of the village of Mamre on the West Cape coast of South Africa were surveyed.

Figure 3.1 The historical village of Mamre

The people in this village have the same ethnic background as "coloureds" residing elsewhere in the Western Cape Province. The village has maintained its distinctive ethnic characteristics and has been the site of several previous epidemiological surveys undertaken by the Department of Community Health of the University of Cape Town and the Centre of Epidemiological Research in Southern Africa of the Medical Research Council.[11] The cooperation of the population has been earned by these previous efforts to detect systemic disease and the number of persons living in the village, as well as their ages and sex are known.

3.2 Patients and Methods

Mamre is situated 56 km from Cape Town (Figure 3.2). The total population of the village is approximately 5000 and at the time of the survey 1194 people were 40 years of age or older. Mamre has a large day-clinic perfectly suitable for the establishment of a temporary eye clinic. The survey was performed during a two week period in May and June 1992 and the targeted population was people of 40 years of age or older.

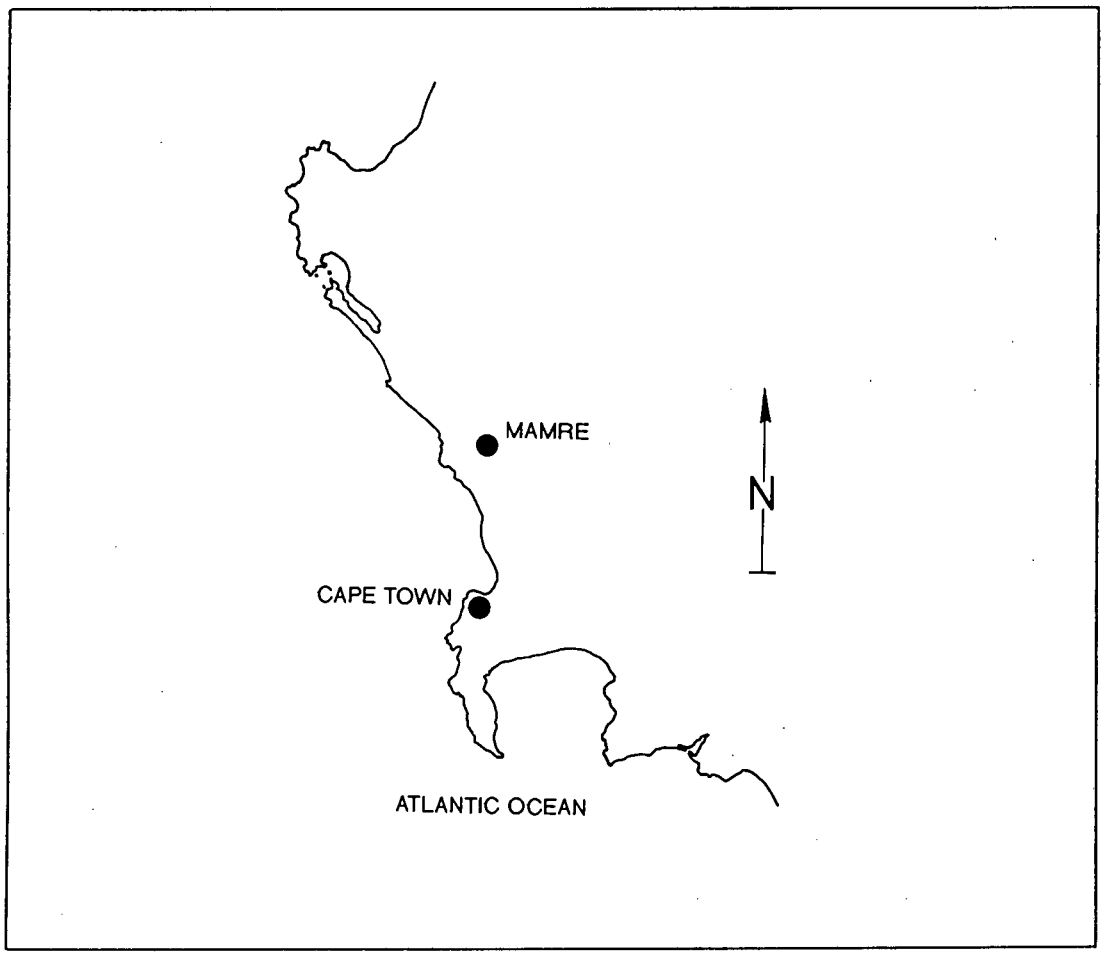

Figure 3.2 Map of Cape Peninsula showing the geographical position of Mamre.

Because of the practical and financial implications of referring large numbers of individuals at risk of having glaucoma to a tertiary teaching hospital, a strategy was planned whereby people were completely examined, and a final diagnosis made,

without them having to leave the village. Approximately 5% of the study population was re-examined at a teaching hospital after the initial period in order to institute therapy.

The field team consisted of three ophthalmologists (two with a sub-speciality interest in glaucoma), an optometrist, an ophthalmic technician and four trained ophthalmic nurses. Two research assistants (motivators) visited the targeted population and made appointments for those willing to take part in the study. Because of a high level of unemployment, many could be examined during the day, but those who were working were examined in the evening or during the weekend. An even daily distribution of people was achieved and the maximum number seen on any one day was 130.

Demographic information was collected from all survey participants, using an interview specifically designed to assess the presence of previous symptoms of intermittent angle closure (headaches, eye pain, haloes). The visual acuity was measured and all sighted patients underwent automated refraction using a Topcon refractor. A complete slit-lamp examination of the anterior segment was performed. The intraocular pressure was measured with a Goldmann applanation tonometer, which was standardised each day.

The drainage angle was examined in both eyes, using a Goldmann one-mirror gonioscope. Angles were graded according to the Shaffer classification, which is based on the angular width of the angle recess. Grade 1 represents a geometric angle of 10°, Grade 2 an angle of 20°, Grade 3 an angle of 25-35° and Grade 4 an angle of 35-45°. A note was made of the numbers of quadrants in which the angle was <10°(a "slit-like" angle). In order to compare these results with others, an

"occludable" angle was considered to be an angle where the pigmented trabecular meshwork was not visible in three quarters of the circumference. A recessed angle was considered to be an angle where significant irregular widening of the ciliary body band was present and particular attention was paid to asymmetry between the eyes.

The optic disc was examined with a direct ophthalmoscope and Goldmann contact lens and the vertical and horizontal cup : disc ratios were recorded. The pupil was dilated in individuals not considered at risk of having angle closure if the fundal view was obscured. A Humphrey "three zone" threshold-related suprathreshold screening visual field test of the central 30° was performed (88 points) in all sighted individuals with an intraocular pressure >21 mmHg, a vertical cup : disc ratio of >0.4 or a vertical cup : disc asymmetry of >0.2. In people with >8 absolute or relative defects, a full threshold field was repeated. These fields were then classified as "definitely" glaucomatous, "probably" glaucomatous or "unlikely" to be glaucomatous. Definitely abnormal fields had medium to large defects (>10° in diameter centrally, twice that beyond 30° from fixation) of at least 0.5 log-unit depth and a shape and distribution typical of optic nerve damage rather than artifact; probably abnormal fields had defects that were either slightly smaller or less dense, but still were atypical for artifact; and unlikely abnormal fields were unreliable or of atypical configuration.[12] In patients who were unable to perform full threshold field analysis, but who had a reliable screening visual field, a glaucomatous field was considered to be one in which at least 17 absolute or relative defects were present in a characteristic pattern.[13]

The diagnosis of acute angle-closure glaucoma was made in individuals with a verified history of acute angle closure attack and an "occludable" angle. Asymptomatic individuals who had either an intraocular pressure of >21 mmHg or

a glaucomatous visual field in the presence of an "occludable" angle, were considered to have chronic angle-closure glaucoma. Subacute cases were defined as those with characteristic symptoms (headaches, eye pain, haloes), an intraocular pressure of <22 mmHg, a full visual field and an "occludable" angle. Provocative tests were not performed. Secondary causes of angle closure such as iris neovascularisation, lens intumescence, lens subluxation and trauma were specifically excluded. Open-angle glaucoma was diagnosed if an open angle was found in the presence of glaucomatous field loss with an optic nerve appearance consistent with that field loss, regardless of intraocular pressure. In those individuals unable to complete the visual field analysis, definite glaucomatous optic nerve damage was present. Post-traumatic glaucoma was diagnosed if >2 quadrants of angle recession was present in association with other features of blunt ocular trauma and the parameters for open-angle glaucoma.

Standard definitions for blindness were used, as proposed by the World Health Organisation and people with a visual acuity of <6/120 in the better eye or with a visual field of less than 10° in the better eye were classified blind.[14]

Statistical analysis was performed using the Wilcoxon 2-sample test and Chi-square analysis. Correlation analysis was performed using Spearman's rank correlation coefficients. A finding was considered significant at $P < 0.05$.

3.3 Results

Of a total of 1194 people who were 40 years of age or older, we examined 987 during a two-week period, achieving a total response rate of 82.7% (987/1194). The median age for men was 52 years (range 40 to 96) and for women was also 52 years (range 40 to 98). Table 3.1 presents the age and sex distribution of those examined.

TABLE 3.1
SEX AND AGE DISTRIBUTION

AGE	MALES		FEMALES	
40 - 49	164	(41.7)	256	(43.1)
50 - 59	99	(25.2)	155	(26.1)
60 - 69	86	(21.9)	116	(19.5)
70 - 79	28	(7.1)	47	(7.9)
80 - 100	16	(4.1)	20	(3.4)
	393	(100)	594	(100)

Numbers of people with percentage in parenthesis.

The median refraction of the right eye in spherical equivalents for each decade is shown in Figure 3.3. Spearman's rank correlation coefficients between the right and left eyes for each decade were greater than 0.79 for both sexes. The differences in men and women were statistically significant for people in their 6th ($P = 0.006$), 7th ($P = 0.002$) and $\geq$ 8th ($P = 0.004$) decades.

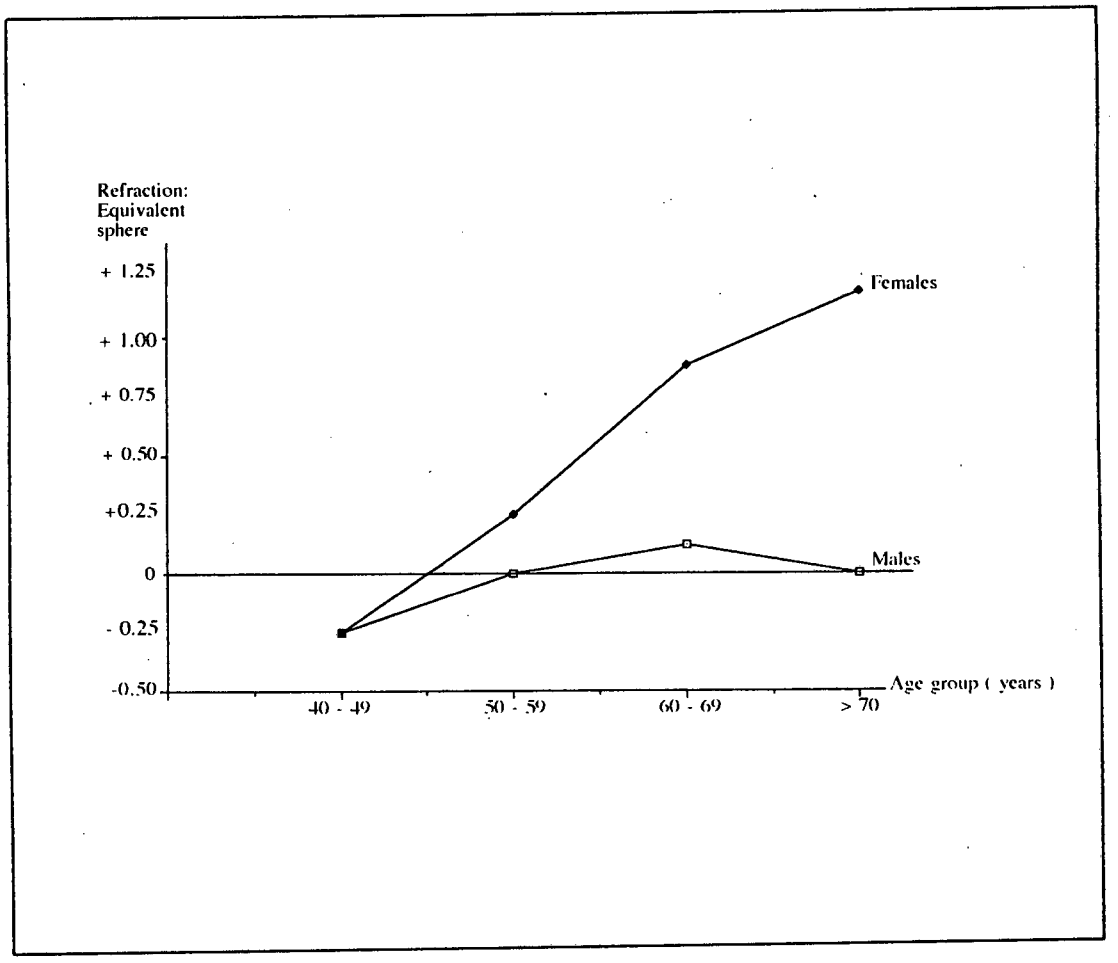

Figure 3.3 Median refraction of the right eye in spherical equivalents for each decade. The differences between men and women is statistically significant for people in their 6th, 7th and ≥8th decades.

The mean intraocular pressure (and one standard deviation) for the population 40 years of age and older was 17.0 mmHg (S.D. 4.7) for men and 17.0 mmHg (S.D. 4.5) for women. The median intraocular pressure for men and women, right and left eyes, was 16 mmHg (with 5% of the population below 12 mmHg and 5% above 23 mmHg).

Gonioscopy identified Shaffer Grade I angles in 5.9% (23/392) of men and 11.1% (66/594) of women. While the proportion of women was greater than the proportion of men for each group, the difference between men and women was statistically significant only for those in the 7th decade (P = 0.012) (Figure 3.4).

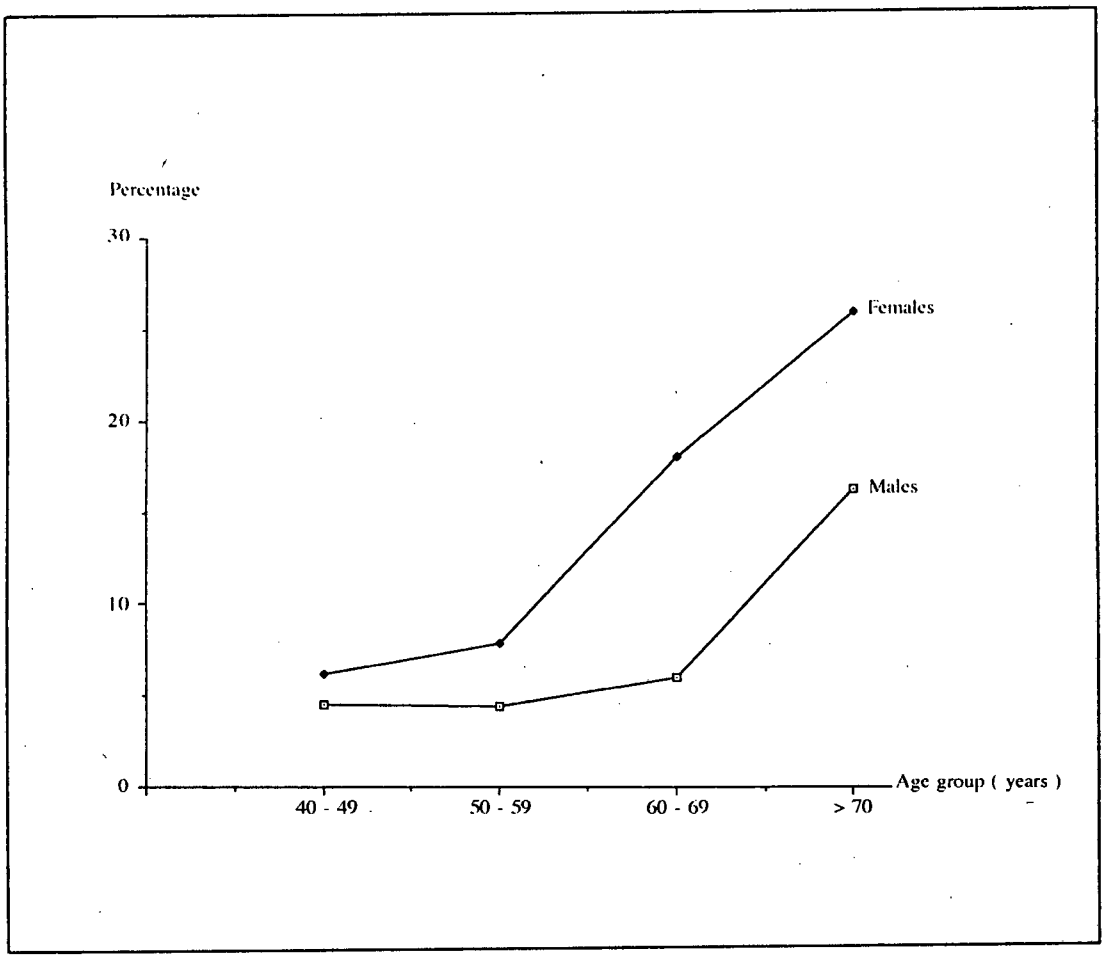

Figure 3.4 Prevalence of Shaffer Grade 1 angle for men and women in decades. The difference between the sexes is statistically significant for people in the 7th decade (P = 0.012).

"Slit-like" angles of 1 to 4 quadrants were found in 2.0% of men (8/392) and 5.4% of women (32/594). The difference between men and women was statistically significant for people in the 7th decade (P = 0.045). Because of a small sample size, the difference between people $\geq$ 8th decades was not statistically significant (P = 0.054) (Figure 3.5). Of 89 people with Shaffer Grade 1 angles, asymmetry was present in 9 (10.1%). Two people had pseudocapsular exfoliation without glaucoma and one had pigment dispersion syndrome.

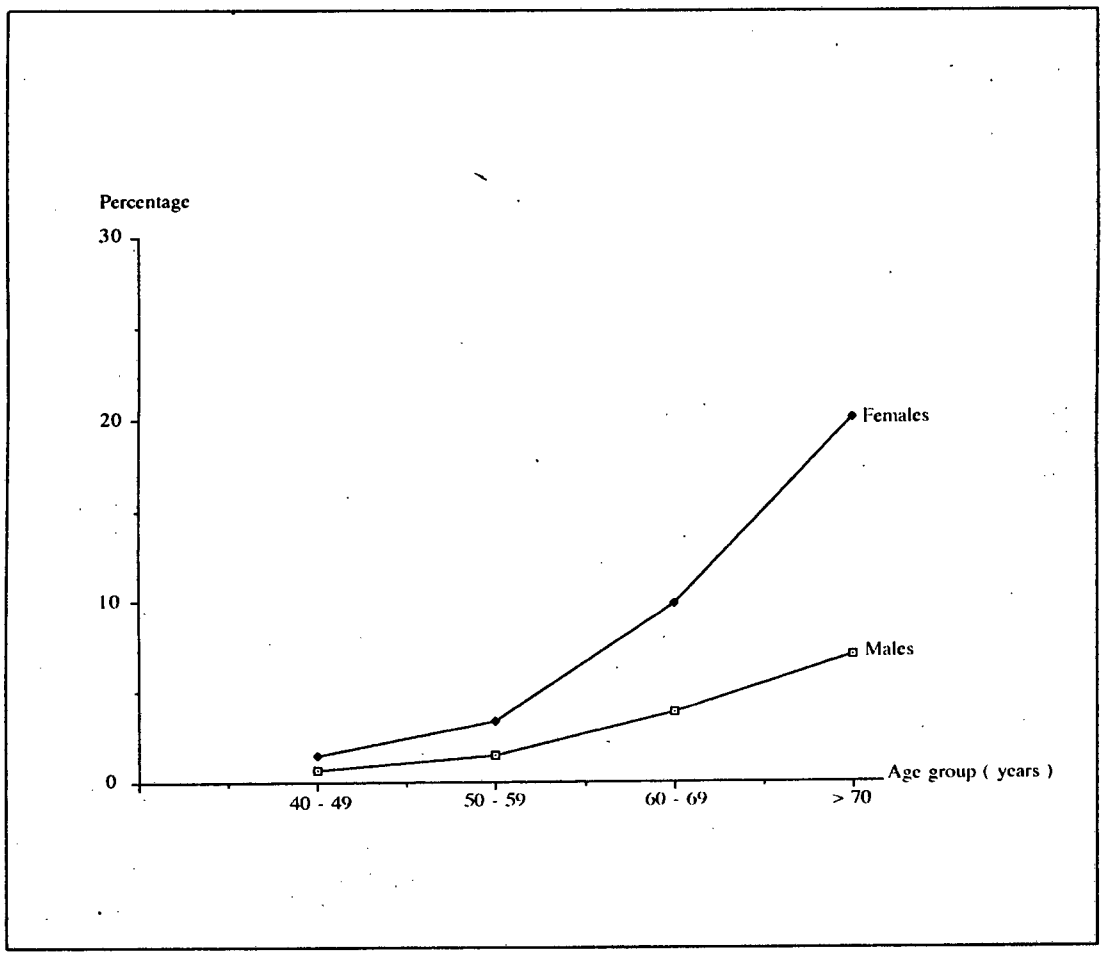

Figure 3.5 Prevalence of "slit-like" angles (an angle of <10° in at least one quadrant) for men and women in decades. The difference between the sexes is statistically significant for people in the 7th decade (P = 0.045). The difference between those older than 70 years is not statistically significant (P = 0.054).

The overall prevalence of primary angle-closure glaucoma for men was 1% (4/392) and for women was 3.2% (19/594). Chronic angle-closure glaucoma was diagnosed in 8 people with glaucomatous visual fields or a blind eye and in 12 with full visual fields. Of these 20 people, all of whom were asymptomatic on examination, four gave a history of previous intermittent ocular pain and three gave a history of observing haloes. In an additional 3 individuals, subacute angle-closure glaucoma was diagnosed. No acute glaucoma was diagnosed. Chronic open-angle glaucoma was diagnosed in 15 people: ten had either elevated intraocular pressure or a history of previous intraocular pressure elevation and five had intraocular pressures below 21 mmHg (range 16 - 20 mmHg) (Table 3.2).

TABLE 3.2
FINDINGS IN PATIENTS WITH PRIMARY GLAUCOMA AND GLAUCOMATOUS VISUAL FIELD LOSS

Primary Angle-closure Glaucoma

No	IOP (mmHg)		Vertical cup : disc ratio		Full threshold fields +	
	R	L	R	L	R	L
1	17*	20*	1.0	1.0	-	-
2	12*	14*	1.0	-	-	-
3	72	72	0.9	1.0	-	-
4	40	34	1.0	0.1	-	-
5	34	22	0.7	0.5	Definite	Probable
6	22	21	0.8	0.9	Definite	Definite
7	44	48	0.5	0.5	Unlikely	Probable
8	20	18	0.6	0.6	Definite	Definite

Primary Open-angle Glaucoma

No	IOP (mmHg)		Vertical cup : disc ratio		Full threshold fields +	
	R	L	R	L	R	L
1	18	16	0.7	0.5	Definite	Definite
2	20	19	0.5	0.7	Unlikely	Definite
3	30	45	0.7	0.8	-	-
4	21	21	0.7	0.7	-	-
5	14*	12*	1.0	1.0	-	-
6	20	18	0.6	0.7	Probable	Definite
7	22	23	0.2	0.6	Unlikely	Definite
8	18	18	0.5	0.6	Definite	Definite
9	42	50	0.7	0.8	Definite	Definite
10	15*	15*	1.0	1.0	-	-
11	22	22	0.6	0.5	Definite	Definite
12	31	25	0.6	0.3	Definite	Definite
13	18	18	0.6	0.6	Probable	Probable
14	22	22	0.7	0.7	Definite	Definite
15	16	22	0.4	0.5	Unlikely	Probable

** Indicates an intraocular pressure on glaucoma therapy.

+ Full threshold fields: "Definite" indicates a glaucomatous visual field with medium to large defects and a shape and distribution typical of glaucomatous optic neuropathy; "Probable" indicates a glaucomatous visual field with slightly smaller or less dense defects atypical for artifact.

The prevalence of primary angle-closure glaucoma and chronic open-angle glaucoma for each sex, in decades, is shown in Table 3.3. Post-traumatic angle recession glaucoma was diagnosed in eight people.

TABLE 3.3
PREVALENCE OF PRIMARY GLAUCOMA

AGE	MALES		FEMALES		TOTAL	
	PACG+	COAG+	PACG	COAG	PACG	COAG
40-49	-	2(1.2)	4(1.5)	-	4(0.95)	2(0.48)
50-59	1(1.0)	1(1.0)	1(0.7)	1(0.7)	2(0.78)	2(0.78)
60-69	2(2.3)	4(4.7)	6(5.2)	2(1.7)	8(3.96)	6(2.97)
>70	1(2.3)	2(4.6)	8(11.9)	3(4.4)	9(8.11)	5(4.50)
TOTAL	4(1.0)	9(2.3)	19(3.2)	6(1.0)	23(2.33)	15(1.52)

+PACG represents primary angle-closure glaucoma and COAG represents chronic open angle glaucoma. Numbers of people with percentage in parenthesis.

The number of individuals with Shaffer type 1 angles or with primary angle-closure glaucoma and symptoms suggestive of intermittent angle closure, is shown in Figure 3.6. None had a family history of glaucoma, which probably reflects a lack of knowledge of the disease rather than an accurate statistic.

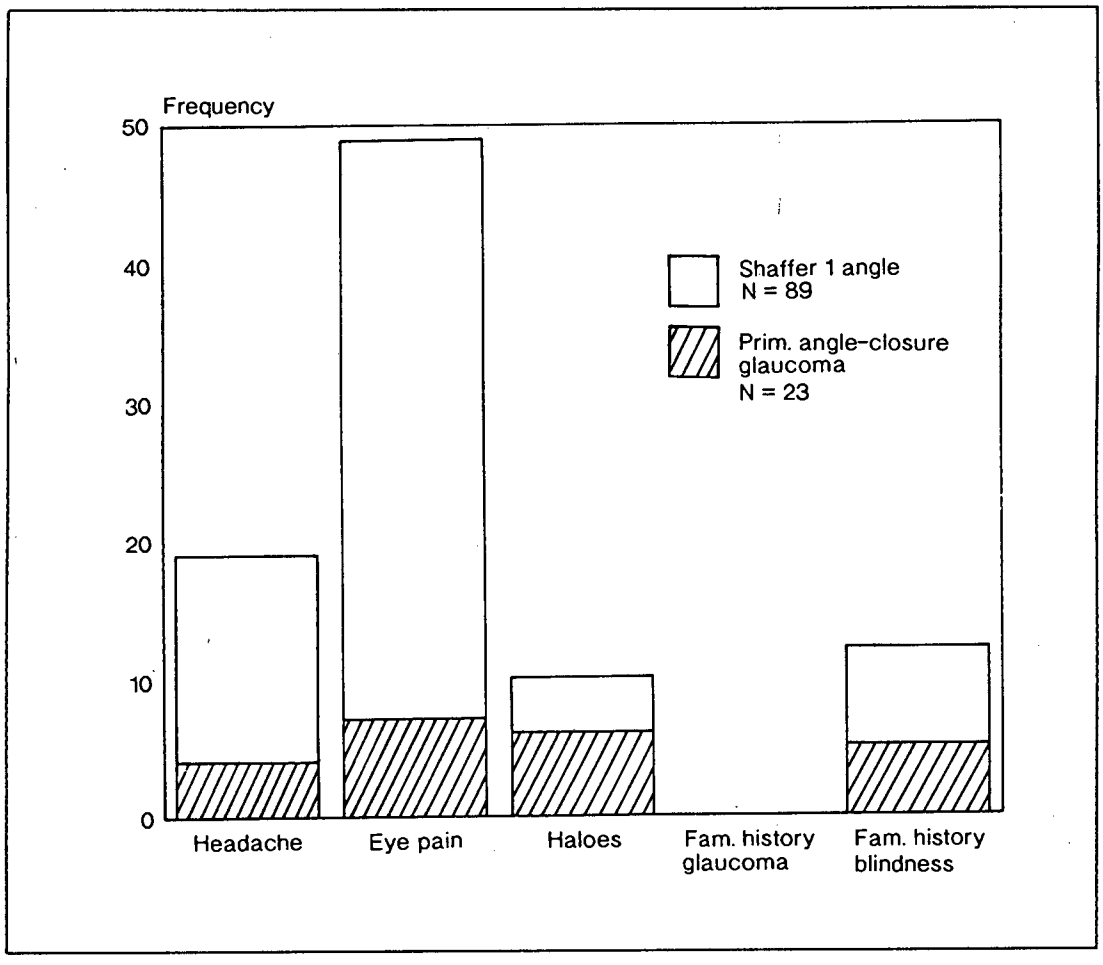

Figure 3.6 Symptoms of intermittent angle-closure glaucoma and family history

Seven people (0.7%) were blind as a result of glaucoma: three had chronic angle-closure glaucoma, two had open-angle glaucoma and two had traumatic glaucoma. All but one were under the management of an ophthalmologist and five had undergone previous drainage surgery. One asymptomatic 42 year-old woman presented for the first time with no light perception in the left eye and 6/12 with split fixation in the right eye. Her intraocular pressure was 72 mmHg in both eyes but no signs of congestion were present. The right eye had three quadrants of angle closure and the left eye had a completely closed angle. An additional 7 people were blind as a result of other eye diseases (four as a result of cataracts, two of degenerative myopia and one of age-related macular degeneration). The prevalence of blindness in people 40 years of age and over was 1.4% (14/987).

3.4 Discussion

The prevalence of primary angle-closure glaucoma depends on the ethnic background of the population studied. In Europeans a prevalence rate of 0.1% has been reported, whereas in Eskimos the rates rise to between 2.1% and 5.1%.[15-18] Falling between these two extremes are Africans and Orientals. In the only studies of homogenous African tribes, the prevalence of primary angle-closure glaucoma in individuals over the age of 40 years has been reported to be 0.25% in Pondos and 1.0% in Tswanas.[19-20] Although the prevalence rates in Japanese and Chinese people have been reported to be 0.3% and 1.3% respectively, no prevalence figures are available for Southeast Asia.[1,4,5]

Although selection bias plays a role, hospital-based case series in Southeast Asia have suggested that primary angle-closure glaucoma makes up 80% to 90% of patients with primary glaucoma.[2,3] This is a reversal of the typical pattern found in Europe and Africa.[15,19] For example, it has been reported that the overall proportion of primary angle-closure glaucoma amongst cases of primary glaucoma does not differ significantly between South African blacks and whites (glaucoma clinic figures of 17% and 20% respectively).[21] This study provides the first population-based evidence that the prevalence of primary angle-closure glaucoma in Cape people of mixed racial background is similar to that found in Eskimos and significantly different from that found in Europeans or black Africans.[15,16,19,20]

The results of any population-based survey are influenced by the sensitivity of the screening methods used and are dependent on the criteria proposed for diagnosis. In order to achieve a high level of sensitivity in this survey, the drainage angle was

assessed gonioscopically in all individuals. Surveys in Greenland Eskimos have used a similar screening examination, but in Asia this has not been undertaken.[1,5,6,18] Because of the potential risk of inducing acute angle closure, provocative testing was not undertaken. A weakness of our survey was that visual field examinations were not performed on every person.[22] The Baltimore Eye Survey, which was performed over a four year period, demonstrated that by using screening criteria consisting of an intraocular pressure of >21 mmHg or a vertical cup : disc ratio of $\geq$0.5, glaucoma would be diagnosed with a sensitivity of 61% (but a specificity of 84%).[22] This suggests that early open-angle glaucoma would have been missed by our survey and that the prevalence of primary open-angle glaucoma in this community is higher than that reported.

The concept of an "occludable" angle is interpreted differently by different observers, as demonstrated for example by the finding that the rate of primary angle-closure attacks in whites with "occludable" angles varies between 7% and 37%.[23,24] To compare our results with those of others, we chose similar criteria to those proposed by the Dana Centre for Preventive Ophthalmology, Baltimore, in their population-based survey of Alaskan Eskimos.[16] In their study, four mirror Zeiss gonioscopy was performed and an angle was considered "occludable" if the trabecular meshwork was not visible in three quarters of the angle and the ciliary body was not visible in two quadrants.

The definition of primary angle-closure glaucoma used in our study was in accord with that adopted by other authors.[17,25,26] Primary angle-closure glaucoma was considered to be present if the intraocular pressure was more than 21 mmHg or if glaucomatous visual field loss was present in the presence of an "occludable" angle. Care was taken to include those individuals with previous acute or intermittent

symptoms of angle closure. Using a different nomenclature, the twelve people found to have an "occludable" angle associated with raised intraocular pressure but full visual fields, could have been described as having "ocular hypertension with narrow angles" rather than chronic angle-closure glaucoma.[27] Individuals with symptomless "slit-like" angles capable of closure and normal intraocular pressure were considered to be angle-closure suspects, but did not undergo provocation testing.[17] They were not included in the prevalence figures of primary angle-closure glaucoma, although many may have developed the disease without receiving therapy.

Predisposing factors for primary angle-closure glaucoma relate mainly to the configuration of the eye itself and those at greater risk for primary angle-closure glaucoma have small, crowded, anterior segments.[28,29] Previous studies have noted the close correlation between hypermetropia and primary angle-closure glaucoma.[1,29] Our survey found an age-related trend towards hypermetropia that was greatest in women over the age of 50 years. A significant difference was found between the median refractive error in women and in men for the 6th, 7th and $\geq$8th decades. The reasons for the trend towards hypermetropia with age and the sexual differences in refraction are unclear. However, this finding may explain why older women in this population tend to have a higher prevalence of Shaffer Grade 1 angles and primary angle-closure glaucoma than do men. The slight trend towards myopia in men in their 8th decade or older might be explained by lenticular changes in these individuals.[29] The fact that people in their 5th decade were on average significantly less hypermetropic than people in higher decades may mean that the prevalence of "occludable" angles and primary angle-closure glaucoma will reduce in the years to come.

Gonioscopy identified Shaffer Grade 1 angles in 9% (89/987) of the population screened and "slit-like" angles in at least one quadrant, in 4% (40/987). In Alaskan Eskimos "occludable" angles were found in 16.9% (45/267) of individuals of 50 years of age or more, compared to 11.7% (66/566) in the same age group in our survey.[16] Women were four to five times more likely to have "occludable" angles than were men. In both sexes, the percentage of people with "occludable" angles increased significantly with age. A sex and age predisposition for "occludable" angles and for primary angle-closure glaucoma has been shown in Eskimo and in Chinese surveys.[5,16,17]

In comparison with Eskimo studies and in keeping with the Southeast Asian and African experience, no acute glaucoma was diagnosed.[10,19-21,30] An elderly woman gave a history of intermittent acute attacks that occurred many years earlier and was found to have iridoschisis in association with chronic angle-closure glaucoma. This finding is not unexpected, as iridoschisis has been linked to intermittent intraocular pressure elevation in primary angle-closure glaucoma.[31] (Chapter 7). Chronic angle-closure glaucoma was diagnosed in twenty people and subacute angle-closure glaucoma in three, resulting in an overall prevalence rate of 2.3% (23/987). Since it has been reported that asymptomatic angle-closure glaucoma is significantly more common than symptomatic congestive angle-closure glaucoma in these people, the rate of intermittent angle-closure may be higher than 0.3%.[9,30] This fact is well illustrated by the remarkable case of a 42-year-old woman who was seen for the first time with no symptoms or signs of congestion, an intraocular pressure of 72 mmHg and advanced chronic angle-closure glaucoma. Only 30% (7/23) of individuals with primary angle-closure glaucoma had symptoms compatible with intermittent angle occlusion.

The overall prevalence of primary angle-closure glaucoma in men was 1% (4/393) and in women was 3.2% (19/594). Whereas the prevalence rate increased with age in women; from 1.5% in the 5th decade to 11.9% in the 8th/9th decades, a similar trend was not found in men. The prevalence of primary open-angle glaucoma in men was 2.3% (9/393) and in women was 1.0% (6/594), giving an overall rate of 1.5% (15/987) in people 40 years or age or older. This rate is significantly less than the 8.8% rate reported in blacks in the West Indies and the 5.0% rate of definite or probable primary open-angle glaucoma reported in urban American blacks, but it is the same rate as that found in urban American whites.[12,32] Significantly, our survey revealed a reversal of the typical pattern found in Europe and North America, since 60.5% of all individuals with primary glaucoma had angle-closure glaucoma.[12,15] This proportion is less than the 79% reported in a Chinese population-based survey and the 86% reported in Greenland Eskimos.[5,18]

A high level of interpersonal violence, as well as a significant degree of alcohol and drug abuse, have been reported among the inhabitants of the village and may explain the high prevalence of post-traumatic angle recession glaucoma.[33,34] This diagnosis was made in eight people and two of these were blind. In all of these individuals, marked irregular widening of the ciliary body band was present typical of angle recession, as well as other ophthalmic features of blunt trauma.

Primary glaucoma was the leading cause of bilateral blindness in the community, with a prevalence rate of 0.5% (5/983). Three people had primary angle-closure glaucoma and two had chronic open-angle glaucoma. The overall prevalence of blindness as a result of primary or secondary glaucoma was 0.7%, which is similar to that found in a homogenous black tribe in South Africa.[19] Overall, glaucoma is

considered to be third on the list of causes of blindness in blacks and whites in South Africa.[35] Because of an easy access to surgery, only four individuals were blind as a result of cataracts and all were old (average age 83 years).

In addition to the diagnosis of 36 new cases of glaucoma, the survey had the benefit of identifying at least 40 individuals at risk of developing angle closure. These people were referred to Groote Schuur Hospital for treatment and will be followed-up at a glaucoma clinic. In South Africa, 10.5% of a population of 28.14 million people have a similar ethnic background to the people described in this study.[36] Our survey indicates that more than 16,000 of these people have some degree of primary angle-closure glaucoma. This disease clearly constitutes a major public health problem in South Africa. If a similar prevalence is found in Southeast Asia, then the problem is of even greater magnitude because of the large numbers of potentially involved people.

3.5 References

1. Congdon N, Wang F, Tielsch JM. Issues in the epidemiology and population-based screening of primary angle-closure glaucoma. *Surv Ophthalmol* 1992; **36** : 411-423.
2. Lim ASM. PACG in Singapore. *Aust J Ophthalmol* 1979; **7** : 23-30.
3. Hung PT. Etiology and mechanism of PACG. *Asian Pac J Ophthalmol* 1990; **2** : 82-84.
4. Shiose Y, Kitazawa Y, Tsukahara S *et al.* Epidemiology of glaucoma in Japan: A nationwide glaucoma survey. *Jpn J Ophthalmol* 1991; **35** : 133-155.
5. Hu Z, Zhao ZL, Dong FT. An epidemiological investigation of glaucoma in Beijing and Shun-yi County. *Chin J Ophthalmol* 1989; **25** : 115-118.
6. Kitazawa Y. Epidemiology of PACG. *Asian Pac J Ophthalmol* 1990; **2** : 78-81.
7. Botha MC. Blood group gene frequencies. An indication of the genetic constitution of population samples in Cape Town. *S Afr Med J* 1972; 46(suppl) : 1-27.
8. Marais JS. *The Cape Coloured People. 1652-1937.* 1st ed. Johannesburg, Witwatersrand University Press; 1957 : 1-31.
9. Sacks S. The glaucomas at the Cape. *S Afr Med J* 1964; **38** : 594-595.
10. Lowe RF, Lim ASM. *Primary angle closure glaucoma* 1st ed. Singapore, PG Publishing; 1989 : 33-39.
11. Klopper JML, Tibbit L. The Mamre Community Health Project (Editorial). *S Afr Med J 1988;* **74** : 319-320.
12. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma. *JAMA* 1991; **266** : 369-374.

13. Kosoko O, Sommer A, Auer C. Screening with automated perimetry using a threshold related three-level algorithm. *Ophthalmology* 1986; **93** : 882-886.

14. *Manual of the International Classification of Diseases, Injuries and the Causes of Death.* Geneva, Switzerland : World Health Organisation; 1977.

15. Hollows FC, Graham PA. Intraocular pressure, glaucoma and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966; **50** : 570-586.

16. Arkell SM, Lightman DA, Sommer A, Taylor HR, Korshin OM, Tielsch JM: The prevalence of glaucoma among Eskimos of Northwest Alaska. *Arch Ophthalmol* 1987; **105** : 482-485.

17. Drance SM. Angle closure glaucoma among Canadian Eskimos. *Can J Ophthamol* 1973; **8** : 252-254.

18. Clemmesen V, Alsbirk PH. Primary angle closure glaucoma in Greenland. *Acta Ophthalmol* (Kbh) 1971; **49** : 47-58.

19. Bartholomew RS. Glaucoma in a South African black population. A population study of the Pondo tribe of South Africa. *S Afr Arch Ophthalmol* 1976; **3** : 135-150.

20. David R, Stone D. The prevalence of glaucoma in a homogenous African population. In David R, Ticho U (Eds.) Recent Advances in Glaucoma, Elsevier Science Publishers BV; 1984 : 145-153.

21. Luntz MH. Primary angle-closure glaucoma in urbanised South African Caucasoid and Negroid communities. *Br J Ophthalmol* 1973; **57** : 445-456.

22. Javitt J, Sommer A. A population-based evaluation of glaucoma screening : The Baltimore Eye Survey *Am J Epidemiol* 1991; **134** : 1102-1110.

23. Lowe RF. Primary angle-closure glaucoma : A review of provocative tests. *Br J Ophthalmol* 1967; **51** : 727-732.

24. Panek WC, Christensen RE, Lee DE. Biometric variables in patients with occludable anterior chamber angles. *Am J Ophthalmol* 1990; **110** : 185-188.

25. Pollack IP. Chronic angle-closure glaucoma. Diagnosis and treatment in patients with angles that appear open. *Arch Ophthalmol* 1971; **85** : 676-689.

26. Leighton DA, Phillips CI, Tsukahara S. Profile of presenting states in eyes in angle-closure glaucoma. *Br J Ophthalmol* 1971; **55** : 577-584.

27. Romano JH, Hitchings RA, Pooinasawmy D. Role of Nd-YAG peripheral iridectomy in the management of ocular hypertension with a narrow angle. *Ophthalmic Surg* 1988; **19** : 814-816.

28. Sugar HS. The mechanical factors in the etiology of acute glaucoma. *Am J Ophthalmol* 1941; **24** : 851.

29. Lowe RF. Aetiology of the anatomical basis for primary angle-closure glaucoma. *Br J Ophthalmol* 1970; **54** : 161-169.

30. Salmon JF. Presenting features of primary angle-closure glaucoma in patients of mixed ethnic background. In press. *South Afr Med J* 1993.

31. Salmon JF, Murray ADN. The association of iridoschisis and primary angle-closure glaucoma. *Eye* 1992; **6** : 267-272.

32. Mason RP, Kosoko O, Wilson R, *et al.* National survey of the prevalence and risk factors of glaucoma in St. Lucia, West Indies : Part 1. Prevalence findings. *Ophthalmology* 1989; **96** : 1363-1368.

33. Bourne DE, Midgley A, Yach D, Katzenellenbogen J. Mortality in Mamre, 1981-1987. *S Afr Med J* 1988; **74** : 355-358.

34. Yach D, Joubert G. Determinants and consequences of alcohol abuse and cigarette consumption in Mamre. *S Afr Med J* 1988; **74** : 348-351.

35. Van der Walt SJ, Lombard P. The opacified view of statistics on visual impairment in South Africa. Imfama; *Journal of the S.A. Bureau for the Prevention of Blindness* 1987; **27** : 5-6.

36. Central Statistical Services. Population Census 1985 (Report No 02-85-02). Pretoria : The Government Printer, 1985.

4.0 The Dimensions of Eyes with Chronic Angle-Closure Glaucoma.

4.1 Introduction

The measurement of eyes with primary angle closure glaucoma and the relationship of one intraocular structure to another, has been comprehensively documented in people of European ethnic background.[1-6] In comparison, ocular biometry has been reported in only one group of Chinese patients and in one group of African patients with primary angle-closure glaucoma.[7,8] However, these studies have established that, irrespective of race, eyes with primary angle-closure glaucoma are shorter and have a shallower anterior chamber than age-matched normal eyes.[1,2,5-8] Shallowing of the anterior chamber has been related to a relatively forward position of the lens, a more than average lens thickness for age and progressive lens thickening as a result of continued lens growth with age.[2]

To determine whether patients of mixed ethnic background with chronic angle-closure glaucoma have similar ocular characteristics to those reported in other racial groups, the eyes of patients with chronic angle-closure glaucoma were measured and the measurements were compared with those found in matched individuals with normal eyes.

4.2 Patients and Methods

Ocular measurements were determined in both eyes of 46 patients with chronic angle-closure glaucoma. The diagnosis of chronic angle-closure glaucoma was made in asymptomatic patients with an intraocular pressure of > 21 mmHg or with

disc cupping and glaucomatous visual field loss in the presence of some degree of permanent angle closure. All had undergone a previous peripheral laser iridotomy and attended the glaucoma clinic at Groote Schuur Hospital. The age of the patients ranged from 50 years to 80 years (mean 63.26 years) and 39 were women (84.8%). A control group of 23 individuals was selected from the hospital outpatient department of comparable race, age and sex. Each had 6/9 or better uncorrected vision, normal intraocular pressures and open angles. The age of the controls ranged from 50 years to 82 years (mean 60.48 years) and 16 were women (69.6%).

Contact ultrasonography was performed using a Sonametrics Ocuscan A400 instrument. A drop of local anaesthetic was instilled into the eye before corneal contact was made. An A-scan pattern was displayed and at the same time the measurement was automatically shown in millimetres. The anterior chamber depth, lens thickness and axial length was recorded in both eyes when an acceptable A-scan pattern with high peaks was observed (Figure 4.1). The anterior chamber depth was measured from the anterior surface of the cornea to the anterior surface of the lens. The radii of corneal curvature were measured in the two principal meridians with a Humphrey autokeratometer and the mean of the two measurements used. The refractive error was determined and the spherical equivalent recorded in dioptres.

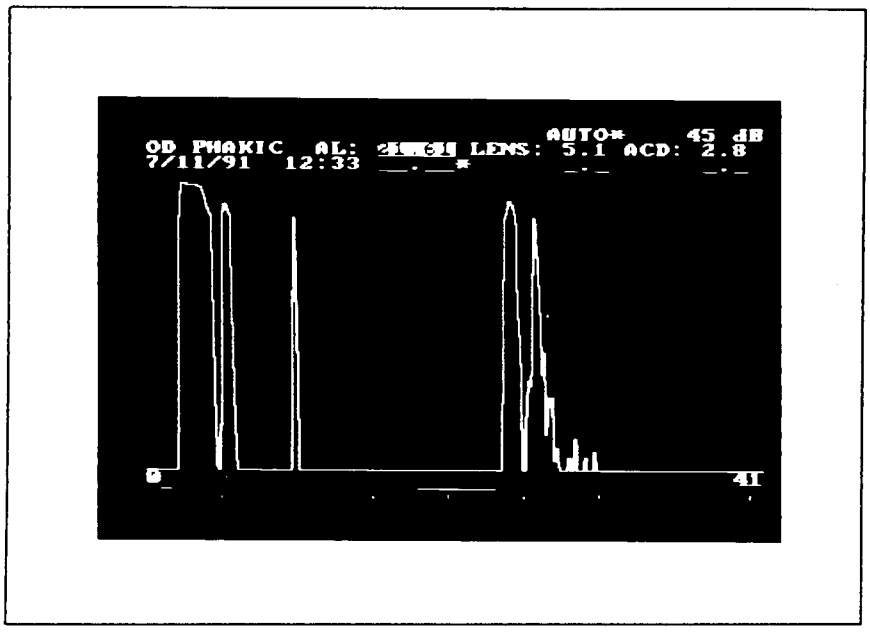

Figure 4.1 Typical A-scan ultrasound of patient with chronic angle-closure glaucoma, showing high peaks

The relative position of the centre of the lens was determined by adding the anterior chamber depth to half the lens thickness and then dividing the sum by the axial length.[6] The ratio between lens thickness and axial length was determined and a biometric unit obtained by multiplying this ratio by ten.[13]

Statistical analysis of variance was determined using the Wilcoxon 2-sample test and the Kruskal-Wallis test. Correlation analysis was performed using Spearman's rank correlation coefficients. A finding was considered significant at $P < 0.05$.

4.3 Results

The refraction in equivalent spheres in patients with primary angle-closure glaucoma is shown in Figure 4.2

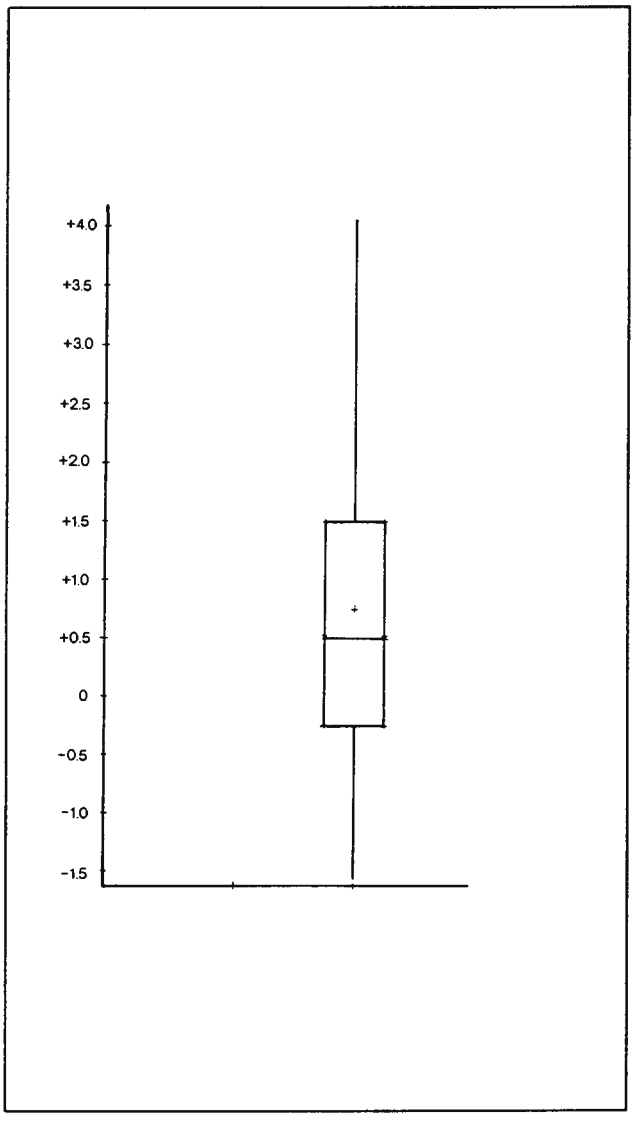

Figure 4.2 Refraction in equivalent spheres in patients with chronic angle-closure glaucoma. The mean value is indicated with a cross; the median values with a box graph (horizontal lines indicate 25th percentiles).

The correlation between the measurements obtained in the right and left eyes of patients with chronic angle-closure glaucoma and in normal subjects was statistically highly significant (Table 4.1). Only the measurements from the right eyes of the two groups will therefore be reported.

TABLE 4.1: SPEARMAN'S RANK CORRELATION COEFFICIENTS FOR RIGHT AND LEFT EYES

PARAMETER	ANGLE-CLOSURE GLAUCOMA	NORMAL
Axial length	0.886 (P=0.0001)	0.936 (P=0.000)
Anterior chamber depth	0.753 (P=0.0001)	0.596 (P=0.0027)
Lens thickness	0.887 (P=0.0001)	0.700 (P=0.0002)
Radius of curvature	0.819 (P=0.0001)	0.945 (P=0.0001)

In eyes of patients with chronic angle-closure glaucoma, the mean axial length was significantly shorter (P=0.0001) and the anterior chamber depth significantly less (P=0.0002) than matched normal eyes. While the radius of corneal curvature was less in eyes with primary angle-closure glaucoma, statistical significance was not shown (P=0.08).

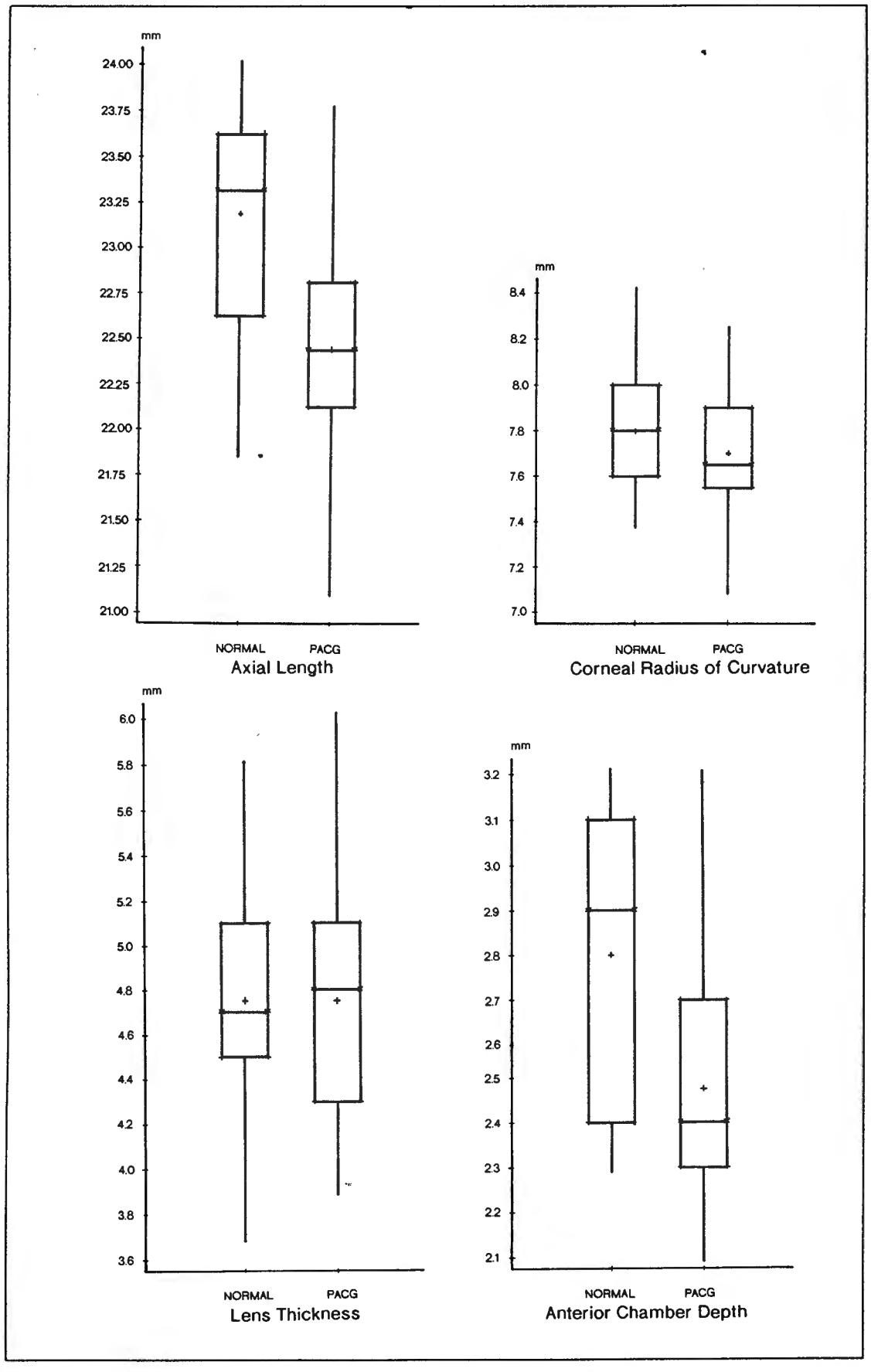

Figure 4.3 Ocular biometry in normal eyes and in eyes with chronic angle-closure glaucoma. The mean value is indicated with a cross; the median values with a box graph (horizontal lines indicate 25th percentiles).

The mean lens thickness of eyes with chronic angle-closure glaucoma was the same as that found in matched normals (F value 0.001) (Table 4.2). Despite these findings, there was considerable overlap between the two groups in respect of the measurements of individual eyes (Figure 4.3).

TABLE 4.2 OCULAR MEASUREMENTS IN RIGHT EYES OF PATIENTS WITH CHRONIC ANGLE-CLOSURE GLAUCOMA AND MATCHED NORMALS

CHRONIC ANGLE-CLOSURE GLAUCOMA				
PARAMETER	**MEAN**	**SD**	**MEDIAN**	**RANGE**
Axial length	22.43	± 0.61	22.41	21.15 - 23.73
AC depth*	2.48	± 0.26	2.4	2.1 - 3.2
Lens thickness	4.73	± 0.48	4.8	3.9 - 6.0
Radius of curvature	7.69	± 0.26	7.66	7.11 - 8.20
Lens: axial length ratio+	2.11	± 0.23	2.14	1.72 - 2.74
Refraction	+0.69	± 1.40	+0.50	-1.50 - +4.00
NORMAL				
Axial length	23.17	± 0.58	23.31	21.89 - 23.97
AC depth*	2.80	± 0.33	2.9	2.3 - 3.2
Lens thickness	4.73	± 0.51	4.7	3.7 - 5.8
Radius of curvature	7.80	± 0.24	7.81	7.38 - 8.39
Lens: axial length ratio+	2.04	± 0.24	2.01	1.67 - 2.65
Refraction	+0.50	± 0.60	+0.50	-0.50 - +1.50

All measurements in millimetres, refraction in equivalent spheres.
*Anterior chamber depth measured from anterior surface of the cornea to anterior surface of lens.
+Lens: axial length ratio = (lens thickness x 10) / axial length)

A significant difference was found between the two groups when the relative position of the centre of the lens was compared. In eyes with chronic angle-closure glaucoma the lens was more anteriorly situated than in normal eyes (mean values of 0.216 and 0.223 respectively; P=0.04). Although the mean ocular lens thickness : axial length ratio was greater in patients with chronic angle-closure glaucoma than in normals (2.11 v 2.04), this difference was not statistically significant.

In eyes with chronic angle-closure glaucoma no correlation was found between age and lens thickness, probably because the age range was small. Refraction was significantly correlated with axial length (r = -0.403, P=0.03) and axial length with corneal radius of curvature (r=0.393, P=0.007). Anterior chamber depth was inversely correlated with lens thickness (r= -0.355, P=0.02).

In normal eyes, a statistically significant correlation was found between age and lens thickness (r=0.501, P=0.02). Anterior chamber depth was inversely correlated with lens thickness (r= -0.656; P=0.0007) and positively correlated with axial length (r=0.435; P=0.04).

4.4 Discussion

Ocular biometry performed on eyes with primary angle-closure glaucoma has consistently revealed a shorter axial length and shallower anterior chamber than normal.[1-9] Lens thickness has been inversely correlated with anterior chamber depth.[8] Similar conclusions can be made from the present study, although when the measurements are compared with those reported in Europeans and Africans with primary angle-closure glaucoma, it is clear that the average axial length is longer and the anterior chamber deeper in the patients discussed here (Table 4.3).

TABLE 4.3 COMPARATIVE ANALYSIS OF THE OCULAR DIMENSIONS OF EYES WITH PRIMARY ANGLE-CLOSURE GLAUCOMA COMPARED TO NORMALS.

PARAMETER*	LOWE		TOMLINSON		LUNTZ		SALMON	
	PACG °	Normal	PACG °	Normal	PACG °	Normal	PACG °	Normal
AC	2.33	3.32	2.31	3.08	2.34	3.19	2.48	2.80
LENS	5.09	4.50	5.23	4.67	4.81	4.16	4.73	4.73
AL	22.01	23.10	22.06	22.58	22.65	23.05	22.43	23.17
RADIUS	7.61	7.67	6.55	7.65	-	-	7.69	7.80
LENS POS.	0.20	0.22	0.224	0.240	0.209	0.229	0.216	0.223

All measurements in millimetres.

*AC = anterior chamber depth measured from anterior surface of cornea to anterior surface of lens; PACG °= primary angle-closure glaucoma; Lens = lens thickness; AL = axial length; Radius = corneal radius of curvature; Lens pos. = relative lens position.

The shallow anterior chamber in patients with primary angle-closure glaucoma is related to a relatively forward position of the anterior lens surface in relation to the root of the iris as a result of an anterior lens position and a lens that is thicker than normal.[2] This results in an iris that lies closer to the lens and thus predisposes to pupillary block.[2] If the marker for the intraocular position of the lens is taken as the midpoint between the anterior and posterior lens surfaces, then the relative lens position can be calculated by dividing the sum of the anterior chamber depth and half the lens thickness by the axial length.[2] This study shows that in patients of mixed ethnic background with chronic angle-closure glaucoma the lens is situated relatively anteriorly in the eye when compared with the lens position in matched normals.

The anterior chamber depth becomes shallower with age because of continued lens growth throughout life. Jansson reported a 0.62 mm increase in women and a 0.71 mm increase in men over a 25-year period and Lowe reported a 0.73 mm increase in lens thickness over 50 years (from 30 years to 80 years).[2,10] In the present study

this was demonstrated in individuals with normal eyes; a similar trend was found in eyes with chronic angle closure although statistical significance was not shown.
The major difference between the findings of this study and most other biometric studies is that the mean lens thickness in the group with chronic angle-closure glaucoma was similar to that in the group with normal eyes (4.73 mm). Although a recent multicentre study reported a mean lens thickness of 4.52 mm in angle-closure glaucoma suspects, Lowe reported a mean lens thickness of 5.09 mm in eyes with primary angle-closure glaucoma compared with 4.50 mm in normal subjects and Tomlinson reported a mean difference between age-matched groups of 0.56 mm.[2,6,11] Similarly, in black African patients, the lens was found to be thicker in patients with primary angle-closure glaucoma than in matched normal subjects.[7] (Table 4.3)

Ocular biometry demonstrates that a relatively anterior lens position rather than a large lens is responsible for shallowing of the anterior chamber in the patients in this study with chronic angle-closure glaucoma. Based on differences in lens thickness between Africans and Danes, Clemmesen and Luntz predicted that "creeping" angle-closure glaucoma might be associated with a thinner than expected lens; an observation that is supported by this study.[7] It can be concluded that the racial differences in lens position and thickness, anterior chamber depth and thus the risk of pupillary block may be partially responsible for differences in the presenting features of patients with primary angle-closure glaucoma.[12-15]

4.5 References

1. Törnquist R. Chamber depth in primary acute glaucoma. *Br J Ophthalmol* 1956; **40** : 421-429.
2. Lowe RF. Causes of shallow anterior chamber in primary angle-closure glaucoma: ultrasonic biometry of normal and angle-closure glaucoma eyes. *Am J Ophthalmol* 1969; **67** : 87-93.
3. Lowe RF. Corneal radius and ocular correlations in normal eyes and in eyes with primary angle closure glaucoma. *Am J Ophthalmol* 1969; **67** : 864-868.
4. Lowe RF. Aetiology of the anatomical basis for primary angle-closure glaucoma. *Br J Ophthalmol* 1970; **54** : 161-169.
5. Phillips CI, Storey JK. Ocular dimensions in angle-closure glaucoma. *Br J Physiol Optics* 1971; **26** : 228-242.
6. Tomlinson A, Leighton DA. Ocular dimensions in the heredity of angle-closure glaucoma. *Br J Ophthalmol* 1973; **57** : 475-486.
7. Clemmesen V, Luntz MH. Lens thickness and angle-closure glaucoma. *Acta Ophthalmol* (Copenh) 1976; **54** : 193-197.
8. Ren-rong W, Bing-kuan G, Xun-chuan J, Shu-chu C. Genetic rules of primary angle-closure glaucoma. *Chin Med J* [Engl] 1986; **99** : 535-543.
9. Markowitz SN, Morin JD. The ratio of lens thickness to axial length for biometric standardisation in angle-closure glaucoma. *Am J Ophthalmol* 1985; **99** : 400-402.
10. Jannson F. Measurements of intraocular distances by ultrasound. *Acta Ophth* 1963; **74** : suppl. 39.

11. Wilensky JT, Kaufman PL, Frohlichstein D, Gieser DK, Kass MA, Ritch R, Anderson R. Follow up of angle-closure glaucoma suspects. *Am J Ophthalmol* 1993; **115** : 338-346.

12. Leighton DA, Phillips CI, Tsukahara S. Profile of presenting states of eyes in angle-closure glaucoma. *Br J Ophthalmol* 1971; **55** : 577-584.

13. Alper MG, Laubach JL. Primary angle-closure in the American Negro. *Arch Ophthalmol* 1968; **79** : 663-668.

14. Lowe RF, Lim ASM. *Primary Angle Closure Glaucoma* 1st ed. Singapore: PG Publishing, 1989; 33-39.

15. Luntz MH. Primary angle-closure glaucoma in urbanised South African Caucasoid and Negroid communities. *Br J Ophthalmol* 1973; **57** : 445-456.

5.0 The Mechanism of Angle Occlusion in Chronic Angle-Closure Glaucoma.

5.1 Introduction

The basic mechanism of angle closure in patients with primary angle-closure glaucoma is considered to be pupillary block.[1] However, in the patients in this study with chronic angle-closure glaucoma, this single mechanism does not explain entirely the asymptomatic gradual "creeping" closure of the angle that is commonly observed.[2]

Provocative tests, once considered useful when evaluating the need for therapy in some cases of primary angle-closure glaucoma, are rarely used today because of the ease and safety of laser iridotomy.[1] However, these tests may be used to explain the mechanisms of angle closure, particularly in eyes where the pupillary block mechanism has been eliminated by means of an iridectomy. This possibility was considered by Hung and Chou, who performed a series of provocative tests on a group of Asian patients who had previously undergone peripheral iridectomy for primary angle-closure glaucoma.[3] They reported that nearly 60% of the eyes demonstrated a positive response when the prone position test was performed in a dark room. Other authors, whose patients were presumably of European ethnic background, have reported significantly less positive responses under similar circumstances.[4,5] No explanation has been given for these racial differences in response to provocative testing.

The aim of this study was to establish whether other mechanisms besides pupillary block play a role in the pathogenesis of chronic angle-closure glaucoma in people of mixed ethnic background. A series of provocative tests were therefore performed

on patients with chronic angle-closure glaucoma who had previously undergone a laser iridotomy. The results may explain why different responses to provocation have been reported in different racial groups.

5.2 Patients and Methods

Thirty-three patients of mixed ethnic background with the diagnosis of chronic angle-closure glaucoma, who regularly attended the glaucoma clinic at Groote Schuur Hospital, were randomly selected for this study. Twenty-eight were women and 5 men and the mean age was 64.3 years. The diagnosis of chronic angle-closure glaucoma was made in asymptomatic patients if the intraocular pressure was >21 mmHg on presentation in the presence of a partially occluded angle. The presence of glaucomatous visual field loss was not considered necessary for this diagnosis and indentation gonioscopy revealed no permanent peripheral anterior synechiae in some eyes (Table 5.1).

For the purposes of this study, only the intraocular pressure response in eyes with a laser iridotomy was considered. A patent Nd-YAG laser iridotomy was present in the periphery of a superior iris quadrant in 51 eyes of 33 patients. Of the 15 fellow eyes, a trabeculectomy or cataract extraction had been performed in 13 eyes and no treatment had been undertaken in 2 blind eyes.

A single observer assessed the anterior segment and gonioscopic appearance of all sighted eyes and divided the eyes into two groups based on the plane of the iris. Those with a "steep iris" plane had an angular width of 10° - 20° and those with a "plateau iris" had an iris root that angulated forward from its insertion point and then angulated sharply centrally giving the surface of the iris a relatively flat

appearance (Figure 5.1). Despite the lack of an objective method of standardisation and some iris appearances that were not clear-cut, 25 eyes of 16 patients were designated as having a steep iris plane and 26 eyes of 17 patients a plateau iris. In three patients the iris plane was considered to be slightly different in the two eyes. (Three eyes designated as having a steep iris plane were included in the study, whereas the three fellow eyes designated as having a plateau iris were not included because the eyes had previously undergone trabeculectomy).

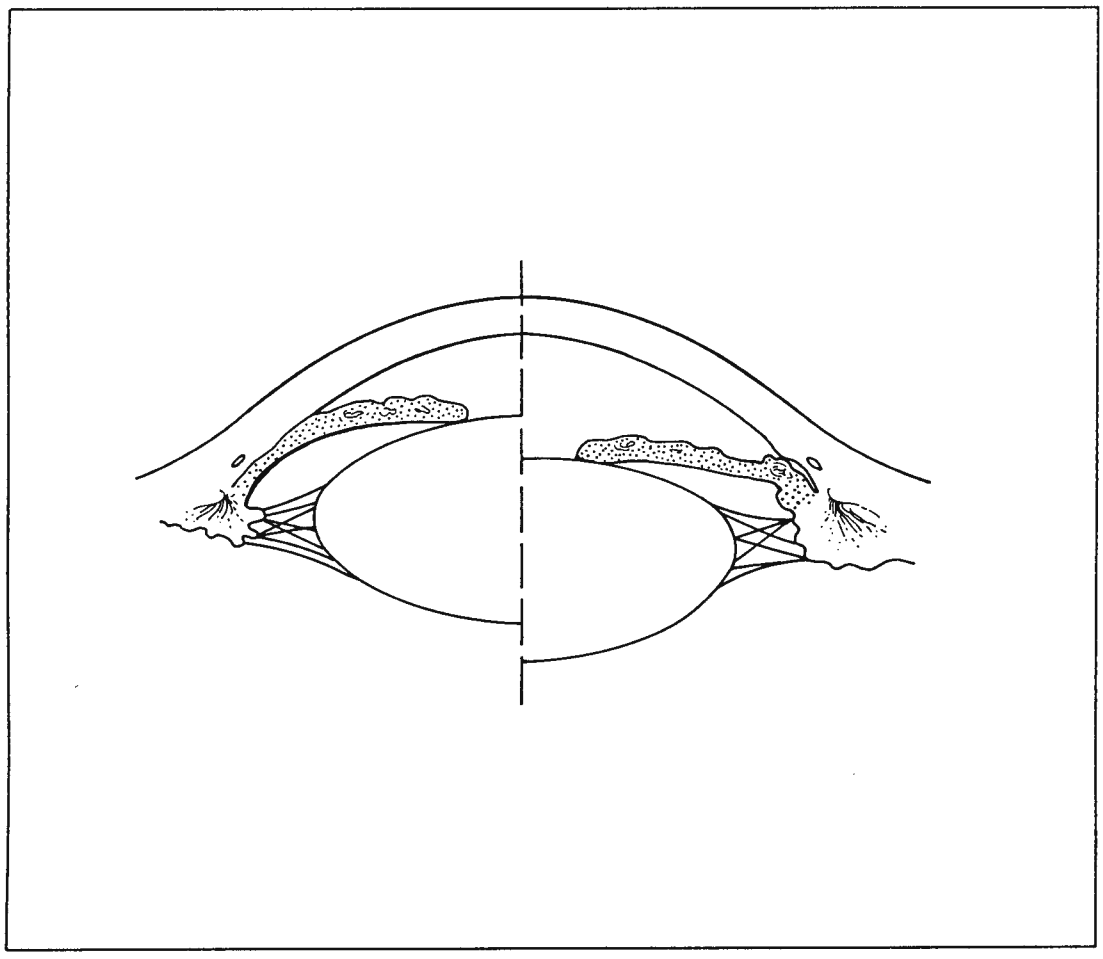

Figure 5.1 Diagram to illustrate a steep iris plane (left) and a plateau iris (right).

The demographic features and ocular findings in each group are summarised in Table 5.1. The group with plateau iris were younger, although statistical significance was not shown (P=0.07; Student's t-test). In those eyes with a steep iris, the mean anterior chamber depth, mean lens thickness and mean axial length were less than that found in eyes with plateau iris, although the differences were not statistically significant. The mean degrees of chronic angle closure was 72°(range 0°- 270°) for those with a steep iris, compared with 145°(range 0°- 270°) for those with a plateau iris, a difference that is statistically significant (P=0.001).

TABLE 5.1 DEMOGRAPHIC AND OCULAR FINDINGS IN 33 PATIENTS (51 EYES) WITH CHRONIC ANGLE-CLOSURE GLAUCOMA

	STEEP IRIS	PLATEAU IRIS
Age (years)	67.3 (± 8.4)	61.4 (± 9.9)
Sex:		
Women	15	13
Men	1	4
Time since PI (months)	33.2 ± 5.6	42.5 ± 7.6
Eyes (No.)	25	26
Mean visual acuity (± SD)	6/12 (± 1 line)	6/12 (± 1 line)
Mean cup : disc ratio (± SD)	0.47 (± 0.05)	0.44 (± 0.05)
Mean degrees of closure (± SD)	72 (± 71)	145 (± 80)
Anterior chamber depth[+] (mm) (± SD)	2.54 (± 0.21)	2.56 (± 0.30)
Lens thickness (mm) (± SD)	4.54 (± 0.44)	4.73 (± 0.48)
Axial length (mm) (± SD)	22.30 (± 0.97)	22.60 (± 1.03)

[+] Anterior chamber depth measured with A-scan ultrasound from the anterior surface of the cornea to the anterior surface of the lens. The standard deviations are placed in parenthesis.

All glaucoma medication was stopped 48 hours before testing. Three provocative tests were performed on all 33 patients. The dark-room test was followed by the prone position test, performed first in the light and then in the dark, with a 5-minute period between each test. In the dark-room test, the patient was seated in a dark room with both eyes open. In the prone position test the patient was seated resting the forehead on the hands and was instructed to open both eyes and told not to sleep. The intraocular pressure was measured with a Goldmann applanation tonometer before each test and 1 hour later. If the intraocular pressure was elevated after a provocative test, digital pressure was applied to the eye to reduce the intraocular pressure before starting the next test. Gonioscopy was not performed between the tests. In each test, a rise of 8 mmHg or more after 1 hour was considered to be a positive result.[6] In the eyes with a positive dark-room prone provocative test, the same test was repeated at a second visit after instilling topical pilocarpine 1%.

Statistical analysis was performed using Student's t-test and Fisher's exact test. Because of the inherent lack of independence of measurements of the two eyes of a single individual, all P values reported in this study have undergone corrective adjustment.[7,8] An interclass correlation was calculated, the statistical test adjusted and the significance levels corrected. A finding was considered significant at a P value of <0.05.

5.3 Results

The numbers of eyes with positive provocative tests are recorded in Table 5.2 Although more eyes designated as having a plateau iris had a positive dark-room test than those with a steep iris plane, this difference was not statistically significant.

However, on testing in the prone position, in the light and in the dark, significantly more eyes designated as having a plateau iris were positive than those with a steep iris plane ($P<0.001$). When the dark-room prone provocative test was repeated in those with a plateau iris after pilocarpine instillation, none was positive; a finding that is statistically significant ($P<0.001$).

TABLE 5.2 **POSITIVE PROVOCATIVE TESTS* IN 33 PATIENTS (51 EYES) WITH CHRONIC ANGLE-CLOSURE GLAUCOMA**

	Narrow Angle	Plateau Iris	Plateau Iris with Pilocarpine
Number of eyes	25	26	20+
Dark-room test	2 (8%)	6 (23%)	-
Light prone test	1 (4%)	17 (65%)	-
Dark prone test	1 (4%)	20 (77%)+	0 (0%)

* A positive test was considered to be a rise of intraocular pressure of 8 mmHg or more, after 1 hour.
+ Indicates a test that was repeated on the same eyes.

The mean intraocular pressure rise (with one standard deviation) after provocation testing is shown in Table 5.3. The differences between the rise of intraocular pressure in eyes with a narrow angle and eyes with a plateau iris configuration is statistically significant ($P=0.02$). Similarly, the difference on prone testing in the light and in the dark is statistically significant ($P<0.001$). On dark-room testing, eyes with a plateau iris showed less intraocular pressure rise after topical pilocarpine was instilled than when the test was performed without pilocarpine ($P=0.001$).

TABLE 5.3 RESULTS OF PROVOCATIVE TESTS: MEAN INTRAOCULAR PRESSURE CHANGES

	Steep Iris Plane	Plateau Iris	Plateau Iris with Pilocarpine
Dark room test			
$P_0 \pm SD$	18.7 ± 5.1	19.2 ± 6.0	
$P_1 \pm SD$	20.2 ± 7.1	25.2 ± 8.9	
$P_1-P_0 \pm SE$	+1.5 ± 0.79	+6 ± 1.5	
Light prone test			
$P_0 \pm SD$	18.3 ± 4.7	19.1 ± 5.6	
$P_1 \pm SD$	21.2 ± 5.4	27.2 ± 7.6	
$P_1-P_0 \pm SE$	+2.9 ± 0.7	+8.3 ± 1.1	
Dark Prone test			
$P_0 \pm SD$	19.2 ± 4.4	18.4 ± 5.5	17.1 ± 6.5
$P_1 \pm SD$	20.2 ± 5.3	27.8 ± 9.1	19.3 ± 3.2
$P_1-P_0 \pm SE$	+1.33 ± 0.7	+9.3 ± 1.3	2.3 ± 1.1

All values in mmHg
P_0 = mean intraocular pressure prior to provocation test; P_1 = mean intraocular pressure after 1 hour; P_1-P_0 = the mean change in intraocular pressure; SD = standard deviation; and SE = standard error.

The number of positive and negative responses to dark-room prone provocative testing relative to the number of quadrants of permanent angle closure is shown for each group in Table 5.4. Significantly more eyes demonstrated a positive response in the group considered to have a plateau iris than was found in the group considered to have a steep iris plane, irrespective of the number of quadrants of angle closure. (For 2 and 3 quadrants $P=0.002$; for 1, 2 and 3 quadrants $P<0.001$).

TABLE 5.4 QUADRANTS OF PERMANENT ANGLE CLOSURE RELATED TO RESPONSE TO DARK ROOM PRONE PROVOCATION

Quadrants of Closure	STEEP IRIS		PLATEAU IRIS	
	Negative	Positive+	Negative	Positive+
0	10	0	2	2
1	10	1	2	3
2	3	0	2	12
3	1	0	0	3
Total	24	1	6	20

+ A positive test was considered to be a rise of intraocular pressure of 8 mmHg or more, after 1 hour.

5.4 Discussion

Eyes that are predisposed to angle-closure glaucoma tend to be hypermetropic, with a crowded anterior segment.[9] Shallowing of the anterior chamber is related to a relative forward position of the lens, and progressive lens thickening as a result of continued lens growth with ageing.[9] The basic mechanism of angle closure in eyes with primary angle-closure glaucoma is considered to be pupillary block, which is eliminated by means of a peripheral iridotomy.[10] The exact mechanism of chronic angle closure in people of Southeast Asian or African ethnic background is not known, but it is suspected that more than one mechanism may play a role in the pathogenesis of this condition.[11,12] Typically, a gradual asymptomatic "creeping" angle closure occurs in these patients, which usually starts superiorly and progresses circumferentially.[13] The iris is pushed into the depths of the angle of the anterior chamber and the angle consequently appears shortened.[13] The failure of normalisation of intraocular pressure after peripheral iridotomy has been attributed to underlying trabecular damage, peripheral anterior synechiae, angle pigmentation, the presence of a large lens or plateau iris syndrome.[3,14]

Classic "plateau iris" is considered to be an uncommon anatomical variant in which the iris root angulates sharply centrally.[15,16] The surface of the iris appears relatively flat, giving the iris the appearance of a plateau in sagittal section. In practice, the plane of the iris is never truly flat and the pupillary iris is 0.6 - 1.0mm anterior to the iris root.[17] This forward displacement of the central iris is considered to be secondary to the lens on which it rests. A more common situation has been termed "incomplete" plateau iris syndrome and occurs when the distance to which the iris surface rises anteriorly in relation to the level of the trabecular meshwork is insufficient to result in complete angle closure.[18] This study shows that plateau iris syndrome occurs significantly more often in the patients in this group than in patients with primary angle-closure glaucoma reported in other series.[4,10,14] A recent study using high-resolution ultrasound biometry of the anterior segment has shown that the anatomical abnormality in plateau iris syndrome is anteriorly situated ciliary processes.[19] In people with plateau iris syndrome the ciliary processes provide structural support beneath the peripheral iris, thus preventing the iris root from falling away from the trabecular meshwork after iridectomy.[18,19]

In a person with narrow angles, a positive dark-room test suggests that pupillary block has occurred and the test usually becomes negative after the performance of a peripheral iridectomy.[4,20] The mechanism of a positive dark-room test in eyes with plateau iris syndrome has been suggested to be related to folding of the peripheral iris secondary to pupil dilation, with occlusion of the angle.[3] Although the mechanism resulting in a positive prone test is unknown, it has been proposed that the prone position allows forward movement of the lens against the iris, which thereby increases pupillary block.[3,21] In addition, it has been suggested that the forward movement of the lens-iris diaphragm may occlude the anatomically predisposed angle.[22] Confirmatory gonioscopy documenting angle closure is the *sine qua non* of angle closure provocation, but in practice is difficult to undertake

because the light of gonioscopic examination reverses the angle closure the examiner is trying to document.[23] Ideally this examination should be performed in the dark using infra-red light.

In this study a significant difference was observed in the response to prone provocative testing between the group with a steep iris plane, and the group with a plateau iris. The results are unlikely to be related to differences in the degree of peripheral anterior synechiae, because those with a plateau iris were significantly more likely to demonstrate a positive response than those with a steep iris plane even when the groups were matched on the basis of quadrants of angle closure. The difference in response is also unlikely to be related to peripheral iris folding secondary to dilation in the dark in those with a plateau iris, because significantly more positive results were obtained after dark-room prone testing than after dark-room testing. However, if the recently described anatomical abnormality in plateau iris is considered, the difference in response between the two groups may be explained by a forward movement of anteriorly positioned ciliary processes in the prone position in those with a plateau iris, resulting in anterior displacement of the peripheral iris root and subsequent occlusion of the angle (Figure 5.2).

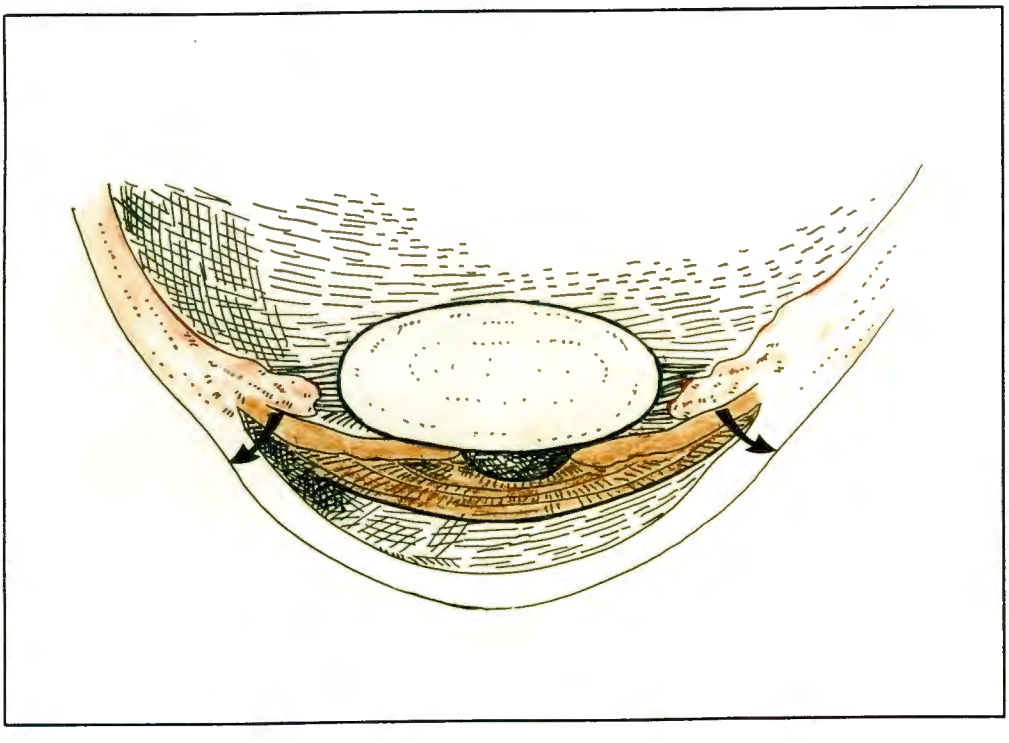

Figure 5.2 Possible explanation of positive results to prone provocative testing

Although a pupillary block mechanism undoubtedly plays an important role in the pathogenesis of angle occlusion in patients with primary angle-closure glaucoma, this study suggests that plateau iris syndrome is not uncommon in patients of mixed ethnic background and therefore also in Asians and Africans. In an eye with a crowded anterior segment, chronic angle-closure glaucoma may be caused in some individuals by abnormal anteriorly positioned ciliary processes (Figure 5.3). Mizuno *et al* made a similar observation in Japanese patients with primary angle-closure glaucoma.[24] By using "cycloscopy" (indirect observation of the ciliary processes), the ciliary processes were found to be hypertrophic in both width and length and lay in an anterior position.[24] This anatomical abnormality may explain the differences in response to provocative testing previously reported in Asian and European studies and may explain the angle appearance described by Gorin as "shortening of the angle" and by Lowe as "creeping angle closure".[3,4,25,26] To resolve this issue, high resolution ultrasound of the anterior segment would be useful in these patients.

Figure 5.3 Gonioscopic appearance of anteriorly positioned ciliary processes seen through a periphery iridectomy.

5.5 References

1. Salmon JF. Presenting features of primary angle-closure glaucoma in patients of mixed ethnic background. *S Afr Med J* 1993; **84** : (in press).
2. Hyams A. *Angle-closure Glaucoma* 1st. ed. Amsterdam: Kugler and Ghedini, 1990; 16-18.
3. Hung PT, Chou LH. Provocation and mechanism of angle-closure glaucoma after iridectomy. *Arch Ophthalmol* 1979; **97** : 1862 - 1864.
4. Friedman Z, Neumann E. Comparison of prone-position, dark room and mydriatic tests for angle-closure glaucoma before and after peripheral iridectomy. *Am J Ophthalmol* 1972; **74** : 24-27.
5. Karmon G, Vender T, Savir H. Evaluation of laser iridectomy in angle-closure glaucoma. *Br J Ophthalmol* 1982; **66** : 471-473.
6. Foulds WS. Observations on the darkroom test and its mechanism. *Br J Ophthalmol* 1957; **41** : 200-207.
7. Newcombe RG, Duff GR. Eyes or patients? Traps for the unwary in the statistical analysis of ophthalmological studies. *Br J Ophthalmol* 1987; **71** : 645-646.
8. Thompson JR. The chi-square test for data collected on eyes. *Br J Ophthalmol* 1993; **77** : 115-117.
9. Lowe RF. The aetiology of the anatomical basis of angle closure glaucoma. *Br J Ophthalmol* 1970; **54** : 161-169.
10. Lowe RF. Natural history and principle of treatment of primary angle-closure glaucoma. *Am J Ophthalmol* 1966; **61** : 642-651.
11. Ritch R, Lowe RF, Reyes A. Therapeutic overview of angle-closure glaucoma. In: Ritch R, Shields MB, Krupin T, eds. *The Glaucomas* St. Louis: CV Mosby, 1989: 856-857.

12. Hung PT. Etiology and mechanism of PACG. *Asian Pac J Ophthalmol* 1990; **2** : 82-84.

13. Lowe RF, Lim ASM. *Primary angle closure glaucoma.* 1st Ed. Singapore: PG Publishing, 1989; 33-39.

14. Murphy MB, Spaeth GL. Iridectomy in primary angle-closure glaucoma. *Arch Ophthalmol* 1974; **91** : 114-122.

15. Wand M, Grant W, Simmons RJ, Hutchinson BT. Plateau iris syndrome. *Trans Am Acad Ophthalmol Orolaryngol* 1977; **83** : 122-129.

16. Lowe RF. Plateau iris. *Aust J Ophthalmol* 1981; **9** : 71-78.

17. Tripathi R, Tripathi B. In: Jakobiec FA, ed. *Ocular Anatomy, Embryology and Teratology*. Philadelphia: Harper & Row, 1982; 197-284.

18. Ritch R. Plateau iris is caused by abnormally positioned ciliary processes. *J Glaucoma* 1992; **1** : 23-26.

19. Pavlin CJ, Ritch R, Foster FS. Ultrasound biomicroscopy in plateau iris syndrome. *Am J Ophthalmol* 1992; **113** : 390-395.

20. Lowe RF. Primary angle-closure glaucoma : investigations after surgery for pupil block. *Am J Ophthalmol* 1968; **65** : 548-551.

21. Harris LS, Galin MA. Prone provocative testing for narrow angle glaucoma. *Arch Ophthalmol* 1972; **87** : 493-496.

22. Hyams SW, Friedman A, Neumann E. Elevated intraocular pressure in the prone position. *Am J Ophthalmol* 1968; **66**: 661-672.

23. Gorin G. Provocation tests in angle closure glaucoma. Importance of gonioscopic control. *Am J Ophthalmol* 1965; **60** : 235-241.

24. Mizuno K, Kimura R, Miroi S. Cycloscopy of angle-closure glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1977; **204** : 247-254.

25. Gorin G. Shortening of the angle of the anterior chamber in angle-closure glaucoma. *Am J Ophthalmol* 1960; 141-146.

26. Lowe RF. Primary creeping angle-closure glaucoma. *Br J Ophthalmol* 1964; **48** : 544-550.

6.0 Presenting Features of Primary Angle-Closure Glaucoma in Patients of Mixed Ethnic Background

6.1 Introduction

Primary glaucoma is classified into two main entities: open-angle glaucoma and angle-closure glaucoma. The conditions are differentiated by examination of the drainage structures of the eye with a gonioscope. In patients with angle-closure glaucoma, the trabecular meshwork is partially or totally closed by the iris root. Accurate differentiation between these two entities is important because the therapy of angle-closure glaucoma is significantly different from that of open-angle glaucoma.

Clinically, patients with primary angle-closure glaucoma may present with a red, painful eye (so-called acute glaucoma) or with a white eye and gradual, painless loss of vision (so-called chronic angle-closure glaucoma). The relative frequency of the two presenting profiles are dependent on the race of the individual. In whites, acute glaucoma is significantly more common than chronic angle-closure glaucoma.[1,2] However in black and oriental people the reverse is true, and most of these individuals present with chronic angle-closure glaucoma.[3-7] The presenting features of primary angle-closure glaucoma and the effect of this disease on vision, have not previously been reported in "coloured" people.

6.2 Patients and Methods

All new "coloured" patients who presented at Groote Schuur Hospital between January 1986 and December 1990 with the diagnosis of primary angle-closure glaucoma were evaluated.

The diagnosis of primary angle-closure glaucoma was made on presentation if the intraocular pressure was >21 mmHg, or if glaucomatous disc cupping with a corresponding glaucomatous visual field was found, in the presence of a partially or totally closed angle or peripheral anterior synechiae. Provocation tests were not performed. Patients with secondary angle closure (for example secondary to uveitis, angle neovascularisation and lens intumescence) were excluded.

Patients were classified according to the features on presentation into one of two groups: acute or chronic. Patients who presented with a red, painful eye, raised intraocular pressure and a closed angle were classified as having acute glaucoma. Those who presented with a history of painless visual loss, a non-inflamed eye, raised intraocular pressure and a partially closed angle were classified as having chronic angle-closure glaucoma. The appearance of the optic disc was not taken into account when classifying either of these groups.[11] Those patients who presented with a previous history of intermittent ocular pain or headache associated with a partially occluded angle, a normal intraocular pressure and glaucomatous disc cupping, were included in the chronic angle-closure glaucoma group. A record was kept of all patients with acute or chronic angle-closure glaucoma whose history suggested previous intermittent closure of the angle. Fellow eyes with a shallow anterior chamber, an occludable angle but a normal intraocular pressure and optic disc, were considered to be "predisposed" to primary angle-closure glaucoma.

All patients were assessed by the same observer and underwent a full ophthalmic examination including slit lamp examination, applanation tonometry and direct ophthalmoscopy. The best corrected visual acuity was recorded after control of the acute episode of intraocular pressure rise. The drainage angle was assessed by means of manipulative Goldmann gonioscopy or indentation gonioscopy. In the areas classified as closed, only Schwalbe's line was visible. The angle was divided into four quadrants and noted as 1/4, 2/4, 3/4, or 4/4 closed (Figure 6.1).

Figure 6.1 Gonioscopic appearance of chronic angle closure. An arrow shows the sharply defined transition between an open angle and a closed angle.

The average of the vertical and horizontal cup : disc ratios was recorded. Visual fields were examined in all sighted patients by means of a Humphrey automated field analyser. Abnormal fields had defects of at least 0.5 log-unit depth and a shape and distribution typical of optic nerve damage rather than artifact. In those patients unable to perform full threshold field analysis, a "three zone"

threshold-related suprathreshold screening visual field was performed. In patients with optic disc cupping, a field was considered glaucomatous if seventeen or more absolute and/or relative defects were present in the full test area.[8] If visual field analysis could not be performed on presentation the examination was performed once the acute condition had been controlled.

Statistical analysis was performed using the t-test and Pearson's test of correlation. A finding was considered significant at $P < 0.05$.

6.3 Results

In the 5-year period, 92 new patients presented with the diagnosis of primary angle-closure glaucoma. The mean age at presentation was 62.2 years (44-82 years) and 69 (75%) were women.

Thirty-three (36%) patients presented with acute angle-closure glaucoma and 59 (64%) with chronic angle-closure glaucoma, a ratio of nearly 1 : 2. Six patients had bilateral acute glaucoma and 38 had bilateral chronic angle-closure glaucoma on presentation (Table 6.1). Twenty patients with chronic angle-closure glaucoma gave a definite history of previous intermittent ocular pain and headache.

TABLE 6.1
Diagnosis in presenting and fellow eyes of 92 patients seen over a 5-year period with primary angle-closure glaucoma

FELLOW EYE	PRESENTING EYE		
	Acute	Chronic	Total
Acute	6	-	6
Chronic	8	41	49
Predisposed	17	15	32
Other[+]	2	3	5
Total	33	59	92

[+] Other indicates a blind eye secondary to trauma or neovascular glaucoma

The mean intraocular pressure in eyes presenting with acute angle-closure glaucoma was 51.0 mmHg; with chronic angle-closure glaucoma 34.4 mmHg; and in eyes that were considered to be predisposed to closure, 16.2 mmHg. Despite a mean intraocular pressure of 34.3 mmHg in eyes with chronic angle-closure, the intraocular pressures were found to be between 40 and 49 mmHg in 22 eyes and between 50 and 59 mmHg in 13 eyes.

The intraocular pressure on presentation was compared with the number of quadrants of angle closure (Figure 6.2). The superior quadrants were consistently involved in all eyes. The greater the number of closed quadrants, the higher the initial intraocular pressure. The correlation between the intraocular pressure on presentation and the number of closed quadrants was good. (Correlation coefficient : $r = 0.73$; $P < 0.001$).

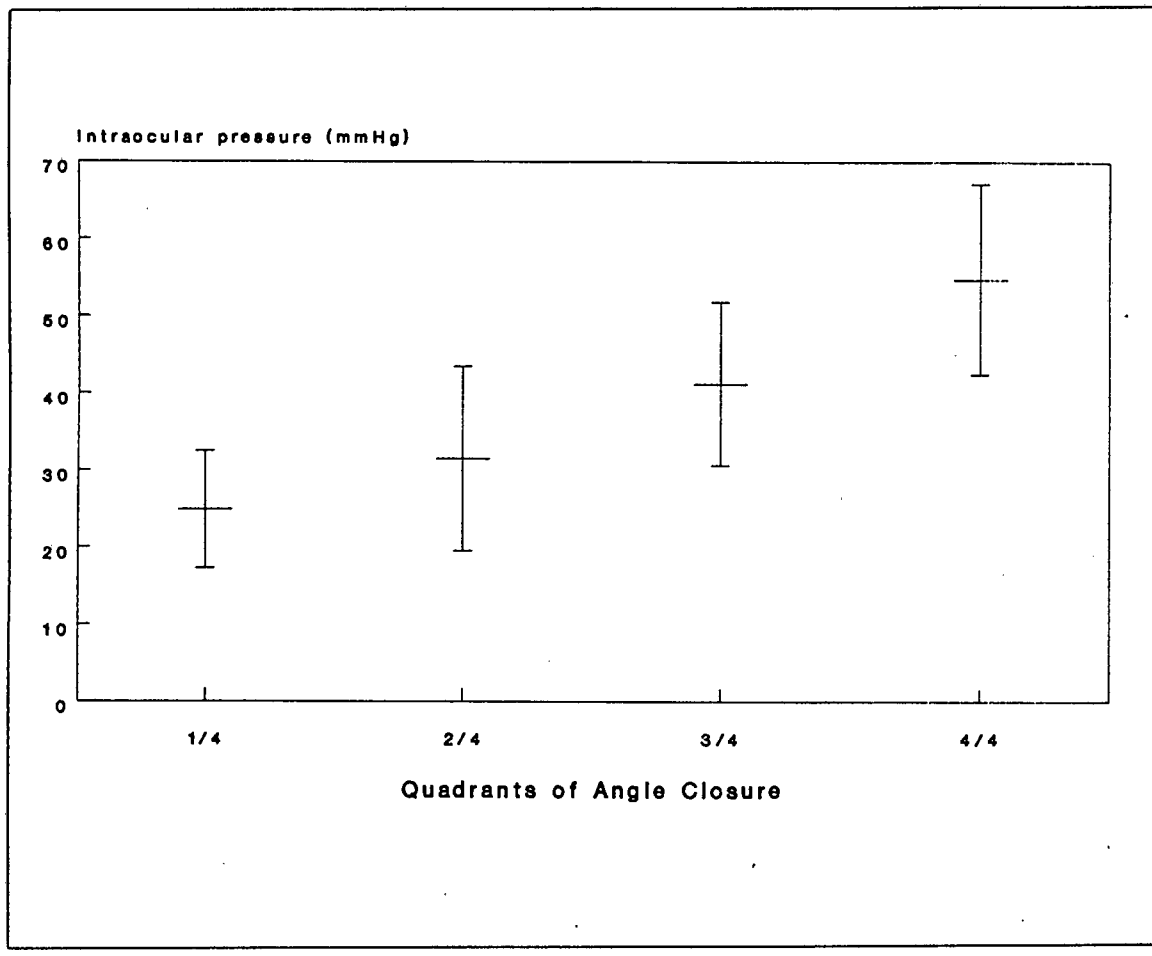

Figure 6.2 The mean intraocular pressure on presentation with one standard deviation compared with the number of quadrants of angle closure

The mean cup : disc ratio was greater than 0.7 in 65 of 184 eyes (35%) and the visual acuity assessed after control of the acute episode, was worse than 6/12 in 79 eyes (43%) (Figure 6.3). In 51 patients, the reduction in visual acuity was related mainly to nuclear sclerosis, although early corticular lens opacity and posterior subcapsular cataract were also observed. While cataract formation prevented examination of the optic disc in 3 eyes, intumescence of the lens was not found. Glaucomatous visual field loss was found in 24 eyes with signs of acute glaucoma and in 80 eyes with chronic angle-closure glaucoma (56.5%, 104/184). In 15 eyes with acute and in 28 with chronic angle-closure, full visual fields were present.

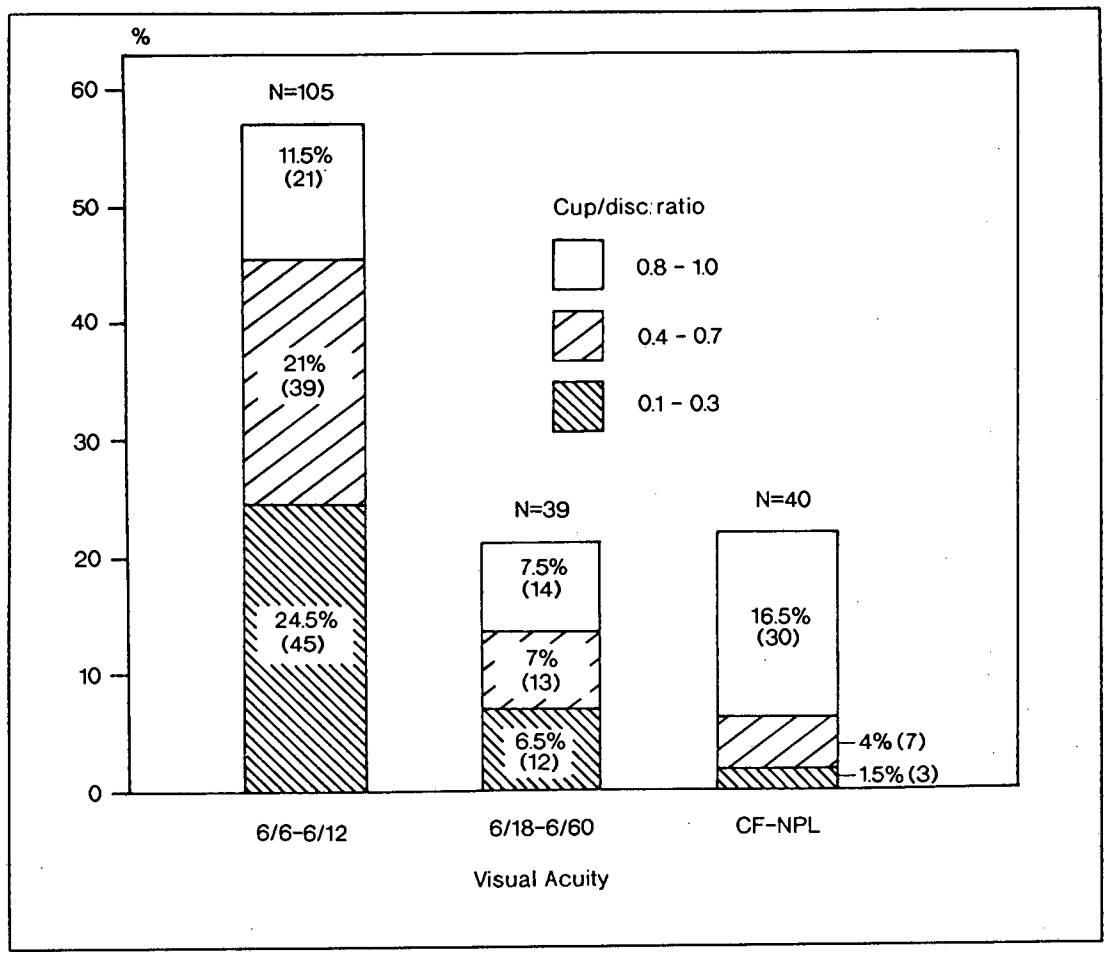

Figure 6.3 Best corrected visual acuity and mean cup : disc ratio in 184 eyes of 92 patients

Eighteen patients presented with no light perception in one eye. The cause of the blindness was absolute angle-closure glaucoma in 13 patients (4 with acute glaucoma), neovascular glaucoma secondary to a central retinal vein occlusion in 3 patients and phthysis bulbi secondary to trauma in 2 patients. The fellow eyes in these 18 patients were also found to have experienced severe visual loss. (Figure 6.4). A diagnosis of chronic angle-closure glaucoma was made in 12 fellow eyes (mean intraocular pressure = 33.7 mmHg) and acute angle-closure glaucoma in 5 fellow eyes (mean intraocular pressure = 50.2 mmHg). One eye was considered to be predisposed to angle closure (mean intraocular pressure 16mm Hg). Only 4 of these 18 patients had a visual acuity of more than 6/12 with a normal optic disc and full visual fields.

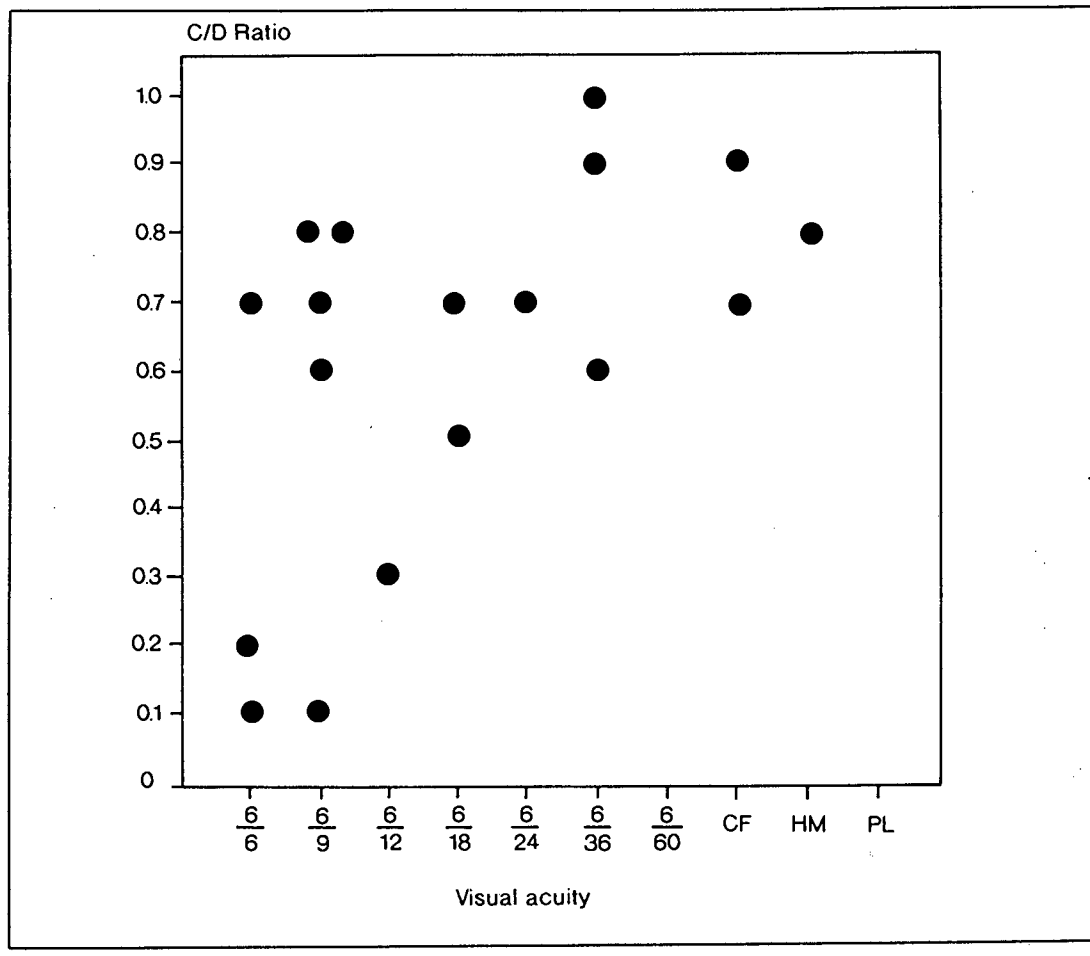

Figure 6.4. Best corrected visual acuity and mean cup : disc ratio in the 18 fellow eyes of patients with uniocular absence of light perception.

6.4 Discussion

The presenting features of primary angle-closure glaucoma depends on the ethnic background of the patients.[9] The majority of white patients with angle-closure glaucoma in South Africa and Europe present with acute symptoms and signs.[1,7] This has also been shown in Eskimos in Alaska.[9] Blacks in South Africa and America and Orientals tend to present with chronic manifestations[3,4,7,10] (Figure 6.5). These patients give a history of gradual visual loss that, without treatment, may progress to irreversible blindness.[3]

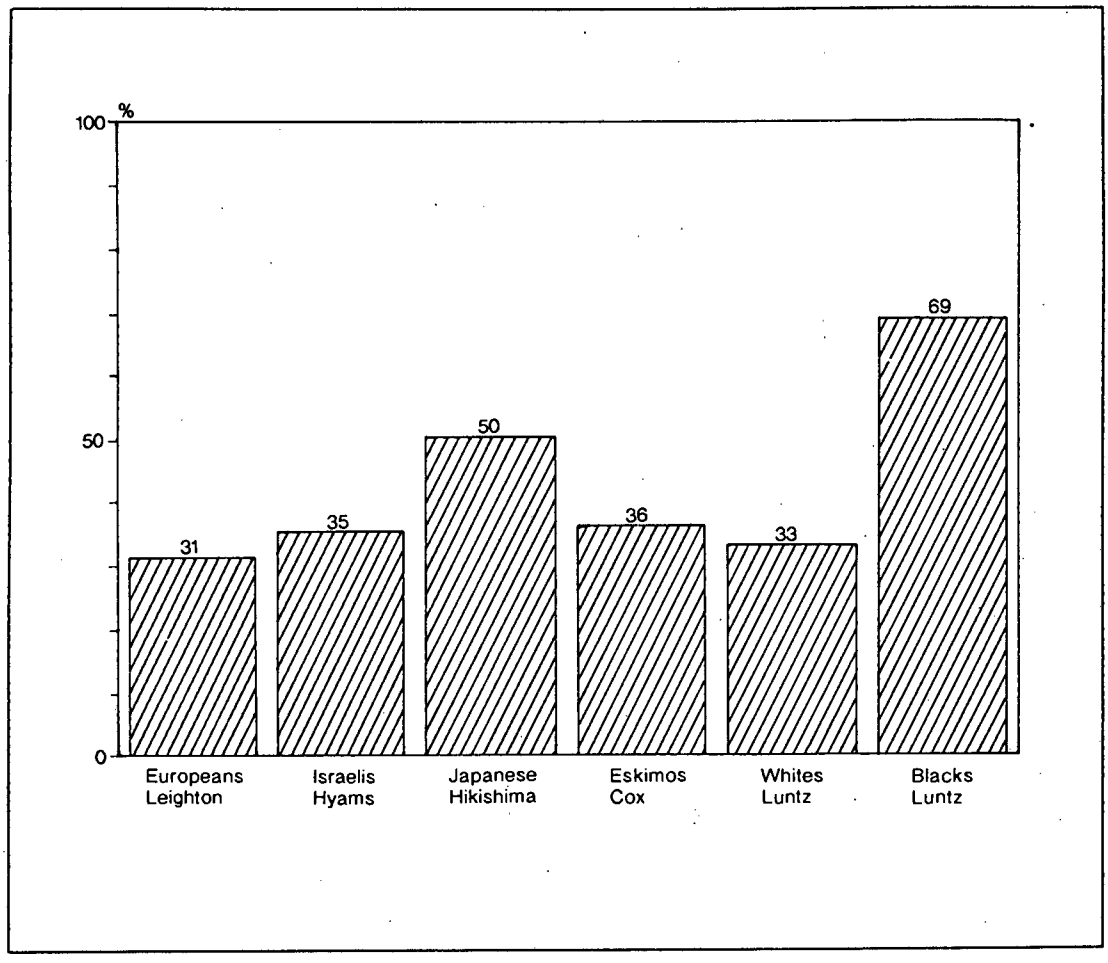

Figure 6.5 Frequency of chronic angle-closure glaucoma as presenting feature of primary angle-closure glaucoma in eye clinic surveys.

Patients with angle-closure glaucoma may present with an acute, subacute (intermittent) or chronic condition. This classification is an over-simplification, because a combination of these types is often seen.[11] A patient presenting with an acute attack may have a deeply excavated disc in one or both eyes due to long-standing chronic angle-closure glaucoma. Similarly, a patient with chronic angle-closure glaucoma may also be suffering from asymptomatic intermittent episodes of angle-closure. In this study therefore, the features on presentation were assessed irrespective of glaucomatous disc damage and the patients were divided into only two categories, acute or chronic angle-closure glaucoma. Seven patients

who presented with quiet eyes, shallow anterior chambers, partially occluded angles, normal intraocular pressures, cupped discs and glaucomatous visual field loss were included in the chronic angle-closure glaucoma group.

Chronic angle-closure glaucoma is also referred to as "creeping" angle closure or "shortening of the angle".[12,13] This disease is often misdiagnosed because it closely resembles primary open-angle glaucoma, in that patients are asymptomatic, have quiet eyes and often have cupping of the optic disc and visual field loss. Gonioscopy is the key to the diagnosis of chronic angle-closure glaucoma and it reveals a narrow angle with apposition between the iris and the trabecular meshwork. Apposition may result in permanent occlusion of the angle with peripheral anterior synechiae.

Of the 92 patients, 69 (75%) were women and the mean age at presentation was 62.2 years. European and Eskimo studies have reported an identical sex distribution.[1,4,9] (Figure 6.6.). Other studies show that most patients present in their sixth and seventh decades.[1,7,14] There were no differences between the demographic characteristics of patients with acute glaucoma and those with chronic angle-closure glaucoma.

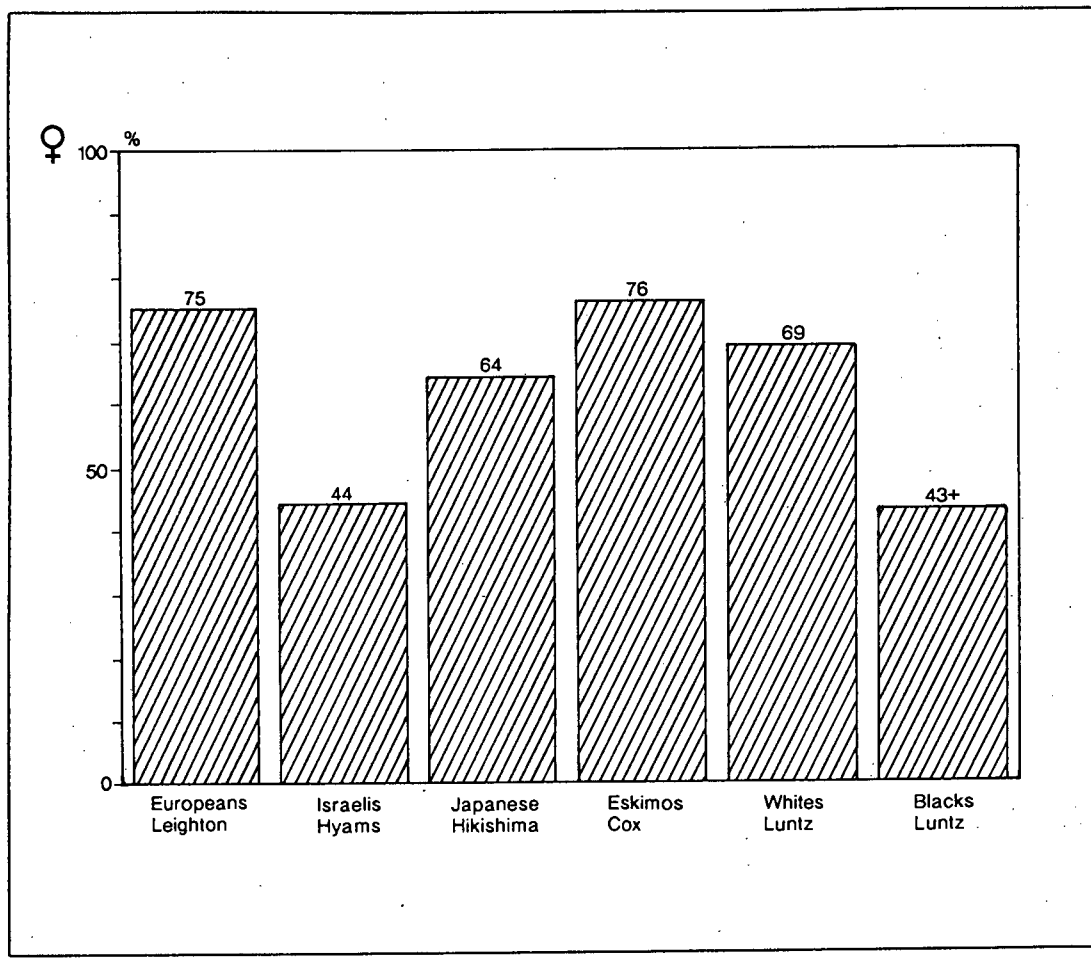

Figure 6.6 Sex distribution of patients with primary angle-closure glaucoma. (+ indicates selection bias)

During this 5-year period, 33 (36%) patients presented with an acute episode of angle closure and 59 (64%) patients with signs of chronic angle-closure glaucoma, a ratio of 1 : 2. Although it has been reported that acute angle-closure glaucoma is rare in blacks, Luntz found an incidence of 32% and therefore a similar acute : chronic ratio.[5,6,7] Twenty (21.7%) patients gave a definite previous history of intermittent ocular pain before presentation. In a study from Israel, 23% of patients with primary angle-closure glaucoma gave a history of subacute episodes, but Lowe reported that nearly 50% of patients who presented with acute glaucoma had experienced similar symptoms in the past.[9,15] Because of the asymptomatic nature of the intraocular pressure spikes in our patients, the incidence of previous

subacute episodes of angle-closure glaucoma may have been higher than 21.7% All the fellow eyes of the 32 (35%) patients who presented with unilateral acute or chronic angle-closure glaucoma, were predisposed to angle closure. Six (6.5%) patients presented with bilateral acute glaucoma; a figure in accordance with previous reports.[2]

The mean intraocular pressure on presentation was higher in patients with acute angle-closure glaucoma (51.0 mmHg) than in patients with chronic angle-closure (34.4 mmHg). The mean intraocular pressure for eyes predisposed to angle closure was 16.2 mmHg. It was remarkable how high the intraocular pressure was on presentation in some patients with chronic angle-closure glaucoma (13 patients had an intraocular pressure of more than 50 mmHg) who had no symptoms or signs of acute congestion or corneal oedema (Figure 6.7). Similar findings have been noted in blacks in Africa and in America and have not been explained.[4-6]

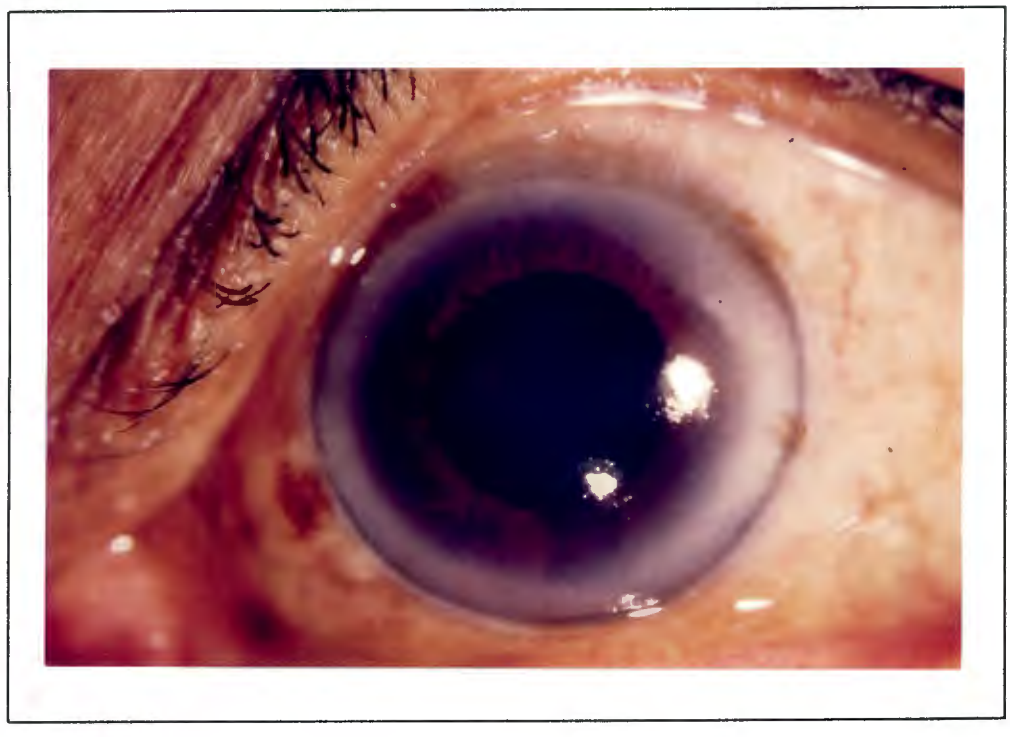

Figure 6.7 Patient with chronic angle-closure glaucoma without signs of congestion and an intraocular pressure of 60 mmHg.

The level of intraocular pressure on presentation correlated well with the number of closed quadrants of drainage angle assessed gonioscopically (r = 0.73). It has been previously suggested that the height of the intraocular pressure is directly related to the extent of angle closure and a linear relationship and correlation coefficient of 0.46 has been shown before.[13,16]

Most of these patients presented with reduced visual acuity and glaucomatous visual fields. In 51 patients early cataract was found. These lens changes were probably age-related, although Lowe has suggested that nuclear sclerosis may be a complication of primary angle-closure glaucoma.[17] In addition, the effects of acute or chronically raised intraocular pressure were present in many eyes. Only 15 patients with acute glaucoma were found to have a normal disc with full visual fields. Advanced disc excavation was present in 35% of eyes and glaucomatous visual field loss in 56.6% of eyes. Unilateral blindness was evident in 13 patients with absolute glaucoma and in 3 patients with neovascular glaucoma secondary to a central retinal vein occlusion; the latter is a complication of primary angle-closure glaucoma that has been recognised previously.[18] Evidence of advanced optic disc damage was present in the fellow eyes of most of the patients who presented with one blind eye. A similar pattern of destructive eye disease has been noted in Southeast Asia.[19] This is in marked contrast to the findings of Leighton *et al*, who reported that 5 of 77 (6.5%) English patients had a blind eye (one with neovascular glaucoma, one with a central retinal vein occlusion and three with absolute angle-closure glaucoma).[1]

The effects of raised intraocular pressure on other anterior segment structures was not significant. Corneal oedema was present in only 23 patients on presentation.

Of these, 9 had acute glaucoma with a normal optic disc and 14 had acute glaucoma with a cupped disc. Patients with chronic angle-closure glaucoma had no corneal oedema despite high intraocular pressures and in 10 patients with acute glaucoma, a clear cornea was found. This finding has been recognised previously, and is difficult to explain as significant corneal endothelial cell loss has been demonstrated following acute intraocular pressure elevation.[17,20]

Primary angle-closure glaucoma and chronic open-angle glaucoma may both occur in the same eye, resulting in so-called "mixed mechanism" glaucoma. This occurs as a result of the chance co-existence of the two mechanisms of glaucoma and is rare. In a retrospective review of 1,861 glaucoma patients this diagnosis was only made in 3 patients.[21] Hyams found 3 definite cases of mixed mechanism glaucoma out of 267 eyes that had undergone peripheral iridectomy for primary angle-closure glaucoma.[22] In my series of 92 patients with primary angle-closure glaucoma the diagnosis of mixed mechanism glaucoma was not made in any patient. In most cases of mixed mechanism glaucoma careful examination will reveal an open-angle glaucoma with a narrow but functionally open angle, open-angle glaucoma with a false positive provocative test, angle-closure glaucoma with trabecular damage (seen clinically as granular pigmentation of the meshwork) or plateau iris syndrome.[11]

In conclusion, the study has shown that "coloured" patients with primary angle-closure glaucoma are more likely to present with chronic symptoms and signs and that the disease may result in devastating ocular damage and visual loss. In "coloured" patients with signs of primary glaucoma, chronic angle-closure glaucoma should be excluded by careful gonioscopic evaluation of the drainage structure of the eye.

6.5 References

1. Leighton DA, Phillips CI, Tsukahara S. Profile of presenting states of eyes in angle-closure glaucoma. *Br J Ophthalmol* 1971; **55** : 577-584.
2. Hyams SW, Friedman Z, Keroub C. Fellow eye in angle-closure glaucoma. *Br J Ophthalmol* 1975; **59** : 207-210.
3. Lowe RF, Lim ASM. *Primary Angle Closure Glaucoma.* 1st ed. Singapore, PG Publishing 1989 : 52.
4. Alper MG, Laubach JL. Primary angle-closure in the American Negro. *Arch Ophthalmol* 1968, **79** : 663-668.
5. Avshalom A, Berson D, Blumenthal M, *et al.* Israeli Ophthalmologists in Africa. *J Isr Med Ass* 1966; **70** : 250-254.
6. Neumann E, Zauberman H. Glaucoma survey in Liberia. *Am J Ophthalmol* 1965, **59** : 8-12.
7. Luntz MH. Primary angle-closure glaucoma in urbanised South African Caucasoid and Negroid communities. *Br J Ophthalmol* 1973; **57** : 445-456.
8. Kosoko O, Sommer A, Auer C. Screening with automated perimetry using a threshold-related three-level algorithm. *Ophthalmology* 1986; **93** : 882-886.
9. Cox JE. Angle-closure glaucoma among the Alaskan Eskimos. *Can J Ophthamol* 1973; **8** : 252-254.
10. Hikishima H, Takahashi N, Yuki Y. A clinical analysis of primary angle-closure glaucoma patients. *Folia Ophthalmol Jpn* 1986; **37** : 737-740.
11. Hyams S. *Angle-closure glaucoma.* 1st ed. Amsterdam. Kugler and Ghedini Publications 1990 : 2-3, 64.
12. Lowe RF. Primary creeping angle-closure glaucoma. *Br J Ophthalmol* 1964; **48** : 544-550.

13. Gorin G. Shortening of the angle of the anterior chamber in angle-closure glaucoma. *Am J Ophthalmol* 1960; **49** : 141-146.

14. Teikari J, Raivio I, Nurminen M. Incidence of acute glaucoma in Finland from 1973 to 1982. *Graefe's Arch Clin Exp Ophthalmol* 1987; **225** : 357-360.

15. Lowe RF. Angle-closure glaucoma : acute and subacute attacks : clinical types. *Trans Ophthalmol Soc Aust* 1961; **21** : 65-75.

16. Bhargava SK, Leighton DA, Phillips CI. Early angle-closure glaucoma. Distribution of iridotrabecular contact and response to pilocarpine. *Arch Ophthalmol* 1973; **89** : 369-372.

17. Lowe RF. Primary angle-closure glaucoma : damage to cornea and lens. *Br J Ophthalmol* 1965; **49** : 460-465.

18. Sonty S, Schwartz B. Vascular accidents in acute angle-closure glaucoma. *Ophthalmology* 1981; **88** : 225-228.

19. Lim ASM. Prevention of blindness in Singapore. *S'pore Med J* 1965; **6** : 96-102.

20. Markowitz SN, Morin JD. The endothelium in primary angle-closure glaucoma. *Am J Ophthalmol* 1984; **98** : 103-4.

21. Abrams JD. Mixed glaucoma. *Br J Ophthalmol* 1961; **45** : 503-510.

22. Hyams SW, Keroub C, Pokotilo E. Mixed glaucoma. *Br J Ophthalmol* 1977; **61** : 105-106.

7.0 The Association of Iridoschisis and Primary Angle-Closure Glaucoma

7.1 Introduction

In 1945, Loewenstein and Foster proposed the term "iridoschisis" to describe a localised cleavage of the iris stroma into two layers, which had occurred in an elderly patient with absolute glaucoma.[1] The anterior leaf of iris was atrophic and had disintegrated into fibrils which were floating freely in the anterior chamber.

Since the original study by Schmitt in 1922, most descriptions of iridoschisis have been limited to individual case reports.[1-15] However, two series have been reported, each describing six patients.[16,17] Although the pathogenesis of iridoschisis is unknown, it has been associated mainly with primary angle-closure glaucoma or has occurred as an apparently idiopathic atrophy in elderly individuals. Other less common associations include congenital abnormalities, congenital syphilis or a history of antecedent trauma.[12,13,18,19]

In this chapter, the clinical features found in twelve patients with iridoschisis are described and the relationship of iridoschisis to raised intraocular pressure in chronic angle-closure glaucoma is discussed.

7.2 Patients and Methods

During a five-year period, from June 1985 to May 1990, a total of seventeen patients with iridoschisis were seen at Groote Schuur Hospital. Twelve of these

patients were referred to the glaucoma clinic because of acutely raised intraocular pressure or because of glaucomatous disc damage with visual field loss; and two were referred because of unusual iris changes. Three patients were seen once in a general ophthalmic clinic and failed to return for follow-up. Because of insufficient clinical details on retrospective analysis these three patients have been excluded from analysis. Two patients with a history of ocular trauma and angle recession glaucoma have been separately reported.[20] For the purpose of this study, twelve unrelated patients with iridoschisis in one or both eyes were therefore studied. Three were males and nine females, whose ages ranged from 39 to 76 years (mean 63.3 years).

A detailed ophthalmic and medical history was taken. Each patient underwent a full ophthalmic examination, including best corrected visual acuity, slit-lamp examination, applanation tonometry, gonioscopy and direct ophthalmoscopy. Humphrey computerised field analysis was performed and A-scan ultrasound was used to measure the corneal thickness-anterior chamber depth and the axial length. Anterior segment photography was performed on all patients.

To describe the anterior chamber angle, both Scheie's gonioscopic classification (based on the extent of visible angle structures) and Shaffer's classification (based on the degrees of arc subtended by the inner surface of the trabecular meshwork and the anterior surface of the iris) were used. By using both classifications, an accurate description could be achieved for those patients with a flatter iris who nevertheless had closed angles.

Ocular biometry results for the study patients were compared with two control groups who were matched for age, sex and race. The one control group consisted of 24 "coloured" patients with a mean age of 63.7 years, who had chronic angle-closure

glaucoma without iris pathology. The other control group consisted of 24 healthy "coloured" individuals with a mean age of 60.3 years who had no evidence of ocular pathology or refractive error. In patients with iridoschisis, axial length measurements were obtained in 19 eyes and anterior chamber depth measurements in 17 eyes. In both eyes of each patient with chronic angle-closure glaucoma and each normal individual, axial length and anterior chamber depth measurements were obtained. Because the biometry obtained from the right and left eye was similar in each case, 48 measurements were assessed from both control groups. Statistical analysis of variance was used to compare the measurements. A finding was considered significant at $P < 0.05$.

7.3 Results

Of the twelve patients in this study, six presented initially with a history of gradual, painless loss of vision or with presbyopic symptoms. Six presented with painful loss of vision, including one who had undergone an enucleation in 1979 for absolute glaucoma resulting from untreated acute angle-closure glaucoma.

Ten patients (patients 1-10) had suffered from intermittent headaches or eye pain, for periods ranging from a few months to sixteen years. On presentation, the intraocular pressure in these patients ranged from 12mmHg to 65mmHg (mean 35mmHg). In fourteen eyes (seven patients) there was evidence of glaucomatous disc damage with a corresponding field defect, but in five eyes (three patients) no damage to the optic nerve was detected. All ten patients had gonioscopic evidence of chronic angle closure, particularly involving the superior angle and all experienced symptomatic relief with control of the intraocular pressure (Table 7.1).

TABLE 7.1
CLINICAL DATA FOR TWELVE PATIENTS WITH IRIDOSCHISIS

Patient	Age	Sex	I.O.P. [mmHg]*		Cup: Disc Ratio	
			R	L	R	L
1	57	M	65	50	1.0	0.5
2	72	F	28	20	0.9	0.6
3	60	F	12	14	0.1	0.1
4	75	F	40	48	0.9	0.7
5	69	F	21	21	0.5	0.6
6	54	M	-	40	-	0.4
7	68	F	16	19	0.7	0.8
8	49	F	43	32	0.1	0.1
9	68	F	40	55	0.8	0.9
10	39	F	55	40	0.8	1.0
11	76	F	12	60	0.3	0.5
12	72	M	9	10	0.1	0.1

TABLE 7.1 continued...
CLINICAL DATA FOR TWELVE PATIENTS WITH IRIDOSCHISIS

Patient	Iridoschisis#		Angle+	
	R	L	R	L
1	SUP/INF	INF	IV 180 °(1)	IV 180 °(1)
2	NIL	INF	III 360 °(1)	III 360 °(1)
3	NIL	INF	IV 180 °(1)	IV 90 °(1)
4	INF	INF	IV 270 °(2)	IV 270 °(2)
5	INF	INF	IV 180 °(1)	IV 180 °(1)
6	-	INF	-	IV 180 °(2)
7	NIL	INF	IV 180 °(1)	IV 90 °(1)
8	INF	INF	IV 360 °(1)	IV 360 °(1)
9	INF	INF	IV 360 °(1)	IV 360 °(1)
10	SUP/NIL	INF	IV 180 °(1)	IV 180 °(1)
11	INF	INF	III 180 °(1)	IV 180 °(1)
12	NIL	INF	III 360 °(2)	IV 180 °(2)

Age in years. Sex: M indicates male, F indicates female.
**Intraocular pressure on presentation*
#SUP indicates superior iris involvement. INF indicates inferior iris involvement. NIL indicates iris atrophy without iridoschisis. + Angle description based on Scheie's classification: III indicates posterior trabeculum obscured. IV indicates only Schwalbes' line visible. The maximum amount of angle closure on presentation is indicated in degrees. Shaffers' classification in brackets.

In two patients, no previous headaches or eye pain had been experienced. One of these patients presented with acute glaucoma after pupillary dilation (patient 11). One presented with visual loss secondary to a cataract and was coincidentally noted to have inferior iridoschisis, a closed superior angle but a normal optic disc (patient 12). Eleven patients had heavily pigmented, brown irides and one had brown-grey irides. Seven had iridoschisis in both eyes and 5 in one eye. The inferior quadrants were involved in 17 eyes (Figure 7.1 and 7.2) and both the superior and inferior quadrants in 2 eyes. Iris debris was seen in the inferior angles of three eyes (patients 4 and 10 bilaterally).

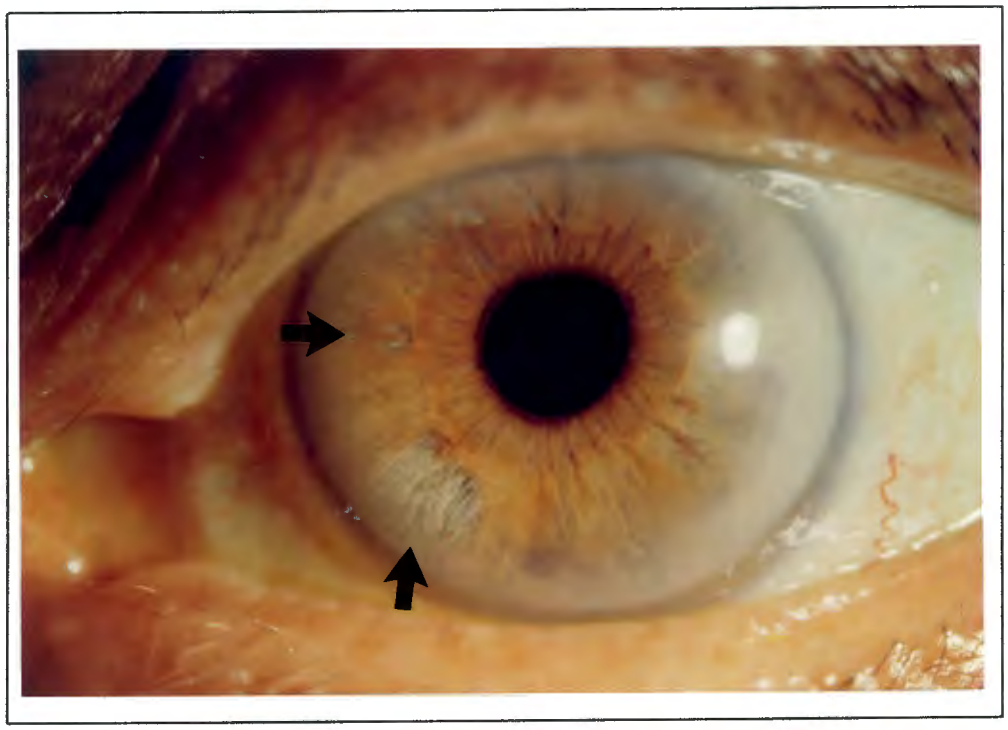

Figure 7.1 An eye demonstrating the earliest form of iris atrophy and iridoschisis (arrows)

Figure 7.2 The typical appearance of iridoschisis. Note the inferior distribution and round pupil.

The area of iridoschisis extended to the pupil margin in six eyes. A fixed dilated pupil was present in one eye, but the remainder had normal, round pupils. The loose strands of iris tissue resulted in limited corneal touch in 12 eyes, with a localised corneal opacity in one and a decompensated, oedematous cornea in another (Figure 7.3). One patient had signs of interstitial keratitis. Clear lenses were present in only two eyes (patients 5 and 10) and one lens was subluxed (patient 10). Nuclear sclerosis or corticular lens opacities were present in all other eyes. Some had fine anterior subcapsular lens opacities suggestive of previous glaukomflecken.

Figure 7.3 Iridoschisis with localised corneal opacity and laser iridotomy

In the fellow eyes of four patients with unilateral iridoschisis, subtle atrophic changes were noted in the inferior stroma of the iris (Table 7.1). Superficial intrastromal cystic changes were present and in addition, in two patients, fine slits were observed in the anterior surface of the iris overlying the cystic changes (Figure 7.1). Two of these four eyes (in patients 3 and 12) had normal discs and two (in patients 2 and 7) had cupped discs.

The A-scan ultrasound measurements obtained from patients with iridoschisis were compared with the measurements obtained in matched patients with chronic angle-closure glaucoma and matched normal individuals. The anterior chamber depths were measured from the anterior surface of the cornea to the anterior surface of the lens (Figure 7.4). The mean axial length of the eyes of patients with iridoschisis was 22.15mm (standard deviation 0.70) and the mean anterior chamber depth was 2.52mm (standard deviation 0.40). In matched patients with chronic angle-closure glaucoma without iris changes, the mean axial length of 48 eyes was 22.42 (standard deviation 0.61) and the mean anterior chamber depth was 2.45mm (standard deviation 0.25). The measurements obtained in these two groups were

statistically similar. In matched normal patients, the mean axial length was 23.14mm (standard deviation 0.55) and mean anterior chamber depth was 2.81mm (standard deviation 0.30). There was a highly significant difference between the measurements found in normal individuals and those found in patients with iridoschisis or chronic angle-closure glaucoma ($P<0.001$).

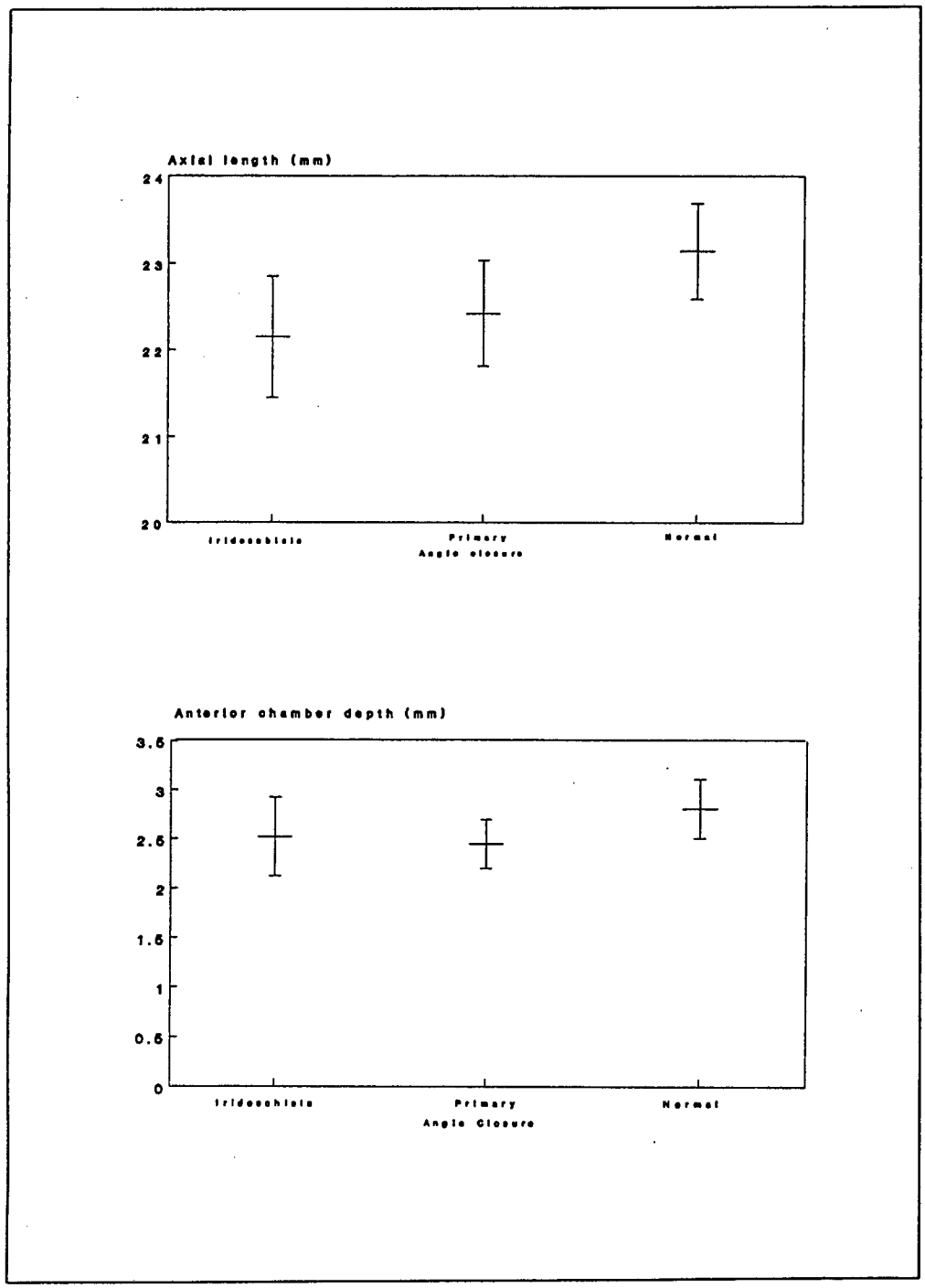

Figure 7.4 A-scan ultrasound results of patients with iridoschisis, chronic angle-closure glaucoma and matched normals; showing mean values with one standard deviation. The anterior chamber depths are measured from the anterior surface of the cornea to the anterior surface of the lens.

The intraocular pressure was controlled medically in all patients before surgery was performed. Eight patients (fourteen eyes) underwent a Nd-YAG laser peripheral iridotomy. In three patients a trabeculectomy was performed and one subsequently underwent uniocular implantation of a Molteno tube because of persistently raised intraocular pressure. Two patients had a cataract extraction with intraocular lens implantation and iridectomy as primary surgical treatment (patients 3 and 12). In one, a corneal graft was performed at the same time as the cataract extraction. Cataract surgery was subsequently performed in a further five patients during the five-year period of follow-up (Table 7.2). After surgery, the structures of the superior angle were clearly visible in all except two patients (patients 1 and 6) who had evidence of peripheral anterior synechiae. Two patients (patient 9 and 10) did not return for follow-up after their initial period of therapy. In the remainder, progressive iris change was not noticed. Long term intraocular pressure control was obtained in all patients, although topical pilocarpine 1% was required after peripheral iridotomy in four patients.

TABLE 7.2: REFRACTION AND OCULAR SURGERY

PATIENT	VISUAL ACUITY* R	L	REFRACTION+ R	L	IRIDOTOMY	TRABECUL-ECTOMY	CATARACT EXTRACTION
1	NPL	6/18	-	+1.50		Left	Left
2	6/24	6/24	+2.50	+1.75	Right/Left		Left
3	CF	CF	-	-			Right/Left
4	CF	6/9	-0.50	-0.25	Right/Left		Right
5	6/9	6/12	+0.75	-0.25	Right/Left		
6	-	6/24	-	+2.75	Left		
7	6/24	CF	+0.75	-	Right/Left		
8	CF	6/18	+1.00	+1.00	Right/Left		Right/Left
9	6/18	NPL	+1.00	-		Right	
10	6/9	NPL	-	-	Left	Right	
11	6/18	6/12	+1.00	+1.25	Rigth/Left		Right/Left
12	6/12	CF	+1.00	+1.00			Right/Left

*NPL indicates no perception of light. CF indicates counting fingers

+Equivalent sphere. No refraction obtained in blind eyes or eyes with cataract.

Nine of the twelve patients had systemic hypertension and in two the diagnosis of congenital syphilis was made (patients 6 & 7). One other patient had a positive serological test for syphilis (patient 12).

7.4 Discussion

During a 5-year period, an attempt was made to examine all the patients with iridoschisis who had presented at Groote Schuur Hospital. This series describes twelve patients with chronic angle closure associated with iridoschisis in one or both eyes. In all involved eyes, the anterior leaf of iris had split from the underlying iris stroma and had disintegrated into fibrils which projected into the anterior chamber. Although the patients had involvement of the inferior quadrants of the iris, two also had involvement of the superior quadrants. These characteristic signs of iridoschisis have been described and illustrated in the past, either in association with angle-closure glaucoma or as an apparently idiopathic atrophy of old age. [1-12, 14-17]

The pupil was round and central in all except one eye, where a fixed and dilated pupil was found. Because of iris touch, one patient had developed a localised corneal opacity and another an oedematous cornea; a complication that has been previously noted in patients with iridoschisis.[15,17] In four patients, subtle atrophy was present in the inferior iris stroma of the fellow eye suggestive of early, incomplete iridoschisis.

The diagnosis of primary angle-closure glaucoma was based on gonioscopic evidence of angle closure, particularly involving the superior angle; a shallow anterior chamber and a short axial length. The slight hypermetropic refraction

found on presentation, was influenced by early nuclear sclerosis in some patients. The mean anterior chamber depth and mean axial length measurements obtained from patients with iridoschisis are similar to previously reported biometric parameters demonstrated in patients with primary angle-closure glaucoma.[21] These measurements were similar to those found in a matched group of patients with chronic angle-closure glaucoma and statistically, significantly different to the findings in matched normals.

Although six patients were asymptomatic on presentation, the history in five was suggestive of subacute angle-closure. Similarly, five of the patients who presented with signs of acute glaucoma gave a history of previous intermittent pain and headache. Examination revealed glaucomatous disc damage and visual field loss in fourteen eyes, but no disc damage was found in nine eyes.

Considering the underlying diagnosis in these patients, it seems likely that raised intraocular pressure may have been responsible in some way for the development of the iridoschisis. Several studies support this suggestion. Anderson and Davis demonstrated that the first permanent effect of acutely raised intraocular pressure in laboratory animals was avascular necrosis of the iris stroma.[22] Histological examination of the specimens taken from patients with iridoschisis has demonstrated marked iris stromal atrophy without evidence of vascular or neural alterations.[1,17] Similarly, fluorescein angiography of the iris has revealed normal vessel perfusion, with normal iris vessels.[23]

Winstanley, in a detailed description of iris atrophy in primary glaucoma, described "iridoschisis-like" changes which had occurred secondary to raised intraocular pressure.[24] The different iris changes found in the involved and fellow eyes of our patients, suggests that a range of atrophic iris stromal changes may occur secondary

to high intraocular pressure. Despite the remarkable appearance of iridoschisis, these characteristic changes may simply be a late and unusual manifestation of iris stromal atrophy.

The question of whether iridoschisis in angle-closure glaucoma is secondary to raised intraocular pressure or is a coincidental finding, is controversial. The patients studied by Posner and Mills developed iridoschisis after an episode of raised intraocular pressure.[9,12] On the other hand, after examination of six cases of iridoschisis with associated angle-closure glaucoma, Romano *et al* came to the conclusion that the iridoschisis was unlikely to be a sequel of the glaucoma, because the iris changes preceded the acute angle-closure attack.[16] Considering the fact that ten of our patients had intermittent episodes of angle closure, the presence of iris changes before a typical episode of acute angle-closure glaucoma may be explained by prior episodes of asymptomatic intermittent intraocular pressure elevation.

Mills, in his analysis of the first seventeen reported cases of iridoschisis, found that nine had features consistent with the diagnosis of angle-closure glaucoma and that in seven cases the nature of the glaucoma was not clear.[12] He suggested that the relationship between glaucoma and iridoschisis might be specific to primary angle-closure glaucoma. The subsequent literature demonstrates a close correlation between iridoschisis and a shallow anterior chamber, with or without glaucomatous changes.[14-17] For example, in the two largest published series, ten out of twelve cases had this anatomical configuration.[16,17] The present study supports the suggestion that the association between iridoschisis and a shallow anterior chamber may not be coincidental and that most previous cases of iridoschisis may have occurred secondary to angle closure.

Most patients with acute intraocular pressure elevation do not develop iridoschisis. The presence of iris atrophy depends on the duration and severity of the intraocular

pressure rise, as well as upon the type of iris pigmentation.[24] Many of our patients had heavily pigmented irides and presented with advanced glaucoma; a feature noted particularly in Asia in patients with subacute angle-closure glaucoma.[21] Iris sphincter damage with tangential distortion of the stroma did not occur in these patients and most had normal pupillary function. This finding has been noted before in eyes with iridoschisis and caused Alberts and Klein to speculate that normal pupillary movements in the presence of iris stromal atrophy might play a role in the development of iridoschisis.[10]

Is has been proposed that iris pigment and degenerative material may occlude the trabecular meshwork in some eyes with iridoschisis and reduce the outflow of aqueous from an already compromised drainage system.[17] The post-operative intraocular pressure control in our patients suggests that this mechanism may not have played a significant role in producing their glaucoma. Any tendency for debris to occlude the trabecular meshwork would have resulted in an intermittent or constant post-operative intraocular pressure elevation in the seven patients (thirteen eyes) who had a peripheral iridotomy only, and in the two patients (four eyes) who underwent an extracapsular cataract extraction with intraocular lens as primary treatment. However, the intraocular pressure was easily controlled for a mean period of three years in ten eyes without additional glaucoma medication and in seven eyes with pilocarpine 1% drops alone. No further disc damage occurred during the period of follow-up.

Iridoschisis has been previously described in association with other conditions.[12,13,18,19] Single cases of iridoschisis secondary to trauma, with and without intraocular pressure elevation have been reported.[3,12,13,20,23] Two patients in this series had suffered from congenital syphilis, an association that has been previously noted, and nine patients had systemic hypertension.[19]

The primary aim of therapy was to control the intraocular pressure and to prevent progression of the glaucoma. This aim was largely achieved by means of surgery, although medical therapy was initially utilised, and in some cases continued. It was unnecessary to treat the iridoschisis *per se*; an approach advocated by Duke-Elder.[25] Progressive iris changes were not seen and the cornea remained clear in the ten patients who were regular clinic attenders.

The differential diagnosis of iridoschisis includes the iridocorneal endothelial (ICE) syndrome and the Axenfeld-Rieger syndrome[26-28] (Figure 7.5). In most cases of the ICE syndrome, the age of onset is earlier, the condition is unilateral, an ectopic pupil with peripheral anterior synechiae is found and iris stromal atrophy with hole formation may occur. Axenfeld-Rieger syndrome is a congenital abnormality occurring in both eyes. Schwalbe's line is prominent, mild iris stromal thinning occurs which may progress to atrophy and hole formation, and corectopia with ectropion uvea may be observed.

Figure 7.5 The iridocorneal endothelial syndrome should be differentiated from iridoschisis.

This study suggests that "iridoschisis" is simply an unusual manifestation of atrophy of the iris, and in most cases is the result of high intraocular pressure. A spectrum of iris changes may be found, from intrastromal atrophy to extensive splitting of the anterior layer of the iris with disintegration into fibrils. While iris pigment and material may occlude the trabecular meshwork in some eyes, this mechanism probably does not play a significant role in producing glaucoma. Chronic closure of the angle, particularly superiorly, is a constant feature of most patients who present with iridoschisis.

7.5 References

1. Loewenstein A, Foster J. Iridoschisis with multiple rupture of stromal threads. *Br J Ophthalmol* 1945; **29** : 277-282.
2. Schmitt A. Ablösung des vorderen Irisblattes. *Klin Monatsbl Augenheilk* 1922; **68** : 214-215.
3. Schoenberg MJ. Case of detachment of the anterior layers of the iris. *Arch Ophthalmol* 1927; **56** : 538-542.
4. Loewenstein A, Foster J, Sledge SK. A further case of iridoschisis. *Br J Ophthalmol* 1948; **32** : 129-134.
5. Garden RR, Wear AR. Iridoschisis in a case of chronic primary glaucoma. *Br J Ophthalmol* 1949; **33** : 509-511.
6. McCulloch C. Iridoschisis as a cause of glaucoma. *Am J Ophthalmol* 1950; **33** : 1398-1400.
7. Haik GM, Lyda W, Waugh RL. Iridoschisis. Report of an additional case. *Arch Ophthalmol* 1952; **48** : 40-43.
8. Carter LF. Progressive senile fibrillar atrophy of the iris stroma (iridoschisis). *Am J Ophthalmol* 1953; **36** : 967-970.
9. Posner A, Gorin G. Iridoschisis and glaucoma. *Am J Ophthalmol* 1958; **45** : 451-452.
10. Albers EC, Klein BA. Iridoschisis. A clinical and histopathologic study. *Am J Ophthalmol* 1958; **46** : 794-802.
11. Payne TD, Thomas RP. Iridoschisis. A case report. *Am J Ophthalmol* 1966; **62** : 966-967.
12. Mills PV. Iridoschisis. *Br J Ophthalmol* 1967; **51** : 158-164.
13. Duncan EN, Rieser JC. Iridoschisis. *Arch Ophthalmol* 1976; **94** : 2004-2005.

14. Zimmerman TJ, Dabazies OH Jr, Kaufman HE. Iridoschisis: a case report. *Ann Ophthalmol* 1981; **13** : 297-298.

15. Weseley AC, Freeman WR. Iridoschisis and the corneal endothelium. *Ann Ophthalmol* 1983; **15** : 955-964.

16. Romano A, Treister G, Barishak R, Stein R. Iridoschisis and angle-closure glaucoma. *Ophthalmologica* 1972, **164** : 199-207.

17. Rodrigues MC, Spaeth GL, Krachmer JH, Laibson PR. Iridoschisis associated with glaucoma and bullous keratopathy. *Am J Ophthalmol* 1983; **95** : 73-81.

18. Summers CG, Doughman DJ, Letson RD, Lufkin M. Juvenile iridoschisis and microphthalmos. *Am J Ophthalmol* 1985; **100** : 437-439.

19. Pearson PA, Amrien JM, Baldwin LB, Smith TJ. Iridoschisis associated with syphilitic interstitial keratitis. *Am J Ophthalmol* 1989; **107** : 88-89.

20. Salmon JF. The association of iridoschisis and angle-recession glaucoma. *Am J Ophthalmol* 1992; **114** : 766-767.

21. Lowe RF, Lim ASM. *Primary Angle Closure Glaucoma.* Singapore, PG Publishing 1989, p3, 35.

22. Anderson DR, Davis EB. Sensitivities of ocular tissues to acute pressure-induced ischemia. *Arch Ophthalmol* 1975, **93** : 267-274.

23. Carnevalini A, Menchini U, Bandello F, Scialdone A, Brancato R. Aspects Fluoroiridographiques de l'iridoschisis. *J Fr Ophthalmol* 1988, **11** : 329-332.

24. Winstanley J. Iris atrophy in primary glaucoma. *Trans Ophthalmol Soc UK* 1961; **81** : 23-37.

25. Duke-Elder S, Perkins ES. Diseases of the Uveal Tract. In: Duke Elder, S (ed) *System of Ophthalmology* Vol 9. St Louis, CV Mosby 1966; pp 694-698.

26. Cross HE, Maumenee AE. Progressive spontaneous dissolution of the iris. *Surv Ophthalmol* 1973; **18** : 186-199.

27. Shields MB, Campbell DG, Simmons RJ. The essential iris atrophies. *Am J Ophthalmol* 1978; **85** : 749-759.

28. Shields MB, Buckley E, Klintworth GK, Thresher R. Axenfeld-Rieger syndrome. A spectrum of developmental disorders. *Surv Ophthalmol* 1985; **29** : 387-409.

8.0 The Role of Prophylactic Peripheral Laser Iridotomy in the Prevention of Chronic Angle-Closure Glaucoma.

8.1 Introduction

In the context of primary angle-closure glaucoma, the term "fellow eye" refers to the unaffected or less affected eye of a patient who presents with acute or chronic angle-closure glaucoma in the primarily affected eye. In a patient with acute glaucoma, the risk of suffering an acute attack in the fellow eye with time has been reported to be between 8% and 68%[1-6] (Figure 8.1). Although it has been shown that a prophylactic peripheral iridectomy will prevent an acute attack of angle-closure glaucoma in the fellow eye, 12 - 22% of eyes may develop a late rise in intraocular pressure secondary to peripheral anterior synechiae formation.[7-14]

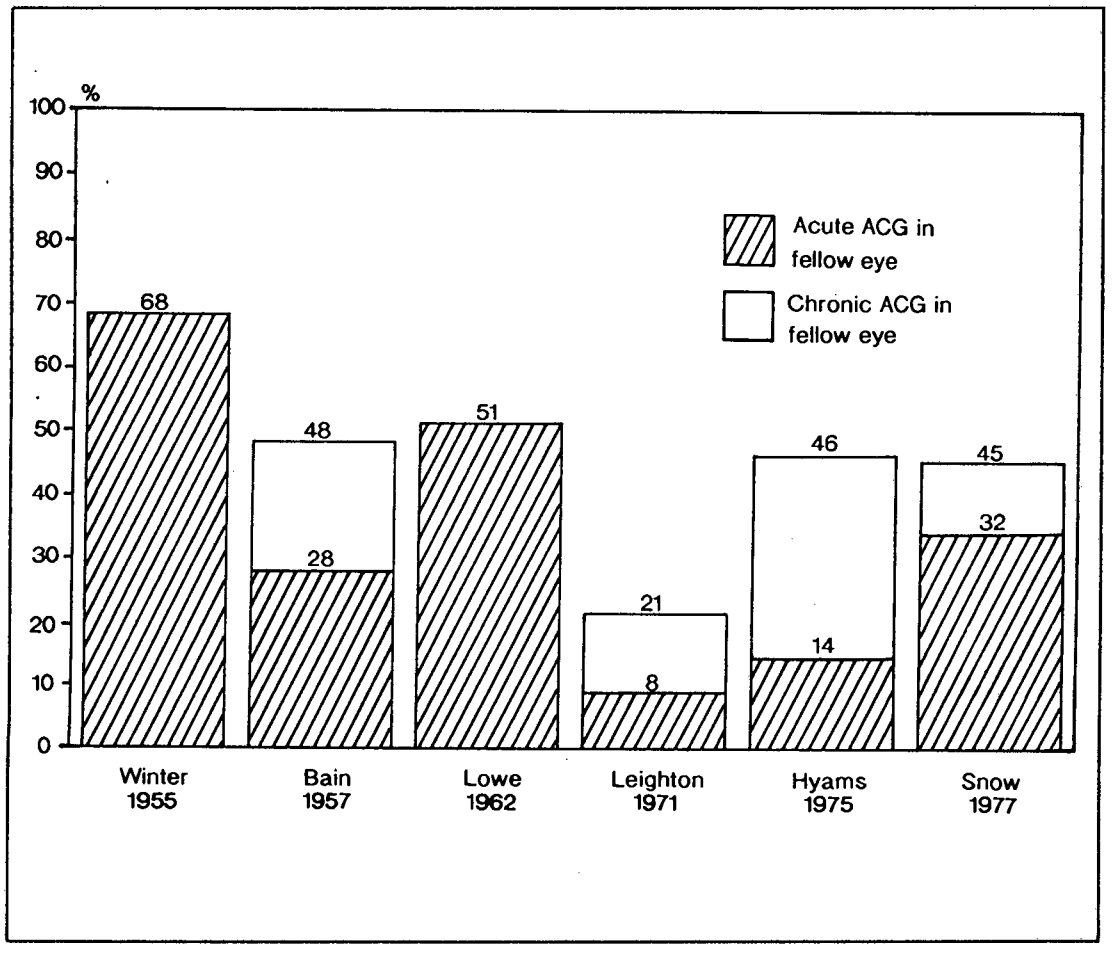

Figure 8.1 Incidence of angle-closure glaucoma in the fellow eye of patients presenting with unilateral acute glaucoma

It is not known whether a prophylactic peripheral iridectomy will prevent chronic angle-closure glaucoma in the fellow eye of patients with unilateral chronic angle-closure glaucoma. More importantly, it is not known whether peripheral anterior synechiae formation and a subsequent intraocular pressure rise can be avoided in individuals of mixed ethnic background who are considered to be at risk of developing primary angle-closure glaucoma.

To determine the risks of prophylactic peripheral iridotomy performed with a Nd-YAG laser and to evaluate the long-term changes in the angle and intraocular pressure after iridotomy, the fellow eye of 17 patients with chronic angle-closure glaucoma was prospectively studied. The preliminary conclusions of this study may provide guidelines to the management of asymptomatic individuals who are considered to be at risk of developing primary angle-closure glaucoma.

8.2 Patients and Methods

From January 1986 to December 1990, a Nd-YAG laser iridotomy was performed in the fellow eye of 17 consecutive "coloured" patients who presented at Groote Schuur Hospital with chronic angle-closure glaucoma in one eye. Their average age was 64.5 years and 15 were women (88%). The mean follow-up was 33 months (range 12 - 60 months).

All patients were asymptomatic on presentation. The diagnosis of chronic angle-closure glaucoma was made if the intraocular pressure was >21 mmHg or if glaucomatous disc cupping with visual field loss was present in association with some degree of permanent angle closure.

The same observer assessed each patient and a full ophthalmic examination was performed. The drainage angle was assessed by means of manipulative or indentation gonioscopy. The quadrants of permanent closure were noted in both eyes. The anterior chamber depth, lens thickness and axial length was measured by A-scan ultrasound using a Sonametrics Ocuscan A400 instrument. (The "anterior chamber depth" was measured from the anterior surface of the cornea to the anterior surface of the lens).

The fellow eye of each patient was considered to be at risk of angle closure because of a crowded anterior segment and ocular biometry that revealed similar mean measurements in both eyes (Table 8.1). Provocative tests were not performed. The mean intraocular pressure was 16.9 mmHg (range 12 - 20 mmHg) on presentation. The visual acuity was 6/12 or better with correction in 15 eyes and 6/24 in 2 eyes with nuclear sclerosis. Using manipulative gonioscopy the anterior trabecular meshwork could be visualised in all quadrants in 11 eyes; one quadrant of permanent angle-closure was present in 3 eyes and two quadrants of permanent closure was present in 3 eyes. In 4 eyes a plateau iris configuration was present and in 13 eyes a steep iris plane was present (Chapter 5). In each case a similar iris plane was found in both eyes. The disc was normal and a full visual field was present in each fellow eye.

TABLE 8.1 OCULAR FINDINGS ON PRESENTATION IN 17 PATIENTS

PARAMETER	FELLOW EYE	CHRONIC ANGLE-CLOSURE EYE
Axial length (mm)	22.25(21.15 - 23.20)	22.32(21.42 - 23.48)
Anterior chamber depth (mm)+	2.39(2.1 - 3.2)	2.45(2.2 - 3.0)
Lens thickness (mm)	4.87(3.9 - 5.3)	4.74(4.0 - 5.2)
Refraction (equivalent sphere)	+1.875(+0.5 - +3.0)	+1.688(+0.5 - +2.75)
Mean quadrants of closure	0.5(0 - 2)	2.6(1 - 4)
Mean cup : disc ratio	0.2(0 - 0.3)	0.6(0.1 - 0.9)

+Anterior chamber depth measured from the anterior surface of the cornea to the anterior surface of the lens.
Mean values with range in parentheses

A peripheral iridotomy was performed using a Nd-YAG laser (Lasertek, CV 2500, Helsinki, Finland) in the Q-switched mode. An Abrahams contact lens was used. The iridotomy was placed in a superior quadrant and, if present, a peripheral iris crypt was selected (Figure 8.2). Three bursts of 1 - 3 mJ were initially applied and the iridotomy was thereafter enlarged using single 1 - 2 mJ laser applications. If the iridotomy was not patent, the procedure was repeated at a second visit. All patients were given oral acetazolamide before treatment and topical prednisolone acetate 1% after the laser therapy (1 drop every 5 minutes for 30 minutes and then hourly for 2 days). The pupil was not dilated post-operatively. The intraocular pressure was monitored for 2 hours after treatment and patients were reassessed the following day.

Figure 8.2 Nd-YAG laser iridotomy

Patients were followed-up at 3 - 4 monthly intervals for at least 12 months (range 12 - 60 months). The intraocular pressure was measured at each visit and gonioscopy was performed every 6 months.

8.3 Results

A patent iridotomy of sufficient size was created in 15 eyes (88.2%) in one treatment session and in 2 eyes (11.8%) in 2 sessions. A small haemorrhage occurred at the iridotomy site in 7 eyes (41%); this stopped after the application of digital pressure to the eye. A mild iritis occurred in all eyes, but settled rapidly on topical corticosteroids without complications. The intraocular pressure rose by more than 10 mmHg in 3 eyes and by more than 20 mmHg in 2 eyes (5/17; 29.4%) within 2 hours of the performance of laser iridotomy, despite the use of pre-laser oral acetazolamide. In each case the intraocular pressure returned to normal within 24 hours.

After a mean follow-up of 33 months the intraocular pressure remained below 21 mmHg in 12 eyes (70.6%). In 5 (29.4%) the intraocular pressure rose by an average of 7 mmHg (range 4 - 10 mmHg). Four of these 5 eyes had a narrow angle with a flat iris plane. In 2 eyes with a plateau iris, two quadrants of permanent angle closure was present on first examination. In 1 eye with a plateau iris progressive chronic angle closure developed; from no quadrants of closure to two quadrants of closure over a period of 18 months. (This patient has not developed further closure of the angle in the 12 months after the start of topical pilocarpine 1%). In 1 eye with a steep iris plane, no further peripheral synechiae developed, but the intraocular pressure rose to 26 mmHg, presumably because of appositional angle closure. In these 5 eyes topical pilocarpine 1% was used four times daily to reduce the intraocular pressure to normal levels and no further closure of the angle was noted during an average follow-up period of 26 months.

All 17 patients remained asymptomatic during the period of follow-up. Two patients with nuclear sclerosis on presentation underwent cataract extraction with intraocular lens implantation 3 months and 12 months respectively after the performance of laser iridotomy. No damage to the optic nerve was documented in any of the 17 patients.

8.4 Discussion

When the mechanism of angle occlusion is pupillary block, acute glaucoma can be prevented by means of a prophylactic peripheral iridectomy.[7-11] In those communities where the prevalence of primary angle-closure glaucoma is high, the use of a portable Nd-YAG laser to create a peripheral iridotomy in those at risk is an appealing concept.[15] However, it has been shown by Wilensky *et al* that there is no parameter or provocative test that is sensitive enough or accurate enough to

detect which eyes with shallow anterior chambers and "occludable" angles will later develop primary angle-closure glaucoma.[16] This means that many individuals considered to be at risk may undergo unnecessary iridotomy. The present study sets out to determine whether the risks of laser iridotomy are justified in subjects with suspected angle-closure glaucoma and whether peripheral anterior synechiae will develop in the presence of a peripheral laser iridotomy in those Asians or Africans considered to be at risk of developing chronic angle-closure glaucoma.

A prospective randomised study would be the ideal method to study the benefits and complications of prophylactic peripheral iridotomy in those at risk of developing chronic angle closure. However, a study of this nature would require considerable time and financial support and would be difficult to undertake in South Africa. The method used in the present study was to examine the effects of laser iridotomy in the fellow eye of patients with unilateral chronic angle-closure glaucoma. The eyes reported here were at considerable risk of developing chronic angle-closure glaucoma because in each case both eyes had similar ocular dimensions and anterior segment anatomy and it has been previously shown that most "coloured" patients with chronic angle-closure glaucoma have bilateral disease (Chapter 6). A distinct weakness of this study is the lack of a control group of untreated eyes. However, the practical problem of demonstrating statistically significant differences between matched groups can be appreciated from the fact that only 17 suitable fellow eyes were found over a 5-year period.

The study demonstrates that a carefully performed prophylactic Nd-YAG laser iridotomy is safe and relatively free of complications. Iridotomy is easily performed as an outpatient procedure, although it may be difficult to penetrate a heavily pigmented iris in one treatment session.[17] It is slightly easier to penetrate the iris in one session when a prophylactic laser iridotomy is performed (88.2%) than when a

therapeutic iridotomy is performed (61.5%) (Chapter 9). Late pigment epithelial proliferation with closure of a small Nd-YAG laser iridotomy has been reported, but was not found in these 17 eyes.[18]

In all eyes a mild transient iritis occurred. The iridotomy provokes inflammation by liberating pigment and tissue debris, releasing prostaglandins and other inflammatory mediators and breaking down the blood aqueous barrier.[19] Posterior synechiae are prone to develop under these circumstances, particularly if topical pilocarpine is used.[20] This complication did not occur in our patients, probably because intensive topical prednisolone 1% was used after the procedure. Bleeding from the iridotomy site has been reported in up to 45% of patients and occurred in 41% of the cases described in this study.[21] The haemorrhage was minimal and was easily stopped by applying digital pressure to the eye. This complication can be avoided by the use of pre-laser topical aproclonidine, an alpha agonist with vasoconstrictive properties.[22] An acute intraocular pressure rise of $\geq$10 mmHg was found in 5 cases (29.4%), but resolved without sequelae. This complication has been previously reported in 30 - 35% of cases and can be limited by the use of glaucoma medication before the performance of iridotomy.[21-23] The acute intraocular pressure rise was not related to pre-existing peripheral anterior synechiae.

In no case was a focal corneal opacity produced. Risk of endothelial damage is greatest where the cornea is in close proximity to the iris. The likelihood of corneal burns can be reduced by careful focusing and by using high magnification.[21] Localised lens damage and cataract formation was avoided by placing the iridotomy as far in the periphery as possible to increase the distance between the iridotomy and the anterior lens surface. Cataract formation has been reported as a late complication of surgical iridectomy, but is unusual after Nd-YAG laser

iridotomy.[9,12-14,24,25] Retinal burns have been described after the performance of laser iridotomy, but do not occur if a converging contact lens (for example: the Abrahams lens) is used.[26] Glare and diplopia have been reported, but these complications were probably avoided by placing the iridotomy in the superior iris, beneath the upper eyelid.[25]

In eyes at risk of developing primary angle-closure glaucoma, chronic closure of the angle may occur if no therapy is instituted.[16] A recent multicentre study of untreated angle-closure glaucoma revealed that 25 out of 129 (19.4%) developed angle closure in at least one eye during a follow-up period of up to six years and that 17 eyes developed peripheral anterior synechiae without clinical symptoms or an increase in intraocular pressure.[16] Although the present study is not strictly comparable, it was found that only 1 of 13 eyes (7.7%) with a steep iris plane (presumably at risk of pupillary block) demonstrated a rise in intraocular pressure, and none of the 13 eyes developed progressive anterior synechiae over a mean follow-up of 33 months (with some eyes followed for up to six years). However, in 4 eyes with a plateau iris configuration the intraocular pressure rose above 21 mmHg. In 2 of these eyes two quadrants of peripheral anterior synechiae were present when the eye was first examined and in 1 eye two quadrants of chronic closure developed despite the presence of a peripheral iridotomy.

Late elevation of intraocular pressure after prophylactic surgical peripheral iridectomy has been reported in 2 - 22% of eyes, but it is not clear from these studies which mechanism was responsible for the late intraocular pressure rise.[8,12-14] (Figure 8.3).

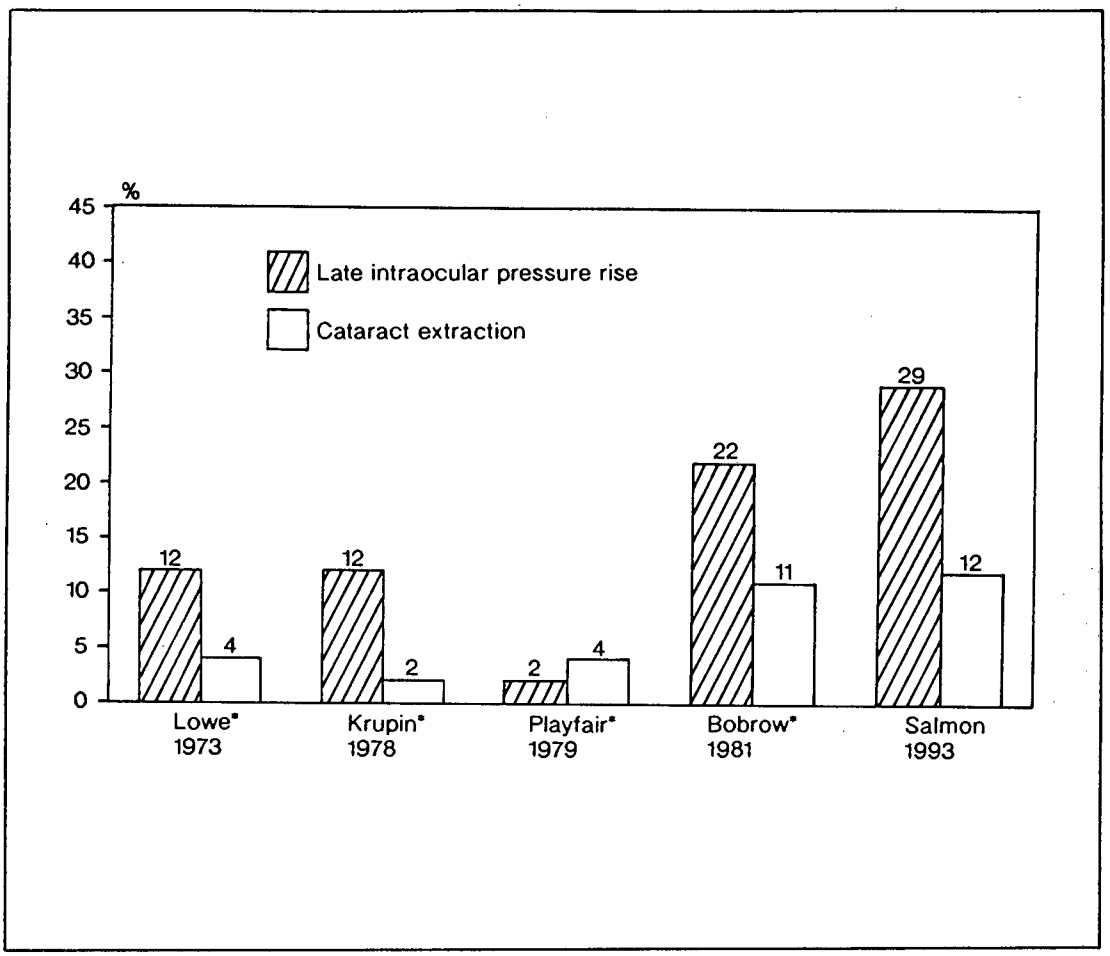

*Figure 8.3 Late occurrence of elevated intraocular pressure and the need for cataract extraction after prophylactic peripheral iridectomy. (*A surgical iridectomy was performed in the fellow eye of a patient with acute glaucoma)*

Although plateau iris is rare in Europeans, it is not uncommon in patients of mixed ethnic background (Chapter 5). In the 4 eyes with a plateau iris dilute topical pilocarpine was used to reduce the intraocular pressure to normal levels and to prevent the development of plateau iris syndrome. No acute glaucoma occurred in any of the 17 eyes treated with prophylactic iridotomy and the pupil could be dilated without an intraocular pressure rise in the 2 patients that underwent cataract extraction.

This study suggests that the risks of Nd-YAG laser iridotomy are small enough to justify the use of this form of therapy in eyes considered to be at risk of developing angle-closure glaucoma. Nevertheless, to reduce the possibility of complications, important precautions include the postoperative use of intensive topical prednisolone and the immediate postoperative control of intraocular pressure. Although long-term follow-up is required before a final conclusion can be reached, it appears that in eyes with a steep iris plane at risk of developing pupillary block, progressive angle closure may be prevented with laser iridotomy. Particular attention should be paid to excluding the presence of a plateau iris, since these patients require careful follow-up and additional dilute topical pilocarpine therapy on a daily basis.

8.5 References

1. Winter FC. The second eye in acute primary, shallow-chamber angle glaucoma. *Am J Ophthalmol* 1955; **40** : 557-558.
2. Bain WES. The fellow eye in acute closed-angle glaucoma. *Br J Ophthalmol* 1957; **41** 193-199.
3. Lowe RF. Acute angle-closure glaucoma. The second eye: an analysis of 200 cases. *Br J Ophthalmol* 1962; **46** : 641-650.
4. Leighton DA. Phillips CI, Tsukahara S. Profile presenting states of eyes in angle-closure glaucoma. *Br J Ophthalmol* 1971; **55** : 577-584.
5. Hyams SW, Friedman Z, Keroub C. Fellow eye in angle-closure glaucoma. *Br J Ophthalmol* 1975; **59** : 207-210.
6. Snow JT. Value of prophylactic peripheral iridectomy on the second eye in angle-closure glaucoma. *Trans Ophthalmol Soc UK* 1977; **97** : 189-191.
7. Williams DJ, Gills JP, Hall GA. Results of 233 peripheral iridectomies for narrow-angle closure glaucoma. *Am J Ophthalmol* 1968; **65** : 548-551.
8. Murphy MB, Spaeth GL. Iridectomy in primary angle-closure glaucoma: classification and differential diagnosis of glaucoma associated with narrowness of the angle. *Arch Ophthalmol* 1974; **91** : 114-122.
9. Krupin T, Mitchell KB, Johnson MF, Becker B. The long-term effects of iridectomy for primary acute angle-closure glaucoma. *Am J Ophthalmol* 1978; **86** : 506-509.
10. Yassur Y, Melamed S, Cohen S, Ben-Sira I. Laser iridotomy in closed-angle glaucoma. *Arch Ophthalmol* 1979; **97** : 1920-1921.
11. Mapstone R. The fellow eye. *Br J Ophthalmol* 1981; **65** : 410-413.

12. Playfair TJ, Watson PG. Management of acute primary angle-closure glaucoma: a long term follow-up of the results of peripheral iridectomy used as an initial procedure. *Br J Ophthalmol* 1979; **63** : 17-22.

13. Bobrow JC, Drews, RC. Long-term results of peripheral iridectomies. *Glaucoma* 1981; **3** : 319-322.

14. Lowe RF. Primary angle-closure glaucoma: a review 5 years after bilateral surgery. *Br J Ophthalmol* 1973; **57** : 457-463.

15. Robin AL, Arkell S, Gilbert SM, Goosen AA, Werner RP, Korshin OM. Q-switched neodymium-YAG laser iridotomy: a field trial with a portable laser system. *Arch Ophthalmol* 1986; **104** : 526-530.

16. Wilensky JT, Kaufman PL, Frohlichstein D, Gieser DK, Kass MA, Ritch R, *et al.* Follow-up of angle-closure glaucoma suspects. *Am J Ophthalmol* 1993; **115** : 338-346.

17. Lim ASM. Angle closure glaucoma in Asia. *Asia Pac J Ophthalmol* 1990; **2** : 77.

18. Wishart PK, Hitchings RA. Neodymium YAG and dye laser iridotomy - a comparative study. *Trans Ophthalmol Soc UK* 1986; **105** : 521-540.

19. Sanders DR, Joondeph B, Hutchins R, *et al.* Studies on the blood-aqueous barrier after argon laser photocoagulation of the iris. *Ophthalmology* 1983; **90** : 169-173.

20. McGalliard JN, Wishart, PK. The effect of Nd-YAG iridotomy on intraocular pressure in hypertensive eyes with shallow anterior chambers. *Eye* 1990; **4** : 823-829.

21. Robin AL, Pollack IP. A comparison of neodymium: YAG and argon laser iridotomies. *Ophthalmology* 1984; **91** : 1011-1016.

22. Robin AL, Pollack IP, de Faller JM. Effects of topical ALO 2145 (p-aminoclonidine hydrochloride) on the acute intraocular pressure rise after argon laser iridotomy. *Arch Ophthalmol* 1987; **105** : 1208-1211.

23. Schwartz LW, Moster MR, Spaeth GL. Neodymium-YAG laser iridectomies in glaucoma associated with closed or occludable angles. *Am J Ophthalmol* 1986; **102** : 41-44.

24. Floman N, Berson P, Landau L. Peripheral iridectomy in closed angle glaucoma: late complications. *Br J Ophthalmol* 1977; **61** : 101-104.

25. Quigley HA. Long-term follow-up of laser iridotomy. *Ophthalmology* 1981; **88** : 218-222.

26. Karmon G, Savir H. Retinal damage after argon laser iridotomy. *Am J Ophthalmol* 1986; **101** : 554-560.

9.0 Long Term Intraocular Pressure Control after Nd-YAG Laser Iridotomy in Chronic Angle-Closure Glaucoma

9.1 Introduction

The recommended initial surgical treatment of chronic angle-closure glaucoma is laser iridotomy, performed once the intraocular pressure has been controlled with glaucoma medication.[1-6] Any subsequent elevation of the intraocular pressure is treated in a stepwise fashion with glaucoma medication and then with drainage surgery if necessary. While the effectiveness of this approach has been demonstrated in early disease, few studies have reported long-term results in patients with advanced chronic angle-closure glaucoma.[5,7] In addition, it is not clear whether the results reported in Western studies apply to patients of Oriental ethnic background with asymptomatic chronic angle-closure glaucoma.[8] In order to clarify these points, the long-term results were examined of Nd-YAG laser iridotomy performed in 52 consecutive patients of mixed ethnic background with chronic angle-closure glaucoma.

9.2 Patients and Methods

From July 1986 to December 1990, Nd-YAG laser iridotomy was performed in 78 eyes of 52 consecutive patients with chronic angle-closure glaucoma. All patients were of mixed ethnic background; 43 were female (82.7%, 43/52) and the mean age was 64.3 years. The mean follow-up was 22 months (range 3 months to 4 years), and 45 patients (64 eyes) were followed for at least one year. One patient failed to

return for follow-up after the three-month post-operative visit and three patients (4 eyes) missed the six-month visit, but were seen thereafter.

The diagnosis of chronic angle-closure was made if the intraocular pressure was >21 mmHg or if glaucomatous disc cupping with visual field loss was present, in association with a partially or totally closed angle. Most patients were asymptomatic. The angle was evaluated using manipulative and indentation gonioscopy. The angle was divided into quadrants and deep circumferential permanent angle closure was present in the quadrants classified as "closed". The average of the vertical and horizontal cup : disc ratios was recorded. Visual fields were performed in all sighted patients using a Humphrey automated visual field analyser. Patients with angle closure secondary to uveitis, trauma, angle neovascularisation and lens intumescence were excluded.

The ocular findings on presentation are summarised in Table 9.1. The mean intraocular pressure on presentation was 35.0 mmHg, the mean number of closed quadrants was 2.0 and the mean cup : disc ratio was 0.58. In 27 eyes (34.6%) the visual acuity was worse than 20/40, mainly because of nuclear sclerosis or corticular lens opacity. In 55 eyes (70.5%) glaucomatous visual field loss was found on presentation.

TABLE 9.1 VISUAL AND OCULAR FINDINGS ON PRESENTATION IN 52 PATIENTS (78 EYES) WITH CHRONIC ANGLE-CLOSURE GLAUCOMA TREATED WITH Nd-YAG LASER IRIDOTOMY

VISUAL ACUITY:	
6/6 - 6/12	51 (65.4%)
6/18 - 6/60	16 (20.5%)
<6/60	11 (14.1%)
VISUAL FIELD:	
FULL	23 (29.5%)
GLAUCOMA	55 (70.5%)
INTRAOCULAR PRESSURE (mmHg):	
20 - 30	32 (41.0%)
31 - 40	21 (26.9%)
41 - 50	19 (24.4%)
>51	6 (7.7%)
QUADRANTS OF ANGLE CLOSURE:	
2 OR LESS	50 (64.1%)
3 OR MORE	28 (35.9%)
MEAN CUP : DISC RATIO:	
0.1 - 0.3	20 (25.6%)
0.4 - 0.7	33 (42.3%)
0.8 - 1.0	25 (32.1%)

All patients had heavily pigmented brown irides. An Nd-YAG laser (Lasertek, CV 2500; Helsinki, Finland) was used in the Q-switched mode. The iridotomy was placed in a superior quadrant and if present a peripheral iris crypt was selected. Initial energy levels of 3 bursts of 1 to 3 mJ were used and the iridotomy thereafter enlarged using single 1 to 5 mJ laser applications. If the iridotomy was not patent

(assessed by direct observation of the posterior chamber or anterior lens capsule), the procedure was repeated in the same site at a second or third visit. All patients were given oral acetazolamide prior to treatment and intensive post-operative topical corticosteroids. The pupils were not dilated after the iridotomy.

For the purpose of this study, a "controlled" post-operative intraocular pressure was defined as an intraocular pressure of less then 22 mmHg. Irrespective of the degree of optic disc cupping or visual field loss, in each case an attempt was made to control the intraocular pressure with topical medication and in some patients with acetazolamide, before trabeculectomy was performed. A Kaplan-Meier survival curve was used to demonstrate the cases that required trabeculectomy after laser iridotomy and glaucoma medication failed to control the intraocular pressure.

In order to determine risk factors for trabeculectomy, the outcome of eyes with findings on presentation above and below the mean value of the presenting intraocular pressure (35 mmHg), quadrants of angle closure (2.0) and cup : disc ratio (0.6), were statistically analysed using Fisher's exact test. A finding was considered significant at $P<0.05$. In order to assess the relative importance of these three parameters, linear discriminant analysis was used, comparing those who required trabeculectomy to control the intraocular pressure (23 eyes), to those who did not require trabeculectomy (55 eyes).

9.3 Results

A patent iridotomy of sufficient size was created in 48 eyes (61.5%) in one treatment session. In 26 eyes (33.3%) two sessions were required, in 3 eyes (3.8%) three sessions and in one eye four sessions. Two patients developed a severe rise in intraocular pressure after completion of the iridotomy. Both presented with asymptomatic chronic angle-closure glaucoma and intraocular pressures of more than 50 mmHg. Topical and systematic medication was prescribed, which resulted in the inferior angle partially opening with control of the intraocular pressure. After performance of a laser iridotomy the intraocular pressure again rose to above 50 mmHg and despite maximum glaucoma therapy could not be brought under control. A diagnosis of malignant glaucoma was excluded because no acute shallowing of the anterior chamber was found. Trabeculectomy was performed the following day without complications.

After a mean follow-up period of 22 months the intraocular pressure was controlled in 7 eyes (9.0%) without medication and in 40 eyes (51.3%) with glaucoma medication (8 on levobutanol drops, 14 on pilocarpine 1% drops, 17 on both of these drops, and one on both drops and acetazolamide). At the last follow-up visit prior to analysis of this data, eight eyes (10.2%) had an intraocular pressure between 22 mmHg and 24 mmHg on an average of two medications. These patients had been controlled on previous visits and were considered controllable on additional medication. In a further 23 eyes (29.5%) trabeculectomy was performed. The indication for trabeculectomy was a persistently raised intraocular pressure despite glaucoma medication in 14 eyes (12 patients) and a severe asymptomatic intraocular pressure spike (to a mean intraocular pressure of 47.6 mmHg) in 7 eyes (7 patients). In all seven patients a patent iridotomy was present. The mean time to trabeculectomy after laser iridotomy was 9.9 months (range 1.5 to 24 months).

The mean intraocular pressure (with one standard deviation) after laser iridotomy and the intraocular pressure control at different time intervals, is summarised in Figures 9.1 and 9.2. At 6 months post-iridotomy 28.8% (21/73) were uncontrolled, at one year 18.8% were uncontrolled (12/64), at two years 10% were uncontrolled (4/40) and at 3 years 14.3% (3/21) were uncontrolled. A Kaplan-Meier survival curve of patients who underwent trabeculectomy after failure of Nd-YAG laser iridotomy and medication is shown in Figure 9.3. It can be seen that most patients underwent drainage surgery within 1 year of laser iridotomy and only one required this surgery after 2 years.

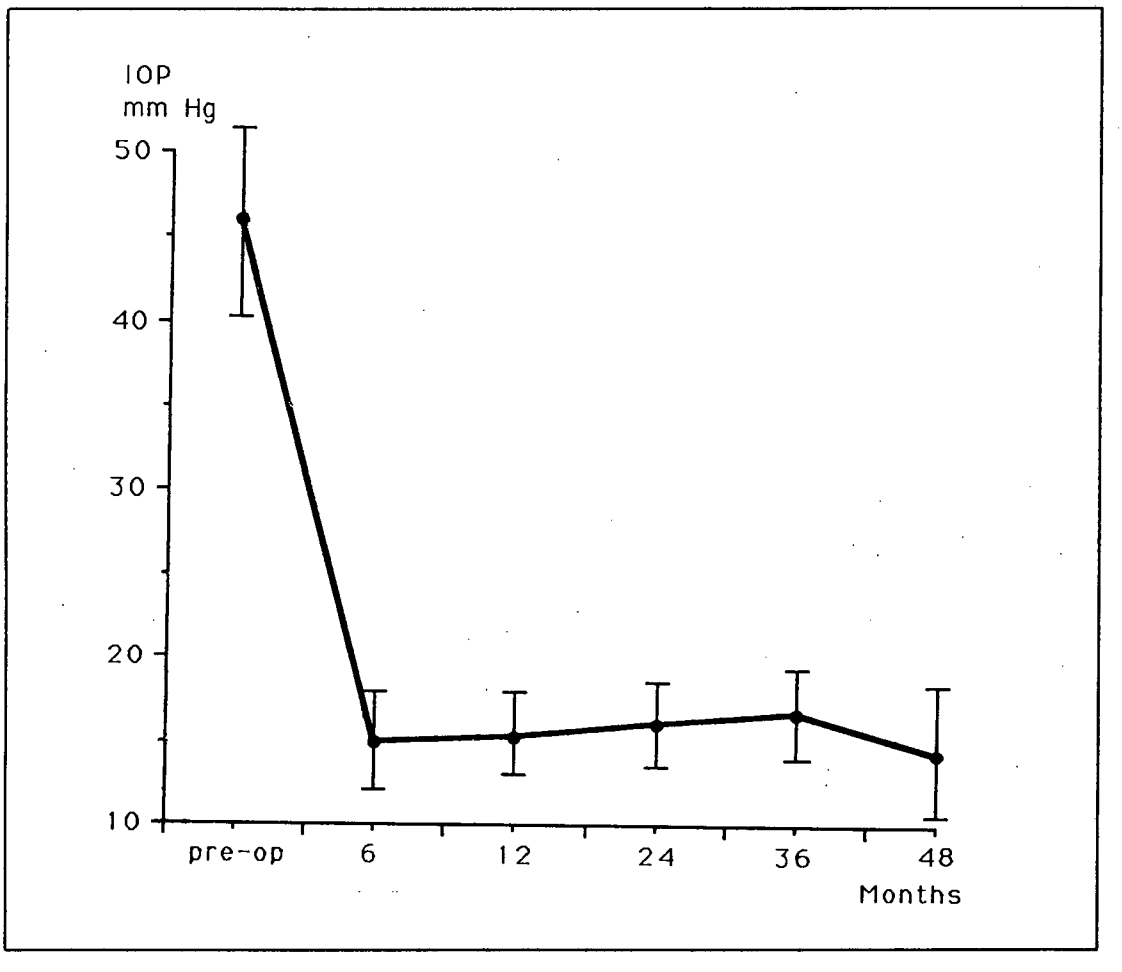

Figure 9.1 Mean intraocular pressures (with one standard deviation) after Nd-YAG laser iridotomy

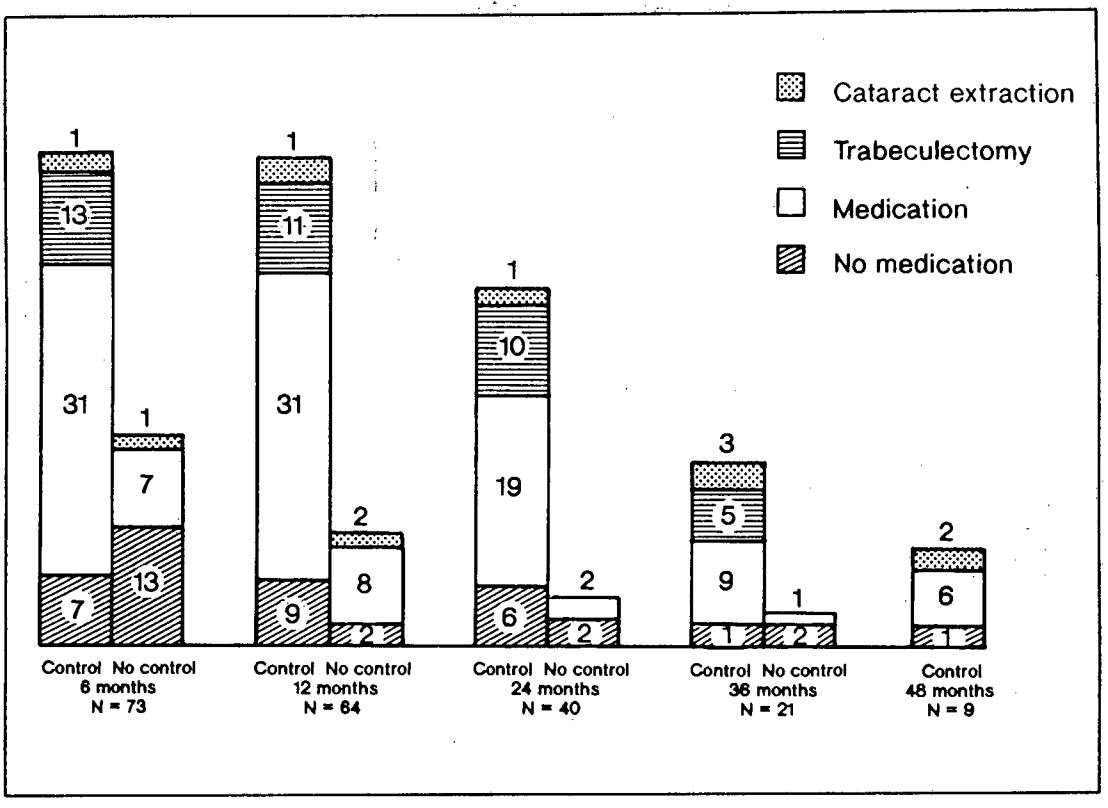

Figure 9.2 Results of Nd-YAG laser iridotomy at 6, 12, 24, 36 and 48 months

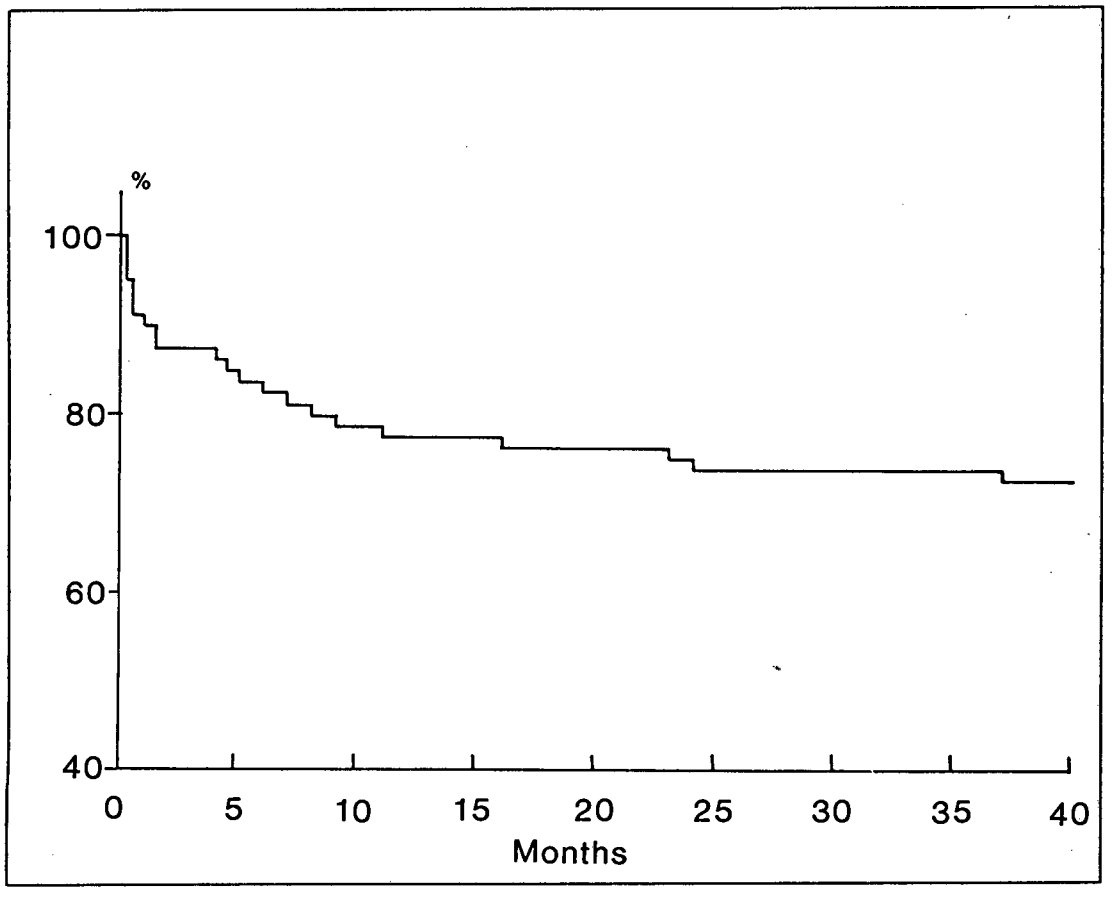

Figure 9.3 Kaplan-Meier survival curve, demonstrating the eyes which underwent trabeculectomy after Nd-YAG laser iridotomy and medication had failed to control the intraocular pressure

Statistical analysis revealed that patients with a presenting intraocular pressure of more than 35 mmHg, or with 3 or more quadrants of angle closure, or with a cup : disc ratio of more than 0.6 were significantly more likely to undergo trabeculectomy ($P < 0.001$) (Table 9.2).

TABLE 9.2
OCULAR PARAMETERS FOR DIFFERENT OUTCOMES AFTER Nd-YAG LASER IRIDOTOMY IN 78 EYES OF 52 PATIENTS

PARAMETER ON PRESENTATION+		NO TREATMENT	MEDICATION	TRABECULECTOMY	SIGNIFICANCE
Intraocular pressure	<36 mmHg	6	33	5	
	>35 mmHg	1	15	18	P< 0.001
Quadrants of angle closure	<3	4	39	7	
	>2	3	9	16	P<0.001
Cup : disc ratio	<0.61	5	28	6	
	>0.60	2	20	17	P=0.006

+On presentation: mean intraocular pressure = 35.0 mmHg, mean quadrants of angle closure = 2.0; mean cup : disc ratio = 0.58.

Using multivariate analysis of the presenting intraocular pressure, quadrants of closure and cup : disc ratio, only 78% of patients who subsequently underwent trabeculectomy could have been predicted on presentation and 36% of patients considered to be at risk, who were subsequently controlled with or without glaucoma medication would have undergone unnecessary trabeculectomy (prediction accuracy 57%; sensitivity 55.4% and specificity 60.9%). Linear discriminant analysis revealed that the cup : disc ratio contributed most towards the decision on trabeculectomy.

9.4 Discussion

Effective management of primary angle-closure glaucoma is important because of the large numbers of people who suffer permanent visual loss from this disease. Most studies describing the treatment of primary angle-closure glaucoma have been undertaken in Europe and North America and it is not clear whether their results apply to patients of Eastern ethnic background; neither is it clear how suitable this treatment is in patients with severe glaucomatous disc damage and visual field loss associated with asymptomatic chronic angle closure.[2,3-6,8] In this retrospective study an attempt was made to clarify these points.

A group of 52 patients of mixed ethnic background with typical features of chronic angle-closure glaucoma was examined. Although a spectrum of disease was found, 32.1% of eyes had an intraocular pressure of more than 40 mmHg on presentation; 36% more than half of the angle permanently closed; and 32.1% a cup :disc ratio of more than 0.7 with corresponding glaucomatous visual field loss. The follow-up was good and 45 patients were followed for at least one year.

The initial therapy was similar for all patients. After control of the intraocular pressure with glaucoma medication, a Nd-YAG peripheral iridotomy was performed. Although a patent iridotomy may be obtained in most patients with blue irides in one session, this is not the case in patients with heavily pigmented brown irides.[8] Using Nd-YAG laser a patent iridotomy was only created in 61.5% of eyes in one session in my series. Any subsequent intraocular pressure rise was treated medically or with trabeculectomy. Management was hampered by a

difficulty in documenting progressive visual field loss in some patients with constricted pupils and early lens opacity. Because the ideal level at which the intraocular pressure should be maintained in patients with chronic angle-closure glaucoma is unknown, decisions on additional therapy were based on the principle that the intraocular pressure should remain below 22 mmHg.[9] Most patients who underwent trabeculectomy required this surgery within one year of presentation and only one two years after presentation.

Although this approach was effective and safe for most patients, the vision in 9 eyes (11.5%) was threatened by an acute elevation of intraocular pressure. In two patients this occurred immediately after Nd-YAG iridotomy and in seven during the period of follow-up. An acute irreversible intraocular pressure rise after Nd-YAG iridotomy has been previously reported.[10] Although this is a potentially serious complication, in both patients the trabeculectomy was uncomplicated, successful post-operative intraocular pressure control was obtained and no loss of vision was documented. The risk of further optic nerve damage was greatest in the seven patients who experienced a marked intraocular pressure rise because of a failure to use the prescribed glaucoma medication (which included topical pilocarpine). In chronic angle-closure glaucoma in people of Oriental ethnic background, plateau iris syndrome may play an important role in the pathogenesis of angle closure[11] (Chapter 5). Relieving pupillary-block with a laser iridotomy may not therefore influence the intraocular pressure control, particularly in eyes with advanced angle damage and particular care should be taken to exclude a plateau iris configuration in these patients.

A significant difference between this study and others, is the high percentage of patients who required glaucoma medication or trabeculectomy to control the

intraocular pressure after laser iridectomy. One reason for this difference may have been the Oriental ethnic background of these patients. Geh, reporting on laser iridotomy used in the treatment of chronic "creeping" angle-closure glaucoma in Chinese patients, revealed that 10% were controlled without medication, 83% with medication and 7% with trabeculectomy after a mean follow-up of 11 months.[12] Studies from North America however, report a low incidence of trabeculectomy after laser iridotomy, with Gieser and Robin reporting a 0% and 8% incidence of trabeculectomy respectively[2,5]. The discrepancy between our results and others may also be explained by the large proportion of patients in our study with advanced disease. Playfair and Watson found that intraocular pressure control in patients with glaucomatous disc damage and visual field loss treated with surgical peripheral iridectomy was significantly worse than in patients with full visual fields.[7] In those with glaucomatous visual field loss, 21% were controlled without medication, 24% were not controlled, 32% required medication and 23% required drainage surgery to maintain the intraocular pressure below 21 mmHg[7].

Despite the good intraocular pressure control after trabeculectomy reported by Watson, drainage surgery as an initial procedure should not be considered in all patients with chronic angle-closure glaucoma.[13] Eltz and Gloor reported severe complications and our results suggest that many patients would undergo unnecessary surgery.[14] Using multivariate analysis of three ocular parameters measured on presentation, only 78% of patients who underwent trabeculectomy could have been predicted on presentation and 36% of patients at risk who were subsequently controlled with or without glaucoma medication would have undergone unnecessary trabeculectomy (prediction accuracy: 57%). It is because of this inability to predict the outcome on presentation, that laser iridotomy and a stepwise approach to trabeculectomy is so effective.

Univariate analysis revealed that patients who were at most risk for failure of iridotomy and glaucoma therapy were those with a presenting intraocular pressure of more than 35 mmHg, or eyes with three of more quadrants of angle closure, or a cup : disc ratio of more than 0.6. While two previous studies found that the intraocular pressure on presentation and the degree of closure do not influence the future intraocular pressure control, a study in Japanese patients revealed a correlation between the extent of pre-operative peripheral anterior synechiae and pressure control after iridectomy.[7,15,16] On multivariate analysis we found that the intraocular pressure and quadrants of closure were less important than the cup : disc ratio in predicting which patients would undergo trabeculectomy. Of these three factors, the cup : disc ratio is the best indicator of the severity of glaucoma; a finding which implies that the decision on surgery was influenced by the degree of optic nerve damage and the need to achieve the lowest intraocular pressure possible in extensively damaged eyes.

This study has demonstrated that the current practice of Nd-YAG laser iridotomy followed by medical therapy and trabeculectomy is effective and safe in most patients with chronic angle-closure glaucoma, even when advanced disease is present. Most will require glaucoma medication to control the intraocular pressure and a significant proportion may require trabeculectomy. In patients with advanced glaucomatous disc damage careful follow-up of the intraocular pressure and visual field performance is particularly important and consideration should be given to early trabeculectomy at the first sign of poor control or progressive disease.

9.5 References

1. Ritch R. The treatment of chronic angle-closure glaucoma. *Ann Ophthalmol* 1981; **13** : 21-23.
2. Robin AL. Pollack IP. Argon laser peripheral iridotomy in the treatment of primary angle-closure glaucoma. *Arch Ophthalmol* 1982; **100** : 919-923.
3. Quigley HA. Long-term follow-up of laser iridotomy. *Ophthalmology* 1981; **88** : 218-224
4. Yamamoto T, Shirato S, Kitazawa Y. Treatment of primary angle-closure glaucoma by argon laser iridotomy : a long term follow-up *Jpn J Ophthalmol* 1985; **29** : 1-12
5. Gieser DK, Wilensky JT. Laser iridectomy in the management of chronic angle-closure glaucoma. *Am J Ophthalmol* 1984; **98** : 446-450.
6. Schwartz LW, Moster MR, Spaeth GI, Wilson RP, Poryzees E. Neodymium-YAG laser iridectomies in glaucoma associated with closed or occludable angles. *Am J Ophthalmol* 1986; **102** : 41-44.
7. Playfair TJ, Watson PG. The management of chronic or intermittent primary angle-closure glaucoma : a long-term follow-up of the results of peripheral iridectomy used as an initial procedure. *Br J Ophthalmol* 1979; **63** : 23-28.
8. Lim ASM. Angle closure glaucoma in Asia. *Asia Pac J Ophthalmol* 1990; **2** : 77.
9. Hyams S. *Angle-closure glaucoma.* Ed 1. Amsterdam, Kugler and Ghedini Publications 1990, p63.
10. Henry JC, Krupin T, Schultz J, Wax M. Increased intraocular pressure following neodymium-YAG laser iridectomy (letter). *Arch-Ophthalmol* 1986; **104** : 178.

11. Hung PT, Chou LH. Provocation and mechanism of angle-closure glaucoma after iridectomy. *Arch Ophthalmol* 1979; **97** : 1862-1864.

12. Geh M, Lim ASM, Ang BC. The results of laser peripheral iridectomy in creeping (chronic) angle closure glaucoma. In Khoo CY (ed.) *New Frontiers in Ophthalmology*, Amsterdam, Elsevier Science Publishers BV. 1991 462-466.

13. Watson PG, Grierson I. The place of trabeculectomy in the treatment of glaucoma. *Ophthalmology* 1981; **88** : 175-196.

14. Eltz H, Gloor B. Trabeculectomy in cases of angle-closure glaucoma : successes and failures. *Klin Monatsbl Augenheilkd* 1980; **177** : 556-561.

15. Gelber EC, Anderson DR. Surgical decisions in chronic angle-closure glaucoma. *Arch Ophthalmol* 1976; **94** : 1481-1484.

16. Iwata K, Abe H, Sugiyama J. Argon laser iridotomy in primary chronic angle-closure glaucoma. *Glaucoma* 1985; **7** : 103-106.

10.0 The Role of Trabeculectomy in the Treatment of Advanced Chronic Angle-Closure Glaucoma.

10.1 Introduction

The currently recommended initial surgical treatment of chronic angle-closure glaucoma is a laser iridotomy and any residual elevation of the intraocular pressure is treated in a stepwise fashion with topical glaucoma therapy and carbonic anhydrase inhibitors and then with trabeculectomy if necessary.[1-6] While numerous studies have demonstrated the effectiveness of this approach, there are few detailed studies describing the cases that subsequently require trabeculectomy.[7-9] Previous reports have warned of the risks of drainage surgery in primary angle-closure glaucoma and complications like a flat anterior chamber with or without malignant glaucoma, haemorrhage and post-operative endophthalmitis have been reported.[7-9] To examine the results and complications of trabeculectomy performed for advanced primary angle-closure glaucoma, I reviewed all patients of mixed ethnic background who had undergone trabeculectomy for chronic angle-closure glaucoma during a five-year period.

10.2 Patients and Methods

From January 1986 to December 1990, trabeculectomy was performed in 46 eyes of 39 patients of mixed ethnic background with chronic angle-closure glaucoma. Twenty-six were females (68.4%, 26/38) and the mean age at surgery was 60.9 years. One patient failed to return for follow-up after the 3 month post-operative visit. The mean period of follow-up was 19 months.

The diagnosis of chronic angle-closure glaucoma was made if the intraocular pressure was >21 mmHg or if glaucomatous disc cupping with corresponding visual field loss was present, in association with a partially or totally closed angle. The angle was assessed using manipulative and indentation gonioscopy and divided into four quadrants. Deep circumferential permanent angle closure was present in the quadrants classified as "closed". Patients with angle closure secondary to uveitis, trauma, angle neovascularisation and lens intumescence were excluded. The average of the vertical and horizontal cup : disc ratios was recorded. Visual fields were performed in all sighted patients with a Humphrey automated field analyser. A-scan ultrasound was used to measure the axial length and anterior chamber depth.

There were three main indications for surgery (Table 10.1). In four patients the intraocular pressure could not be controlled medically on presentation. Two of these patients had an initial drop of intraocular pressure with partial opening of the angle and underwent Nd-YAG laser iridotomy. The intraocular pressure subsequently rose and could not be brought back to normal with medical therapy. In 19 patients (23 eyes), the intraocular pressure remained between 20 mmHg and 30 mmHg on follow-up, despite the use of glaucoma medication (including acetazolamide in 8 patients). Although no further field loss was documented, the intraocular pressure was considered to be too high and trabeculectomy was performed a mean period of 4.6 months after presentation. In 17 patients (19 eyes), initially controlled on glaucoma medication (11 on acetazolamide and topical medication, 6 on pilocarpine and levobutanol drops and 2 on pilocarpine drops), an asymptomatic intraocular pressure rise (to a mean level of 43.1 mmHg) occurred because of failure to use the prescribed medication. Visual field analysis performed after the episode revealed additional field loss in 3 eyes. Because of

their poor compliance and advanced visual field loss trabeculectomy was performed to avoid the risk of a second episode of acute intraocular pressure rise. In these patients surgery was performed a mean period of 11.7 months after presentation, but in 10 patients (52.6%) this was within 3 months of commencing therapy.

TABLE 10.1 OCULAR FINDINGS AND PREVIOUS TREATMENT

INDICATION	UNCONTROLLED ON PRESENTATION	UNCONTROLLED ON FOLLOW-UP	ASYMPTOMATIC SPIKE OFF MEDICATION
Number of eyes:	4	23	19
Mean presenting I.O.P.	50.0 mmHg	45.9 mmHg	48.0 mmHg
Mean quadrants closed:	4/4	3.2/4	2.9/4
Mean AC depth +:	2.55mm	2.41mm	2.45mm
Mean axial length	21.77mm	22.53mm	22.56mm
Mean cup : disc ratio	0.78	0.78	0.74
Congestive signs on presentation	2 (50%)	7 (30.4%)	7 (36.8%)
Previous Treatment:			
Iridectomy* - YAG	2	9	9
B:	-	-	1
PI:	-	4	3
No Iridectomy:	2	10	6
Glaucoma medication prior to surgery:			
Topical	-	15	8
Maximum	4	8	11
Mean time to surgery	2.5 days	4.6 months	11.7 months

+Anterior chamber depth measured from the anterior surface of cornea to anterior surface of lens.
*YAG indicates Nd-YAG laser iridotomy, PI indicates surgical iridectomy and B (both) indicates first a laser iridectomy and then a surgical iridectomy.

A standard trabeculectomy technique was used in all patients. A fornix-based conjunctival flap was raised and a 4 x 4mm scleral flap was cut. A 1 x 2mm sclerectomy was performed, followed by a peripheral iridectomy. The scleral flap was sutured with 4 x 10-0 nylon sutures and the conjunctiva closed with interrupted 10-0 nylon sutures. Topical atropine 1% was inserted on completion of surgery and a subconjunctival injection of 20mg celestone and 20mg gentamicin was given. On the first post-operative day the pupil was intensively dilated with short-acting mydriatics. All patients received topical homatropine and dexamethasone - chloramphenicol for four weeks, followed by topical prednisolone acetate for a further 4 to 8 weeks.

In order to compare these results with others, a successful result was considered to be an intraocular pressure of less than 21 mmHg with or without medication. Linear regression analysis was performed comparing the intraocular pressure on presentation to the change of intraocular pressure achieved after surgery. Separate models were obtained for those receiving post-operative glaucoma medication and for those controlled without medication.

Three subgroups of patients were identified: a group of 19 patients (20 eyes) who had previously undergone an Nd-YAG laser peripheral iridotomy, 6 patients (8 eyes) who had undergone surgical iridectomy and 14 patients (18 eyes) who had undergone no previous surgical treatment. The groups differed in only one respect: the average time from presentation to trabeculectomy in the Nd-YAG laser iridotomy group was 7.4 months, in the group with a surgical iridectomy it was 13.6 months and in the group without an iridectomy it was 3.7 months. The complications of trabeculectomy performed in these groups were compared. Statistical analysis was performed using Fisher's exact test and the Chi-square test. A difference was considered statistically significant at $P < 0.05$.

10.3 Results

The intraocular pressure was successfully maintained below 21 mmHg in 30 eyes (30/45, 66.7%) without medication and in a further 11 eyes (11/45, 24.4%) with the addition of topical medication. In 4 eyes the intraocular pressure was not controlled (4/45, 8.9%). A Kaplan-Meier survival curve demonstrating the cumulative success probability after trabeculectomy, with and without glaucoma medication, is shown in Figure 10.1.

The intraocular pressure was successfully controlled on or off medication in 97.3% (36.37) at 12 months, in 90.9% (20/22) at 24 months and in 87.5% (7/8) at 36 months. The bleb appearance at the last post-operative visit was cystic or microcystic in 21, diffuse in 19 and flat in 5. (Figure 10.2 and 10.3)

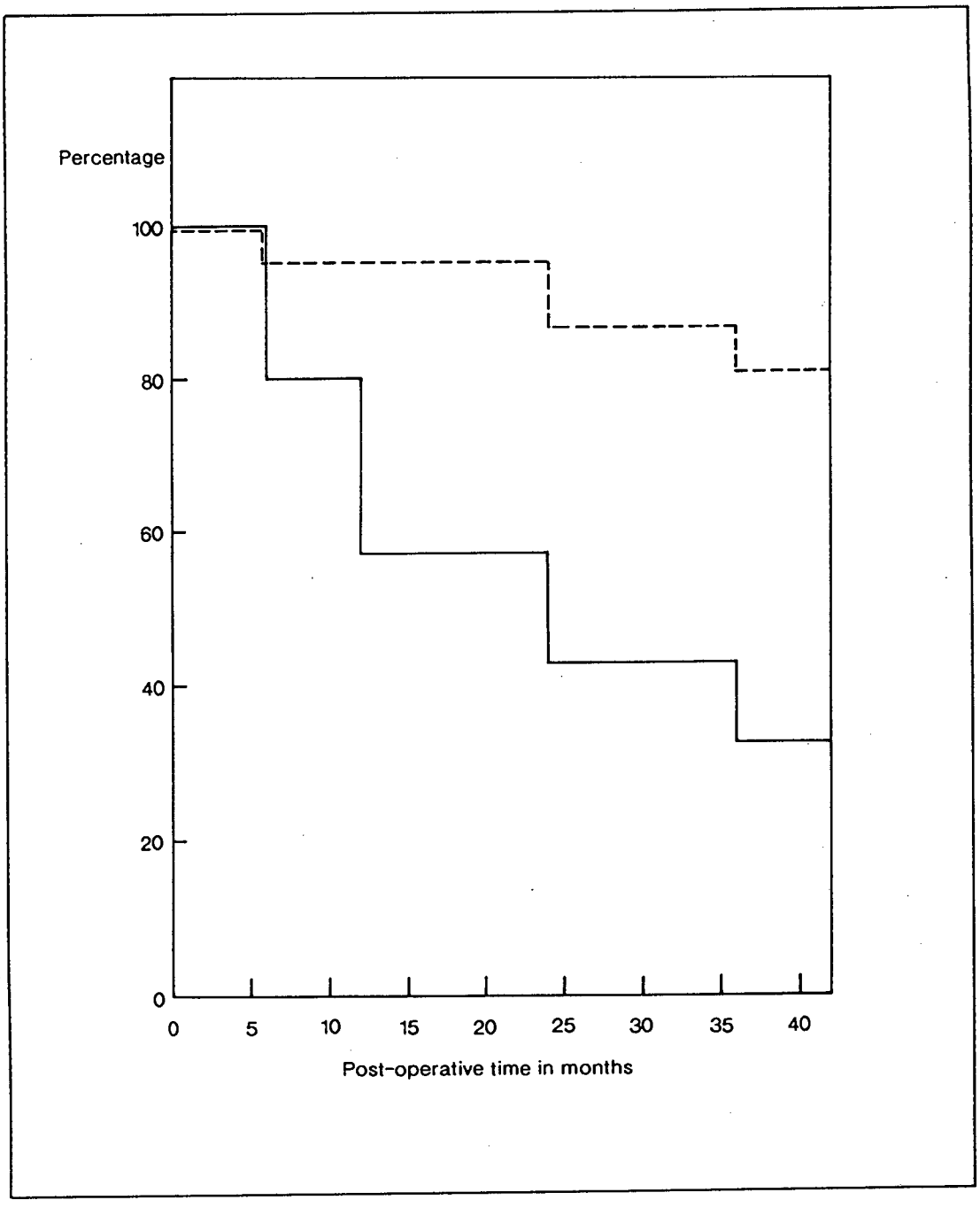

Figure 10.1 Kaplan-Meier survival curve demonstrating the cumulative success probability after trabeculectomy for chronic angle-closure glaucoma. The continuous line indicates those controlled without medication and the broken line those controlled with additional glaucoma medication.

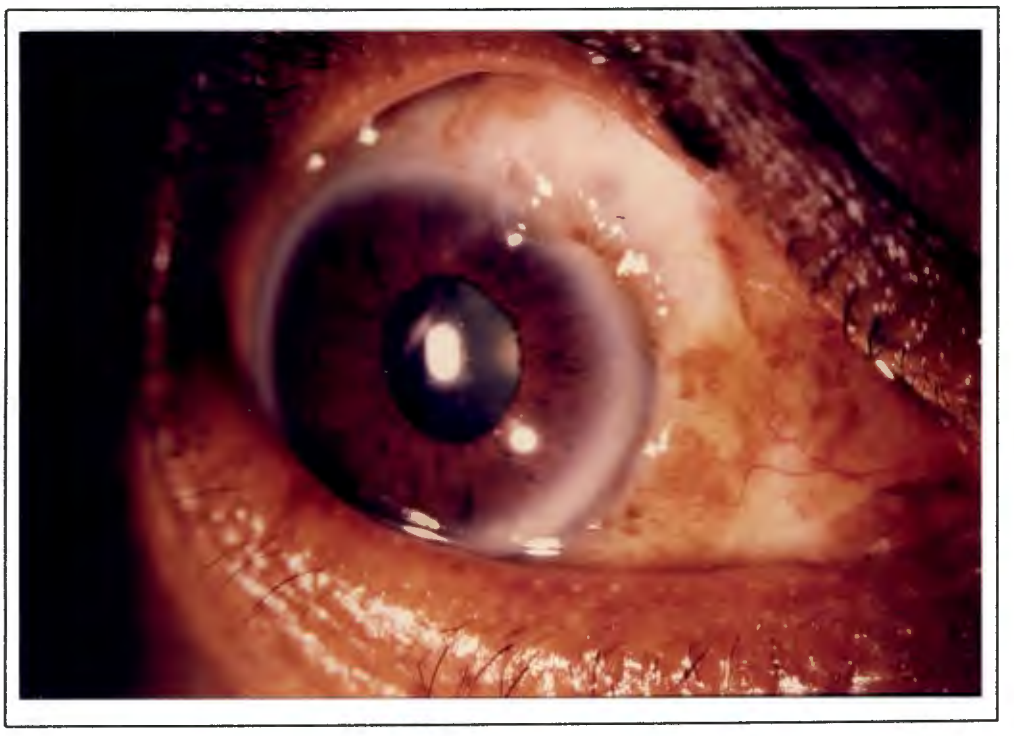

Figure 10.2 Cystic trabeculectomy bleb (present in 47%)

Figure 10.3 Diffuse trabeculectomy bleb (present in 42%)

Trabeculectomy and topical medication failed to control the intraocular pressure in 4 patients, and two (patients 2 and 3, Table 10.2) demonstrated progressive visual field loss. Of the four failures, one had early bleb failure. In order to control these patients a second trabeculectomy was required a mean period of 3 years after the original drainage procedure (Table 10.2).

TABLE 10.2 FAILURE AFTER TRABECULECTOMY

Patient		1	2	3	4
Sex		M	F	M	M
Age		48	59	57	52
Visual acuity		6/9	6/9	6/9	6/24
Previous iridectomy		Nd-YAG	Surgical	Surgical	Nil
Cup : disc ratio		0.95	0.9	0.5	0.9
Post op. I.O.P	1 year:	13	16	22	18
(mmHg)	2 years:	20	24	20+	22+
	3 years	24+	17		
Visit prior to repeat surgery		24+	23*	24*	22+
Time to repeat surgery		41 months	39 months	34 months	29 months

+ indicates additional glaucoma medication
* intraocular pressure not controlled and progressive visual field loss documented.

The result of linear regression analysis (pressure on presentation, Po, versus the change in pressure after surgery, P) is shown in Figure 10.4

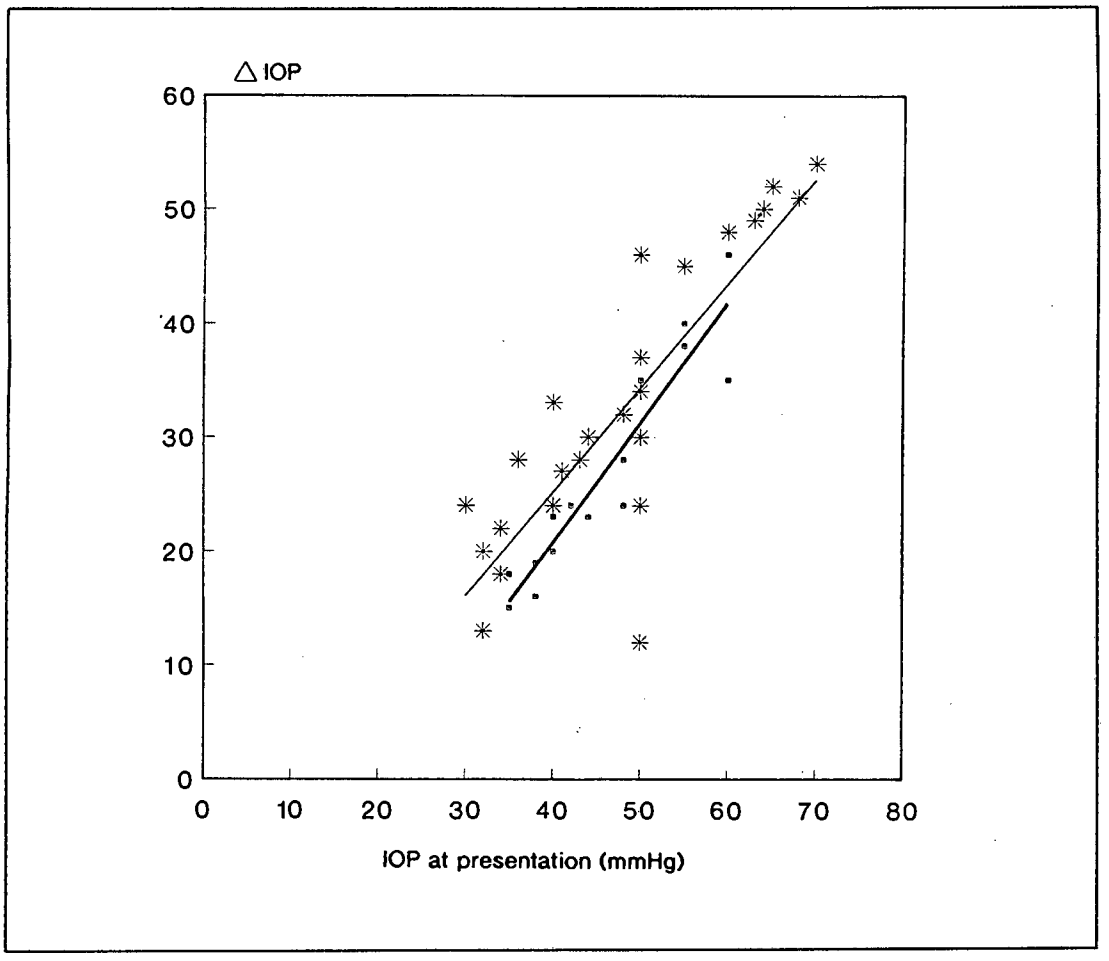

Figure 10.4 Regression analysis comparing the intraocular pressure on presentation to the change of intraocular pressure achieved after surgery. The results of 30 eyes not requiring post-operative glaucoma therapy are represented by stars and the slope with a thin line (r=0.863). The results of 15 eyes requiring post-operative glaucoma therapy are represented by boxes and the slope with a heavy line (r=0.942).

Two slopes were obtained with the following parameters:

A. P = 0.94 x Po - 11.42 (standard error 3.45) for 30 eyes not requiring post-operative glaucoma therapy. The correlation coefficient is 0.863.

B P = 1.05 x Po - 21.19 (standard error 4.82) for 15 eyes requiring post-operative topical glaucoma therapy to control the intraocular pressure. The correlation coefficient is 0.942. In these patients the period of follow-up was significantly longer than in those requiring no additional medication (P = 0.01).

Post-operative complications are summarised in Table 10.3. There were no statistical differences in complications between those patients who had previously undergone a Nd-YAG iridotomy, a surgical iridectomy, or those who had not undergone previous surgery. A small post-operative hyphaema was found in 6 (13%); a complication that was more common in patients who had previously undergone a Nd-YAG laser iridotomy (P = 0.12). A shallow anterior chamber occurred in 11 patients (23.9%) and surgical reformation of the anterior chamber and drainage of choroidal detachments was required in two of these eyes. In no patient was the surgery complicated by malignant glaucoma. Progressive cataract formation resulting in cataract extraction with intraocular lens implantation occurred in 9 patients a mean period of 23.9 months after trabeculectomy.

TABLE 10.3 COMPLICATIONS OF TRABECULECTOMY

Previous Treatment	YAG Iridotomy N = 20	Nil N = 18	Surgical PI N = 8
Shallow anterior chamber	5 (25%)	3 (16.7%)	3 (37.5%)
Reformation of anterior chamber	1 (5%)	1 (5.6%)	0
Hyphaema	5 (25%)	1 (5.6%)	0
Cataract extraction	3 (15%)	4 (22.2%)	2 (25%)
Failure	1 (5%)	1 (5.6%)	2 (25%)

10.4 Discussion

In people of Oriental ethnic background primary angle-closure glaucoma is often diagnosed at a late stage of the disease and severe visual loss may occur. This pattern was clearly demonstrated on reviewing the presenting features of 46 eyes of 39 patients with chronic angle-closure glaucoma who had undergone trabeculectomy. The mean cup : disc ratio was 0.76, glaucomatous visual field loss was present in 93.5% (43/46) and all had significant circumferential areas of angle closure. Twelve patients had one blind eye on presentation.

In our department in recent years, once the intraocular pressure has been controlled with glaucoma medication and any inflammation reduced with topical corticosteroids, the initial surgical treatment of chronic angle-closure has been a laser iridotomy.[1-6] Because of the ease and safety of laser iridotomy and the difficulty in predicting which patients will not be controlled after laser iridotomy, initial treatment with trabeculectomy should only be considered when the intraocular pressure cannot be controlled on presentation[1] (Chapter 9). In the years before Nd-YAG laser was available, some patients underwent a surgical iridectomy. In other patients topical medication was commenced without an iridotomy, because of initial patient refusal to undergo surgery or because the performance of an iridotomy was considered hazardous in the presence of advanced disease. These different approaches to the initial management of chronic angle-closure glaucoma coincidentally enabled me to compare the complications of trabeculectomy performed with or without prior iridectomy.

Irrespective of the initial surgical treatment, trabeculectomy was performed for three indications: an inability to control the intraocular pressure medically on presentation, inadequate control of intraocular pressure on follow-up and an acute intraocular pressure rise on follow-up because of poor compliance. Four patients underwent a trabeculectomy in the acute stage because the intraocular pressure could not be controlled medically. In these patients the angle remained closed without acute anterior chamber shallowing (thus excluding the diagnosis of malignant glaucoma). Argon laser peripheral iridoplasty was not attempted.[10] In 23 eyes of 19 patients the intraocular pressures were found on follow-up to be between 20 mmHg and 30 mmHg despite medication. The "ideal" intraocular pressure for patients with chronic angle-closure glaucoma is unknown and although this level of intraocular pressure may not have resulted in optic nerve damage, accurate follow-up using visual fields was considered unreliable in the presence of a small pupil and lens change.

A third group consisting of 19 eyes of 17 patients, were initially controlled with an intraocular pressure of less than 21 mmHg. Because of a failure to use the prescribed medication (including topical pilocarpine) they were found on follow-up to have a high intraocular pressure and a completely closed angle. Remarkably, these patients had no congestive signs or symptoms at this follow-up visit, despite the level of the intraocular pressure and none had acute shallowing of the anterior chamber suggestive of malignant glaucoma. The mean intraocular pressure was 5 mmHg lower than the mean initial presenting intraocular pressure and was brought back to normal with glaucoma medication without difficulty. Thirteen patients (68.4%) had a patent iridectomy or iridotomy, including one who had experienced a similar episode despite the presence of a patent Nd-YAG laser iridotomy and had undergone a surgical iridectomy in the mistaken belief that the laser iridotomy was not large enough. In six patients in this group no iridectomy

was present and pupillary block may have been responsible for the intraocular pressure spike. Progressive synechial closure of the angle was not documented in these patients and is unlikely to be the cause for the acute rise in pressure because of the ease with which the intraocular pressure was controlled prior to trabeculectomy and the relatively short time from initial presentation. Although there are isolated reports of acute angle-closure glaucoma developing in the presence of a small but patent Nd-YAG laser iridotomy, a more likely explanation in our patients is that the appositional angle closure occurred because of plateau iris syndrome.[1,12] Although plateau iris syndrome is considered rare in Europeans, this anatomic variation is not uncommon in our patients of mixed ethnic origin, as shown in Chapter 4.

The surgery was immediately effective in reducing the intraocular pressure in all except two patients who had an intraocular pressure of greater than 20 mmHg on the first post-operative day. No patient experienced a spike of intraocular pressure during the period of post-operative observation. While the overall results of trabeculectomy in this study are similar to those previously published, this was achieved by using additional topical glaucoma medication in about one in three cases: 66.7% were controlled with trabeculectomy alone and a further 24.4% with the addition of topical medication. Ridgway reported an intraocular pressure below 21 mmHg after trabeculectomy in 85% of eyes with chronic angle closure glaucoma and in a further 7% with additional medical treatment.[12] Watson, using similar success criteria, reported control in 76% without medication and in a further 8% with medication.[7]

Regression analysis demonstrated that the higher the initial intraocular pressure, the greater the drop after drainage surgery. The relationship was predictable ($r = 0.863$) and shows that those eyes with a good drainage bleb will have a

post-operative intraocular pressure similar to episcleral venous pressure (12.2. mmHg).[7] In those requiring additional medication to control the intraocular pressure, an even more predictable relationship was found (r = 0.942). This indicates the tendency to keep the intraocular pressure in the "normal" range with the least possible medication (20.1 mmHg).

The early complications of trabeculectomy were similar to those reported in previous studies, with the exception that no cases of malignant glaucoma were found.[7,9,11] Eltz described 7 cases (13%) of malignant glaucoma in patients with chronic angle-closure glaucoma, but this percentage is higher than other studies have found.[7,8] In my patients the pupil was intensively dilated post-operatively and this may have played a role in reducing the risk of malignant glaucoma. Although statistical significance was not demonstrated, a post-operative hyphaema was present in 25% of the patients who had previously undergone a Nd-YAG laser iridotomy, compared to only 5.6% of those who had not undergone previous surgery (P = 0.12). Watson reported a small post-operative hyphaema in 21.4% (9/42) of patients who had undergone trabeculectomy for chronic angle-closure glaucoma.[7] A shallow anterior chamber occurred post-operatively in 24% (11/46) and two patients required surgical reformation of the anterior chamber and drainage of choroidal detachments. In Watson's series a shallow anterior chamber was found in 21.4% and a choroidal detachment associated with a shallow anterior chamber in 4.8% (2/42), although none required further surgery for this complication.[7] No visual loss was documented after surgery in the present study, even in patients with small central fields.

The major long-term complication was progressive cataract formation, a finding that has been noted in the past after peripheral iridectomy and trabeculectomy.[14,15] In patients who underwent cataract extraction, nuclear sclerosis was present on presentation. Cataract extraction with intraocular lens implantation was performed

in 19.6% of eyes (9/46), a mean period of 2 years after trabeculectomy. Greve described the use of lens extraction as the initial therapy of chronic angle-closure glaucoma, but the value of this approach in our patients is unknown.[16]

Four patients (8.8%) required a second trabeculectomy a mean period of 3 years after the first drainage procedure. Watson reported the need for a second trabeculectomy in five eyes (13.5%) because the first procedure failed to control the intraocular pressure.[7] In three of the eyes in the present series a good microcystic drainage bleb developed initially and the intraocular pressure was well controlled for a long period. These patients were young, had advanced disease and experienced late scarring of the bleb. The role of fibrosis suppression in the prevention of late bleb failure is unknown.[17]

This study has confirmed the effectiveness of trabeculectomy in controlling the intraocular pressure in patients with advanced chronic angle-closure glaucoma. While malignant glaucoma remains a potential hazard, this complication did not occur in our patients and perhaps the danger has been overestimated in the past.

10.5 References

1. Ritch R. The treatment of chronic angle-closure glaucoma. *Ann Ophthalmol* 1981; **13** : 21-23.
2. Robin AL. Pollack IP. Argon laser peripheral iridotomy in the treatment of primary angle-closure glaucoma. *Arch Ophthalmol* 1982; **100** : 919-923.
3. Quigley HA. Long-term follow-up of laser iridotomy. *Ophthalmology* 1981; **88** : 218-224
4. Yamamoto T, Shirato S, Kitazawa Y. Treatment of primary angle-closure glaucoma by argon laser iridotomy : a long term follow-up *Jpn J Ophthalmol* 1985; **29** : 1-12
5. Gieser DK, Wilensky JT. Laser iridectomy in the management of chronic angle-closure glaucoma. *Am J Ophthalmol* 1984; **98** : 446-450.
6. Schwartz LW, Moster MR, Spaeth GI, Wilson RP, Poryzees E. Neodymium-YAG laser iridectomies in glaucoma associated with closed or occludable angles. *Am J Ophthalmol* 1986; **102** : 41-44.
7. Watson PG, Grierson I. The place of trabeculectomy in the treatment of glaucoma. *Ophthalmology* 1981; **88** : 175-196.
8. Eltz H, Gloor B. Trabeculectomy in cases of angle-closure glaucoma : successes and failures. *Klin Monatsbl Augenheilkd* 1980; **177** : 556-561.
9. Wilson P. Trabeculectomy : a long term follow-up. *Br. J Ophthalmol* 1977; **61** : 535-538.
10. Ritch R. Argon laser treatment for medically unresponsive attacks of angle-closure glaucoma. *Am J Ophthalmol* 1982; **94** : 197-204.
11. Fleck BW. How large must an iridotomy be? *Br J Ophthalmol* 1990; **74** : 583-588.

12. Hung PT, Chou LH. Provocation and mechanism of angle-closure glaucoma after iridectomy. *Arch Ophthalmol* 1979; **97** : 1862-1864.

13. Ridgway AEA. Trabeculectomy. A follow up study. *Br J Ophthalmol* 1974; **58** : 680-686.

14. Sugar H.S. Cataract formation and refractive changes after surgery for angle-closure glaucoma. *Am J Ophthalmol* 1970; **69** : 747-749.

15. Godel V, Regenbogen L. Cataractogenic factors in patients with primary angle-closure glaucoma after peripheral iridectomy. *Am J Ophthalmol* 1977; **83** : 180-184.

16. Greve EL. Primary angle-closure glaucoma : Extracapsular cataract extraction or filtering procedure? *International Ophthalmol* 1988; **12** : 157-162.

11.0 Conclusions

Primary angle-closure glaucoma is significantly more common than primary open-angle glaucoma in Asia, whereas in Africa and Europe the reverse is found. Cape people of mixed ethnic background have Southeast Asian, indigenous African and European ancestors. A survey undertaken in the glaucoma clinic at Groote Schuur Hospital revealed that this ethnic group are more likely to present with primary angle-closure glaucoma than whites or blacks are (Chapter 2). This predisposition can be explained by an Oriental genetic influence on their ocular structures.

Hospital-based studies have the disadvantage of being subject to selection bias. A population-based prevalence survey was therefore undertaken in the village of Mamre, situated 56 km from Cape Town. The results are reported in Chapter 3. The study revealed an age-related trend towards hypermetropia, especially in women. The prevalence of Shaffer grade 1 angles in this village was 9% and of primary angle-closure glaucoma 2.3%; this prevalence increased with age in both sexes. Women were affected four times more frequently than men were and the sex difference persisted across all age groups. The prevalence of chronic angle-closure glaucoma was 2.0% and of chronic open-angle glaucoma 1.5%. The prevalence of blindness secondary to chronic angle-closure glaucoma was 0.3%. The survey identified primary angle-closure glaucoma as a significant public-health problem in the Western Cape Province.

The anatomical basis for chronic angle-closure glaucoma in this ethnic group is reported in Chapter 4. The mean axial length and the mean anterior chamber depth were less and the mean "relative lens position" was more anterior in eyes with

chronic angle-closure glaucoma than in normal individuals. The mean lens thickness in patients of mixed ethnic background with chronic angle-closure glaucoma was the same as the mean measurement found in matched normal individuals, whereas in Europeans the mean lens thickness in patients with primary angle-closure glaucoma has been reported to be greater than that found in normal individuals. It can be concluded that an anterior position of the lens is the main reason for the crowded anterior segment found in "coloured" patients with chronic angle-closure glaucoma.

The mechanism of angle occlusion is considered in Chapter 5. Most studies of Western patients suggest that angle closure occurs secondary to pupillary block, and plateau iris syndrome is considered unusual. By using provocative tests in patients of mixed ethnic background with chronic angle-closure glaucoma who had a patent laser iridotomy, it was shown that plateau iris syndrome plays an important role in the pathogenesis of chronic angle-closure glaucoma in this ethnic group. Anteriorly positioned ciliary processes may be responsible for the "creeping" angle closure found in some patients with chronic angle-closure glaucoma.

The presenting features of primary angle-closure glaucoma depend on the ethnic background of the population studied. In Chapter 6 the presenting features and effects of primary angle-closure glaucoma in people of mixed ethnic background are reported. About one-third presented with acute glaucoma and two-thirds with chronic angle-closure glaucoma. Glaucomatous visual field loss was present in more than half the patients and total uniocular blindness secondary to chronic angle-closure glaucoma was present in one-fifth. The results show that if these people develop primary angle-closure glaucoma they are more likely to present with chronic symptoms and signs than with acute symptoms and may suffer significant ocular damage and visual loss before presentation.

In Chapter 7 the relationship of "iridoschisis" to primary angle-closure glaucoma is considered. Iridoschisis appears to be an unusual manifestation of iris stromal atrophy and results from intermittent or acute elevation of intraocular pressure secondary to angle closure.

The management of an asymptomatic eye that is at risk of developing chronic angle-closure glaucoma is considered in Chapter 8. In this series, the performance of a prophylactic peripheral iridotomy using Nd-YAG laser was easy and no serious complications were experienced. The long-term intraocular pressure levels in eyes with a steep iris plane were good. A plateau iris configuration should be excluded because these eyes tend to develop a raised intraocular pressure with time. The risk of further angle occlusion in the presence of a peripheral iridotomy appears to be small, but further follow-up of these patients is required before a definitive conclusion can be reached.

Most Western studies advocate the use of laser iridotomy as the initial surgical treatment for chronic angle-closure glaucoma. In Chapter 9 the use of Nd-YAG laser iridotomy in patients with chronic angle-closure glaucoma is discussed. Analysis of the ocular findings on presentation revealed an inadequate ability to predict which patients would be controlled with iridotomy and glaucoma medication and which would require a trabeculectomy. For this reason, laser iridotomy followed by topical glaucoma medication and then, only if required, trabeculectomy, seems a logical and safe approach in these patients, even in those with advanced glaucomatous disc cupping and visual field loss. Careful follow-up of intraocular pressure levels and visual field performance is particularly important in patients with advanced disease.

The role of trabeculectomy performed for advanced chronic angle-closure glaucoma in this ethnic group is discussed in Chapter 10. Serious surgical complications were uncommon and the intraocular pressure could be reduced to below 21 mmHg in two-thirds of patients without medication and in most of the remainder with additional topical glaucoma medication. One-third underwent a cataract extraction with intraocular lens implantation within three years of initial filtering surgery.

Because of the high prevalence rate of primary angle-closure glaucoma and the severity of ocular involvement, this disease is clearly a major public-health problem in the Western Cape Province. The economic consequences of this disease are important because 10.5% of the population of South Africa have a similar ethnic background to the people described in this thesis. Although the late effects of the disease on visual function are devastating, the treatment is relatively simple, safe and effective if the disease is diagnosed early. Efforts should therefore be made to identify individuals at risk and to heighten awareness of the condition amongst health-care workers and ophthalmic practitioners.

Although this thesis applies specifically to Cape people of mixed ethnic background who have chronic angle-closure glaucoma, there is sufficient evidence to suggest that the conclusions will also be relevant to the people of Southeast Asia.

My hope is that these findings will ultimately result in the prevention of blindness from this disease.