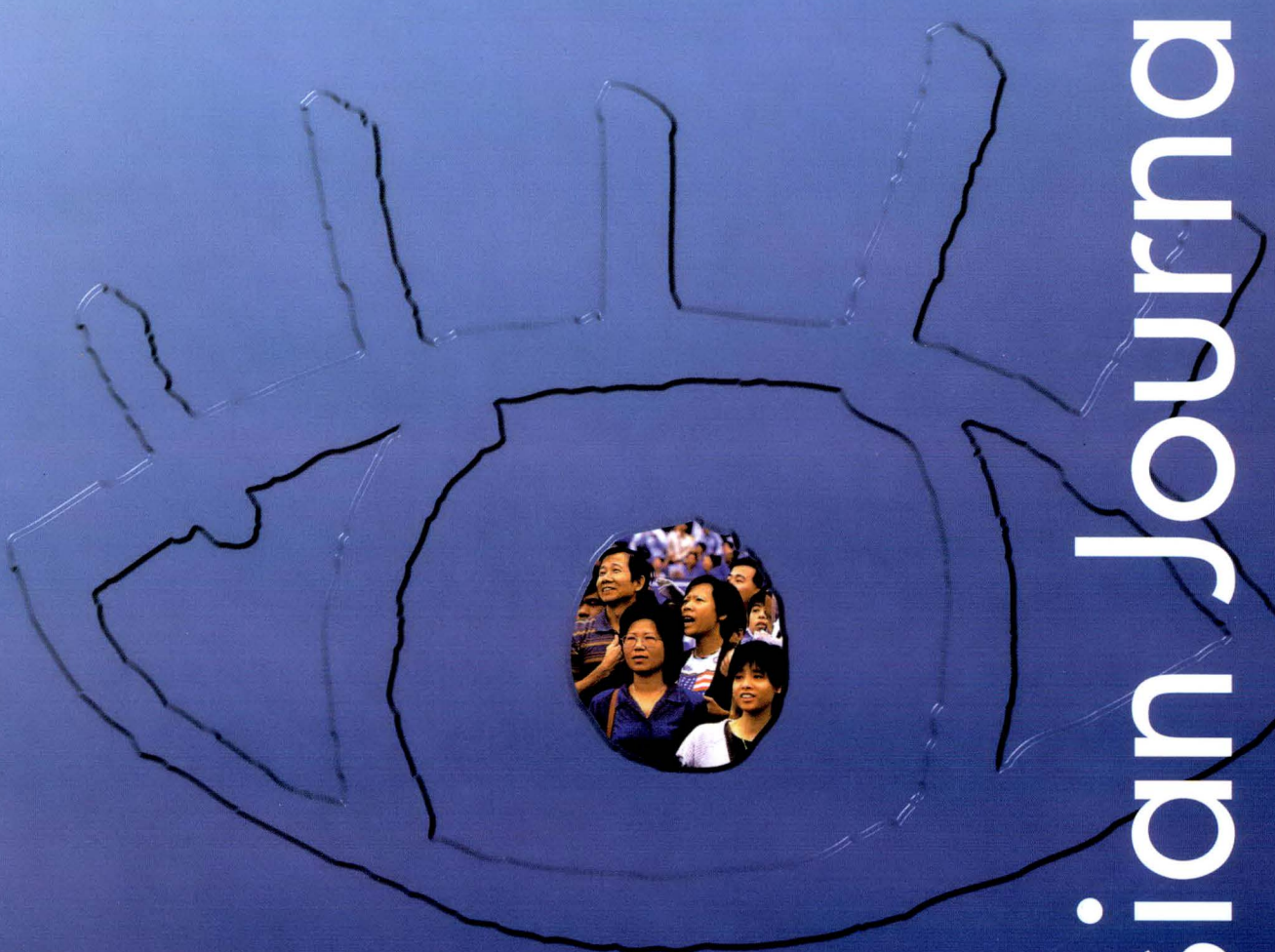


**Latanoprost for Glaucoma and Ocular Hypertension**

**Pulsatile Ocular Blood Flow in Glaucoma**

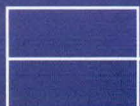
**Diagnosis and Management of Cyclodialysis Cleft**

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<sup>2</sup>Meta-analysis of 3 studies of 6 months (n=717) with open-label extensions up to 2 years (n=113).

<sup>3</sup>Available safety data include a 4-year, open-label long-term study and spontaneous reports.

<sup>4</sup>IMS D&H audit from July 2000 to June 2001 (based on value share).

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# Open Label, Prospective, Multicentre Indian Study of Latanoprost in Primary Open Angle Glaucoma and Ocular Hypertension

Indian Latanoprost (Xalatan) Study Group

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## Indian Latanoprost (Xalatan) Study Group

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**Aims:** To evaluate the intraocular pressure lowering effect and safety of latanoprost 0.005% in patients with primary open angle glaucoma and ocular hypertension.

**Patients and Methods:** 126 patients with primary open angle glaucoma or ocular hypertension were enrolled in this prospective open label study from 15 centres in India. Patients were treated with latanoprost 0.005% once daily as single therapy for 3 months.

**Results:** At all the follow-up visits there was a significant reduction in intraocular pressure compared with baseline values ( $p < 0.05$ ). At 3 months (week 12), a mean intraocular pressure reduction of  $9.1 \pm 3.9$  mm Hg was obtained. The most frequently reported adverse ocular events were mild congestion (4.2%) and itching (2.5%). Few systemic adverse events were reported.

**Conclusion:** Latanoprost eye drops showed a marked intraocular pressure lowering effect during the treatment period. The drug was well tolerated and the intraocular pressure lowering effect was stable during the treatment period.

## Introduction

Latanoprost (PhXA41; Xalatan®) is a new phenyl substituted analogue of prostaglandin F<sub>2α</sub> isopropyl ester that produces an ocular hypotensive effect on topical application for primary open angle glaucoma (POAG) and ocular hypertension (OH). Latanoprost has proven to be an effective ocular hypotensive in healthy eyes and in eyes with elevated intraocular pressure (IOP). Latanoprost has been approved in many countries for the treatment of primary open angle glaucoma and ocular hypertension. This agent reduces IOP by increasing ocular uveoscleral outflow with no effect on aqueous humor production.<sup>1-3</sup> In phase III studies, latanoprost 0.005% was shown to be an effective IOP reducing agent in patients with POAG or OH during 6 to 12 months of treatment.<sup>4-7</sup>

In this open-label, multicentre, non-comparative, prospective study, the efficacy and safety of latanoprost were evaluated in Indian patients with POAG or OH. The purpose of this study was to evaluate the IOP-reducing effect and tolerability of latanoprost 0.005% eye drops during 12 weeks of treatment.

## Patients and Methods

The study was designed as a 3-month open label, multicentre, non-comparative, prospective study, involving 126 patients with POAG or OH at 15 centres across the country. Informed consent was obtained from all patients prior to enrolment.

Patients 18 years aged or older, with unilateral or bilateral POAG or OH, with an IOP of at least 21 mm Hg with previous treatment or 25 mm Hg without treatment were eligible for inclusion. Patients with POAG or OH were enrolled in the study at the discretion of the investigators, according to the manufacturer's indications for latanoprost.

Exclusion criteria included patients with closed or barely open anterior chamber angle or history of angle closure, intra-ocular surgery within the past 6 months, argon laser trabeculoplasty within the past 3 months, any ocular inflammation or infection within the past 3 months, known hypersensitivity to any component of the study drug, or any condition preventing reliable applanation tonometry. Pregnant women or nursing mothers were also excluded.

**Medication and Treatment Schedule**

At each visit, the patient was provided with a bottle of latanoprost eye drops, which was sufficient for 1 month. While in use, opened bottles were stored at room temperature (<25°C). The dropper bottles were used within 4 weeks of opening. Patients were instructed to place 1 drop of latanoprost in the affected eye(s) every evening at approximately 8.00 pm.

The treatment period was 3 months. During the 3-month follow-up period, each patient visited the clinic 4 times, as follows: day 0 (visit 1), week 4 (visit 2), week 8 (visit 3), and week 12 (visit 4). At the end of week 12, the patients were exited from the study and treated at the discretion of the investigators.

**Efficacy and Safety Variable Evaluation**

During every visit, the IOP was measured with a Goldmann applanation tonometer before the pupils were dilated. The same tonometer was used for a given patient at each visit. To minimise diurnal variation, the IOP was consistently measured at the same time of day.

Gonioscopy was performed at the first visit. Visual field acuity and refraction, visual field examination, slit lamp examination, and ophthalmoscopy to evaluate the optic nerve head was performed as clinically required,

**Table 1. Demographic characteristic of patients receiving latanoprost.**

Characteristics	Values
Number of patients	126
Age (years)	
Mean ± SD	53.4 ± 12.8
Range	32-85
Sex	
Male	66 (52.4%)
Female	60 (47.6%)
Diagnosis	
Primary open angle glaucoma	112
Ocular hypertension	14

at the discretion of the investigator. During each visit, patients were evaluated for clinical adverse events. Adverse events were recorded on the case report form (CRF).

**Results**

126 patients were enrolled in this study. The mean age of the patients was 53.4 ± 12.8 years (range, 32 to 85 years). Sixty six patients (52.4%) were male and 60 (47.6%) were female. The diagnoses were POAG (n = 112) and ocular hypertension (n = 14). The demographic characteristics of the patients are presented in Table 1.

Thirty six patients (28.6%) had concomitant illness, which included hypertension (7, 5.5%), diabetes mellitus (6, 4.8%), hypertension with diabetes mellitus (4, 3.2%), and bronchial asthma (3, 2.4%). Ten patients (7.9%) had other ocular diseases, which included nuclear cataract, nuclear sclerosis, immature cataract, myopia, and lenticular sclerosis. Six patients (4.8%) had other systemic diseases, which included hypothyroidism, migraine, carcinoma of the mandible, transient ischaemic episodes with diabetes mellitus, and hypertension

**Table 2. Concomitant disease frequency.**

Disease	Number of patients (%)
Hypertension	7 (5.5)
Diabetes mellitus	6 (4.8)
Hypertension with diabetes mellitus	4 (3.2)
Bronchial asthma	3 (2.4)
Other ocular disease	10 (7.9)
Other systemic disease	6 (4.8)
<b>Total</b>	<b>36 (28.6)</b>

with ischaemic heart disease. The details of concomitant illness are shown in Table 2.

The baseline mean IOP was 27.1 ± 6.0 mm Hg. At the end of 4 weeks treatment with latanoprost, the mean IOP was reduced by 7.2 ± 4.1 (26.7%) from baseline (p < 0.05). After 8 weeks of treatment, the mean IOP was reduced by 8.9 ± 4.1 (32.8%) from baseline (p < 0.05). After 12 weeks, the mean IOP was reduced by 9.1 ± 3.9 (33.6%) from baseline (p < 0.05). The mean ± SD changes in IOP are presented in Table 3 and Figure 1.

Twenty (16.8%) adverse events were reported, which included both ocular and systemic events. The most common ocular events were mild congestion (5, 4.2%), itching (3, 2.5%), dryness of the eye (2, 1.7%), mild discharge and watering (2, 1.7%), and eye pain (2, 1.7%). Other ocular events were swelling of the lid (1, 0.8%), increased thickness and length of eyelashes (1, 0.8%), episcleritis (1, 0.8%), and iris pigmentation (1, 0.8%). Systemic events were headache (1, 0.8%) and diarrhoea (1, 0.8%). The adverse event frequency is shown in Table 4.

Seventeen patients (13.5%) were withdrawn from the study. The reasons for withdrawal included uncontrolled IOP (9,

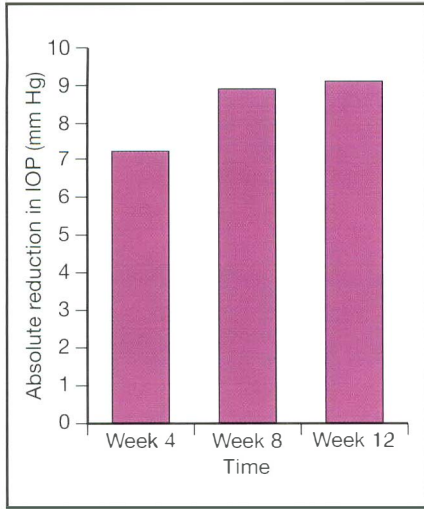


**Table 3. Changes in mean intraocular pressure (IOP) after 12 weeks of treatment with latanoprost.**

Follow up	Mean IOP ± SD (mm Hg)	Absolute reduction in IOP (mm Hg)	Reduction in IOP (%)
Baseline	27.1 ± 6.0	—	—
Week 4	19.8 ± 5.5	7.2 ± 4.1*	26.7
Week 8	18.2 ± 4.4	8.9 ± 4.1*	32.8
Week 12	18.0 ± 3.7	9.1 ± 3.9*	33.6

\* p < 0.05 (by students t test).

**Figure 1.** Absolute reduction in mean intraocular pressure (IOP) after 12 weeks of treatment with latanoprost (n = 109).



7.1%), voluntary withdrawal (1, 0.8%), surgery for glaucoma (1, 0.8%), and lost to follow up (6, 4.7%). No patient was withdrawn due to adverse events. The various reasons for withdrawal are presented in Table 5.

**Discussion**

A combination of 2 or more drugs is common in the treatment of glaucoma. As a rule, a drug that increases uveoscleral outflow such as latanoprost or pilocarpine may be combined with a drug that reduces inflow, such as  $\beta$ -adrenergic antagonists or carbonic anhydrase inhibitors. However, polytherapy may be inconvenient for

**Table 4.** Adverse event frequency.

Adverse event	Number of patients (%)
Mild congestion	5 (4.2)
Itching	3 (2.5)
Dryness of the eye	2 (1.7)
Mild discharge and watering	2 (1.7)
Eye pain	2 (1.7)
Swelling of the lid	1 (0.8)
Headache	1 (0.8)
Diarrhoea	1 (0.8)
Eye lashes feel longer	1 (0.8)
Episcleritis	1 (0.8)
Iris pigmentation	1 (0.8)
<b>Total</b>	<b>20 (16.8)</b>

**Table 5.** Reasons for discontinuation of latanoprost therapy before 12 weeks.

Reasons for withdrawal	Number of patients
Intraocular pressure not controlled	9
Voluntary withdrawal	1
Surgery for glaucoma	1
Lost to follow up	6
<b>Total</b>	<b>17</b>

patients and can result in poor compliance. Therefore, it is preferable to consider the option of switching a patient from 1 monotherapy to another monotherapy when the IOP is inadequately controlled rather than adding another drug to the first treatment.

In the present study, newly diagnosed patients with POAG or OH with inadequately controlled IOP with topical therapy, either alone or in combination, were switched to treatment with latanoprost once daily. The results of the study demonstrate that latanoprost 0.005% administered once daily reduces IOP in patients with POAG or OH. Latanoprost was administered once daily throughout the treatment period and significantly reduced the IOP. The mean baseline IOP of  $27.1 \pm 6.0$  mm Hg was reduced to  $18.0 \pm 3.7$  mm Hg at the end of 12 weeks of therapy with latanoprost 0.005% once daily ( $p < 0.05$ ). A consistent reduction in IOP was observed throughout the study. The mean absolute reduction in IOP

at 12 weeks compared with baseline was  $9.1 \pm 3.9$  mm Hg (33.6%) [Figure 1]. The final IOPs are shown in Figure 2.

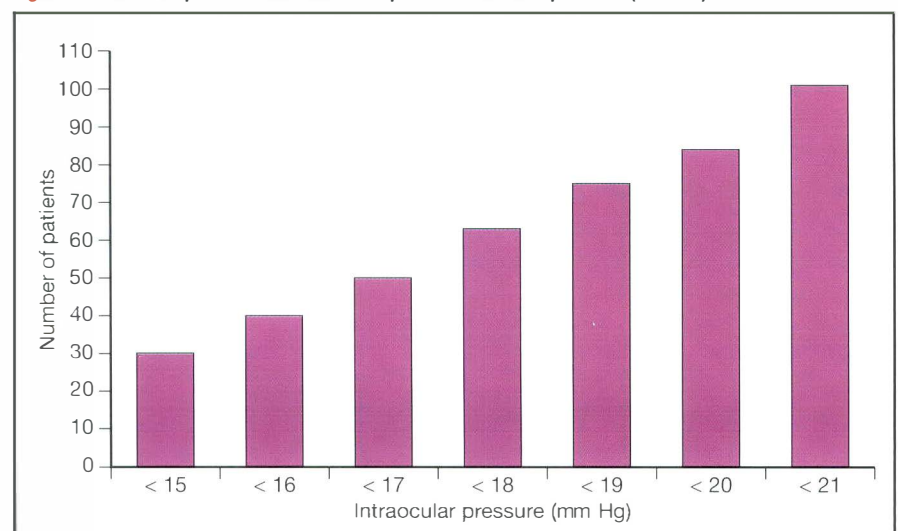
Mishima et al conducted a 12-week comparison study of latanoprost and timolol in POAG and OH.<sup>4</sup> In this study, latanoprost reduced IOP at the end of 12 weeks by  $6.2 \pm 2.7$  mmHg (26.8%), while timolol reduced IOP by  $4.4 \pm 2.3$  mm Hg (19.9%).

Camras et al conducted a 6-month comparative study of latanoprost and timolol in patients with OH and glaucoma.<sup>6</sup> In this study, latanoprost reduced the IOP by  $6.7 \pm 3.4$  mm Hg (27%), while timolol reduced the IOP by  $4.9 \pm 2.9$  mm Hg (20%).

O'Donoghue et al conducted a 3-month comparative study of latanoprost and dorzolamide in patients with glaucoma and ocular hypertension.<sup>8</sup> In this study latanoprost reduced IOP by  $8.5 \pm 3.3$  mm Hg (32%), while dorzolamide reduced IOP by  $5.6 \pm 2.6$  mm Hg (23%).

Alm et al conducted a 6-month comparative study of latanoprost and timolol in patients with glaucoma and OH.<sup>9</sup> In this study, latanoprost administered in the evening showed a superior reduction in IOP — from 24.8 mm Hg to 16.2 mm Hg (35%) — to latanoprost applied in the morning — from 25.5 mm Hg to 17.7 mm Hg (31%) — while timolol reduced the IOP from 24.6

**Figure 2.** Number of patients who achieved specific intraocular pressure (n = 109).



to 17.9 mm Hg (27%). This study seems to indicate a slight advantage of evening administration of latanoprost with regard to IOP reduction.

Twenty adverse events were reported, including mild congestion, itching, dryness of the eye, mild discharge and watering, eye pain, swelling of the lid, eyelash growth, episcleritis, and iris pigmentation. Systemic events included headache and diarrhoea. While 17 patients were withdrawn from the study, no patient was withdrawn due to adverse events.

Latanoprost offers several potential advantages over currently available medications for glaucoma therapy. Unlike  $\beta$ -blockers, carbonic anhydrase inhibitors, and  $\alpha_2$ -agonists, latanoprost acts on uveoscleral outflow rather than formation of aqueous humor. Virtually all glaucoma results from impaired outflow, but not excessive formation of aqueous humor. Avascular ocular structures depend on aqueous flow for metabolic exchanges, therefore chronic excessive reduction of aqueous humor formation may have deleterious effects. Unlike  $\beta$ -adrenergic blockers, which do not further reduce aqueous flow at night beyond the decrease already achieved during sleep, latanoprost reduces IOP equally as well at night as during the day. This represents a potential advantage because glaucomatous damage may occur during sleep when the ocular perfusion pressure may be reduced because of low systemic blood pressure. Furthermore, since latanoprost increases uveoscleral outflow, it can theoretically reduce IOP below the episcleral venous pressure, unlike drugs that act by either reducing aqueous humor production or increasing outflow facility. The evening administration that has been shown to be superior to morning administration<sup>9</sup>

has been chosen for this study to block an early morning diurnal IOP spike.

The present study demonstrates that 0.005% latanoprost administered once daily reduces IOP for 3 months for Indian patients with POAG or OH. These results confirm the efficacy and safety of latanoprost similar to those studies performed in Japanese, North American, and European patients.<sup>5,6,8,9</sup> Latanoprost has a good safety profile, both in terms of ocular and systemic side effects, compared with other currently available ocular medications. Throughout this study, there was a consistent decrease in IOP, which appeared to improve with longer administration. This is probably related to biochemical changes that take place in the uveoscleral outflow.

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# Study of Pulsatile Ocular Blood Flow in Primary Chronic Angle Closure Glaucoma

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6

**Aims:** To estimate pulsatile ocular blood flow in patients with primary chronic angle closure glaucoma and to correlate pulsatile ocular blood flow with the extent of the glaucomatous defect.

**Patients and Methods:** Pulsatile ocular blood flow recordings were taken in both eyes of 42 patients with primary chronic angle closure glaucoma in at least one eye and compared with 42 age- and sex-matched healthy controls. Axial length and intraocular pressure, both factors known to influence pulsatile ocular blood flow, were also recorded. Pulsatile ocular blood flow findings were correlated with measures of disease progression such as cup disc ratio and Humphrey visual field indices.

**Results:** Eyes with primary chronic angle closure glaucoma with advanced visual field defects had significantly lower pulsatile ocular blood flow compared with fellow eyes with no glaucoma ( $p < 0.05$ ). Pulsatile ocular blood flow in the fellow eyes of patients with glaucoma did not differ significantly from that in healthy controls. Mean deviation had a negative correlation with pulsatile ocular blood flow. However, corrected pattern standard deviation, as well as the degree of cupping among eyes with chronic angle closure glaucoma, did not correlate with the pulsatile ocular blood flow.

**Conclusions:** Pulsatile ocular blood flow is significantly lower in eyes with primary chronic angle closure glaucoma with advanced glaucomatous defects than in fellow eyes and eyes of healthy controls, although this relationship is not evident in patients with early or moderate glaucomatous defects.

## Introduction

Clinically available methods of estimating blood flow in the retinal circulation include laser Doppler velocimetry,<sup>1</sup> fluorescein angiography,<sup>2</sup> and

the blue field entoptic technique.<sup>3</sup> Choroidal blood flow is more difficult to measure than the retinal circulation and techniques to measure it include colour Doppler ultrasonography, fundus pulsation measurement with laser interferometer, and the

pneumotonometric method of measuring pulsatile ocular blood flow (POBF).<sup>4,5</sup> Of these methods, the pneumotonographic means of measuring POBF is currently an acceptable means of deriving the pulsatile component of choroidal blood flow; the other methods primarily measure the blood velocity. Estimation of POBF is based on continuous recording of intraocular pressure (IOP) by means of a pneumotonometer that measures the pressure wave of the ocular pulsation during a cardiac cycle. This technique, described by Langham et al, derives blood flow measurements from a pressure volume relationship.<sup>6-9</sup> The pulsatile ocular blood flow is mainly determined by the choroidal circulation and the contribution of the retinal circulation is almost negligible. This is of particular relevance when studying ocular blood flow in glaucomatous eyes since the posterior ciliary arteries, which are responsible for the blood supply to the choroidal circulation, are also the main arterial supply to the anterior optic nerve.<sup>10</sup>

Primary angle closure glaucoma is relatively uncommon in the West but is considered to be the most common type of glaucoma in the world.<sup>11</sup> Population-based prevalence studies among Asians and Eskimos show that primary angle closure glaucoma makes up 80 to 90% of primary glaucomas.<sup>12</sup> With the exception of a study by Cheng et al,<sup>13</sup> there are no studies on the ocular haemodynamics of primary chronic angle closure glaucoma (PCACG). This study was therefore undertaken to investigate the POBF in eyes with PCACG and to compare them with fellow eyes and eyes of healthy controls.

## Patients and Methods

Patients with unilateral PCACG were recruited from the glaucoma clinic of the All India Institute of Medical Sciences in New Delhi. Only patients with previously documented IOPs  $>22$  mm Hg on at least



2 occasions, optic disc cupping >0.5, and visual field defects in the presence of occludable angles with at least 180° peripheral anterior synechiae were designated to have PCACG. An occludable angle was defined as one in which the pigmented trabecular meshwork was not visible throughout 270° or more of the angle circumference without indentation or manipulation.

Forty two patients in whom at least 1 eye had features of PCACG, with the other eye being an uninvolved 'fellow eye', were recruited. Other inclusion criteria were best corrected visual acuity (BCVA) of at least 20/60 or better and an IOP <22 mm Hg with topical antiglaucoma medication at the time of recording the POBF. Only patients who were experienced at visual field testing and had previous reliable visual field tests were included. Exclusion criterion were secondary angle closure glaucomas, refractive error greater than ± 2D, retinal or optic nerve pathology that could cause visual field defects, previous incisional surgery, previous laser procedures within 2 weeks, presence of concomitant systemic disease such as diabetes or hypertension, and systemic medication.

Forty two age- and sex-matched controls were selected from 135 healthy volunteers, in whom POBF was estimated. Exclusion criteria for healthy controls were those who had a family history of glaucoma, large physiological cupping, refractive error greater than ± 2D and those with hazy media.

Informed consent was given by all the participants before starting the study. After recording a detailed history, all participants underwent measurement of their blood pressure, applanation tonometry, gonioscopy, and axial length measurement. The findings were recorded in a database along with the topical medications used by patients. Automated perimetry was performed with central 30-2 full threshold

program of the Humphrey field analyser 645 (Humphrey Instruments, San Leandro, USA). The mean deviation (MD) and corrected pattern standard deviation (CPSD) of all patients were recorded and visual field defects were classified into early, moderate, and severe based on Hodapp et al's classification.<sup>14</sup>

The linear cup disc ratio was measured using the scanning laser ophthalmoscope (Heidelberg retinal tomograph II software version 1.50 ). The system automatically acquires 3-dimensional images with predetermined parameters. Images were taken by a single experienced observer at an imaging head eye distance of 10 mm. POBF was estimated using the OBF system (OBF Labs Ltd., Malmesbury, UK) by an experienced observer who was unaware of the ocular condition of the examinees. The OBF system has a pneumotonometer that transmits IOP change signals that are used to derive ocular volume changes from pressure volume relationship of the human eye.

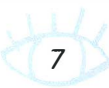
POBF is determined by calculating change in ocular volume over time. The IOP change signals are recorded over a 20-second cycle. The computer automatically selects 5 representative pulses and a record of IOP, pulse amplitude (PA), pulse volume (PV), pulse rate (PR), and POBF is obtained for both eyes. All subjects were re-examined twice more within 1 hour. Average values of the 3 recordings were taken for the analysis.

**Statistical Analysis**

Comparison of POBF values between PCACG eyes and healthy controls were performed using the unpaired students *t* test. A paired students *t* test was used to estimate whether differences between POBF values in those with early, moderate, and severe field defects were different from each other or not. Multivariate linear regression was used to examine the relation between POBF, the dependant variable and cup disc ratio, MD, and CPSD as independent variables. The mean of interocular differences of various parameters among those with bilateral PCACG, those with 1 eye with PCACG, and the fellow eyes were compared with healthy controls using paired students *t* test. The level of statistical significance was set at *p* < 0.05.

**Results**

As shown in Table 1, the age and sex distribution between the patients with PCACG and healthy controls was comparable. The mean axial length of eyes of patients with PCACG was lower than those of healthy controls (*p* = 0.04). The average IOP of patients with glaucoma was higher than, although not significantly different from, the healthy controls. The mean POBF of eyes with PCACG was 1112 ± 281 ml/minute and that of fellow eyes was 1360 ± 312 ml/minute. The overall mean POBF of the 30 patients with glaucoma (1053 ± 245 ml/minute) was lower than that of



**Table 1. Characteristics of patients with primary chronic angle closure glaucoma (PCACG) and healthy controls.**

	Patients with PCACG (n = 42)	Healthy controls (n = 42)	p Value
Age ± SD (years)	58.9 ± 9.8	58.2 ± 9.3	NS
Sex			
Male	22	24	NS
Female	20	18	NS
Axial length ± SD (mm)	21.3 ± 1.1	22.7 ± 1.2	0.04
Intraocular pressure ± SD (mm Hg)	14.4 ± 4.2	12.5 ± 3.8	NS
Pulsatile ocular blood flow ± SD (ml/min)	1053 ± 245	1325 ± 235	0.02

Abbreviations: NS = not significant.

**Table 2.** Clinical parameters of eyes of patients with primary chronic angle closure glaucoma (PCACG) versus the fellow eyes.

Visual field defect	Fellow eyes (n = 42)	Eyes with PCACG (n = 42)		
	None	Early (n = 10)	Moderate (n = 14)	Severe (n = 18)
Mean cup/disc ratio	0.31 ± 0.08	0.67 ± 0.10*	0.78 ± 0.09*	0.88 ± 0.1*
Mean intraocular pressure (mm Hg)	11.1 ± 2.8	14.8 ± 3.3	14.4 ± 3.4	14.6 ± 3.2
Mean axial length (mm)	21.4 ± 1.2	21.3 ± 1.4	21.2 ± 1.5	21.1 ± 1.2
Mean pulse rate	71.2 ± 13.4	68.3 ± 12.1	70.3 ± 11.2	66 ± 10.4
Mean pulsatile ocular blood flow (ml/min)	1360 ± 312	1298 ± 298	1134 ± 321	913 ± 286*

\* Statistically significant difference from fellow eyes; p < 0.05.

healthy controls (1325 ± 235 ml/minute) [p < 0.05]. Table 2 shows the relationship of the degree of glaucomatous field defects to the POBF. Those eyes with field defects had a higher cup disc ratio than the fellow eyes, as expected. The IOP of glaucomatous eyes was, on average, higher than the fellow eyes despite receiving medical treatment for glaucoma. However, the difference was not statistically significant. The mean axial length of eyes with PCACG and fellow eyes was comparable. Eyes with severe field defects had a significantly lower POBF compared with the fellow eyes and eyes of healthy controls. However, the POBF values in eyes with early or moderate field defects were not significantly different from the fellow eyes or those of healthy controls.

There was no statistically significant difference between the mean POBF values of the fellow eyes of patients with glaucoma (1360 ± 312 ml/minute) and the eyes of healthy controls (1325 ± 235 ml/minute). Of the 42 patients with PCACG, 30 were using timolol 0.5% twice daily and 12 were using both timolol 0.5% twice daily and pilocarpine 2% three times daily in the eye with glaucoma. All patients had undergone YAG iridotomy in both eyes, the patency of which was confirmed during examination.

There was no correlation between optic disc cupping and POBF. There was no correlation between the CPSD and POBF while there was a negative correlation with MD values (r = -0.41; p < 0.005).

Interocular differences in various parameters among patients with 1 eye with PCACG and healthy controls were analysed (Table3). The difference in IOP between the 2 eyes of patients with unilateral PCACG was significantly higher than that of the eyes of healthy controls. Interocular differences in the pulse amplitude were not significantly different between the 2 subgroups. However, pulse volume (PV) and POBF differences between the 2 eyes of patients with unilateral glaucoma were significantly higher than among the eyes of healthy controls (Table3).

### Discussion

The 2 mechanisms proposed for glaucomatous optic atrophy are direct damage to the axons caused by raised IOP<sup>15</sup> and a primary problem in the blood circulation to the optic nerve.<sup>16</sup> Several studies have reported reduced ocular blood flow in eyes with normal tension glaucoma (NTG) or high tension primary open angle glaucoma (POAG).<sup>17-21</sup> Hayreh et al experimentally proved reduced blood flow to be the primary cause of glaucomatous optic atrophy and thereby visual field damage.<sup>16</sup> Although it is not possible

to clinically measure optic nerve perfusion directly, POBF gives an indication by estimating the pulsatile component of the choroidal blood flow<sup>8,9</sup> and has been shown to give reproducible results.<sup>22,23</sup>

However, the pitfalls of using POBF are that it relies on standard ocular rigidity and that the ratio of pulsatile to non-pulsatile blood flow may change in relation to systemic blood pressure without altering the total blood flow. The factor of ocular rigidity was controlled by excluding patients who had undergone surgery and those with high refractive error and the second factor was controlled to some extent by excluding patients with systemic hypertension. Comparison of POBF values is also complicated by numerous factors such as age, sex, axial length, and IOP. It was therefore important to select age- and sex-matched individuals for this study. POBF is known to have a negative correlation with axial length.<sup>24</sup> Therefore, a lower axial length would lead to higher POBF values. Compared with healthy controls, eyes with PCACG had a lower POBF despite the fact that they had a lower mean axial length.

Eyes with chronic angle closure glaucoma with advanced field defects had a reduced ocular blood flow in comparison to the fellow eyes and eyes of healthy controls. Fellow eyes did not show significant POBF differences compared with eyes of healthy controls, which is consistent with a previous study where no circulatory changes were observed in eyes with preclinical primary angle closure glaucoma with colour Doppler sonography.<sup>25</sup> However, a study of eyes with NTG without field defects showed

**Table 3.** Interocular differences among patients with primary chronic angle closure glaucoma (PCACG) and healthy controls.

	Healthy controls (n = 42)	1 eye PCACG, (n = 42)
Intraocular pressure (mm Hg)	1.80 ± 1.10	3.2 ± 1.60*
Pulse amplitude (mm Hg)	0.40 ± 0.21	0.42 ± 0.24
Pulse volume (ml)	1.10 ± 0.60	1.65 ± 1.10*
Pulsatile ocular blood flow (ml/min)	140 ± 97	270 ± 132*

\* Statistically significant difference between primary chronic angle closure glaucoma and healthy controls; p < 0.05.

that they had reduced blood flow compared with healthy controls.<sup>17</sup> One of the proposed mechanisms is an inherent abnormality in autoregulation of choroidal blood flow in reply to raised IOP in eyes with NTG.<sup>26</sup> Circulatory abnormalities have been documented on laser Doppler flowmetry even in patients with suspected primary open angle glaucoma without field defects.<sup>27</sup> It is unlikely that primary circulatory abnormalities are causing optic atrophy in the eyes of patients with chronic angle closure glaucoma since eyes with early field defects and glaucomatous cupping did not show a significant POBF reduction. In fact, even eyes with moderate field defects did not have a significant difference in POBF compared with those of healthy controls in this study.

Intraocular pressure is an important lateralising factor in glaucomatous eyes and the IOPs of eyes with chronic angle closure glaucoma was higher compared with those of fellow eyes despite receiving antiglaucoma treatment, although this was not statistically significant. Higher IOP has been found to be the cause of asymmetry in patients with asymmetric primary open angle glaucoma<sup>28</sup> and NTG.<sup>17</sup> The possibility that raised IOP over a period of time impairs the autoregulation of choroidal blood flow or permanently impairs the vascular supply of the optic nerve could explain the lower blood flow in eyes with PCACG with advanced glaucoma.

The effect of topical antiglaucoma medication on ocular haemodynamics has been a subject of much research recently. Baxter et al studied the effect of timolol 0.5% on the ophthalmic artery and concluded that this medication does not affect the blood circulation.<sup>29</sup> Other studies employing tonographic methods of estimating blood flow also did not show any effect of timolol 0.5% on POBF in healthy individuals and patients with glaucoma.<sup>30-31</sup> Pilocarpine was found to have no effect on POBF after 1 week

of therapy when administered alone or in combination with timolol.<sup>32</sup> However, it was found to increase POBF in patients with uncontrolled ocular hypertension when POBF was measured 90 minutes after pilocarpine administration.<sup>33</sup> This was probably due to its effect of decreasing IOP. Thus, we do not believe POBF values were affected by the medication being taken by these patients on a long term basis.

## Conclusion

To date, there is no method of clinically measuring optic nerve perfusion directly. Moreover, there is no gold standard on which to compare these findings of choroidal blood flow. Hence, to attempt to prove whether ocular blood flow reduction is a cause or a consequence in eyes with PCACG can only be presumptuous and beyond the scope of this study. However, the fact that POBF remains normal in fellow eyes and is not found to be significantly affected in eyes with moderate field defects, indicates that it may not be the primary cause of glaucomatous optic atrophy in eyes with PCACG.

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# Ultrasound Biomicroscopy in the Diagnosis and Management of Cyclodialysis Cleft: Case Report and Review of the Literature

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## Introduction

Cyclodialysis clefts result from disinsertion of the longitudinal ciliary muscle fibres, separating the ciliary body from the scleral spur and underlying sclera, allowing direct communication between the anterior chamber and ciliochoroidal space and unrestricted bulk flow of aqueous from the anterior chamber to the supraciliary space. Cyclodialysis may be caused accidentally by trauma, iatrogenically during intraocular surgery, or intentionally for the treatment of glaucoma. Although the diagnosis can often be made by gonioscopy, clefts may be difficult to detect in recently traumatised or operated eyes because of hazy media, hypotony, shallow

anterior chamber, or abnormal anterior segment architecture. The anatomic location of the pathology relative to the other structures of the eye as well as the inherent limitations of the instrument utilised may also prevent direct visualisation. Accurate diagnosis is necessary for appropriate management of hypotony, particularly when associated with decreased vision (Table 1). When direct visualisation of the cleft is difficult or impossible, ultrasound biomicroscopy (UBM) is a valuable tool for identifying and localising the cleft.

Treatment directed at reversing the hypotony aims to either close the cleft or wall it off. We report a case of ocular hypotony secondary to a cyclodialysis cleft that was successfully managed with the aid of

UBM and review the literature on diagnosis and management of cyclodialysis clefts.

## Case Report

A 10-year-old boy was struck in the left eye by a stick. On examination, visual acuity was 20/20 OD and counting fingers OS. Examination of the right eye was unremarkable. Slit lamp examination of the left eye revealed a hyphaema, sphincter tear, iridodialysis, and intraocular pressure (IOP) of 2 mm Hg. Steroid and cycloplegic drops were started. After 2 days, the hyphaema had cleared and the lens was clear. Indirect ophthalmoscopy revealed a vitreous haemorrhage and commotio retinae. One week later, vision had improved to 20/60, IOP was 18 mm Hg, and gonioscopy showed a 360° angle recession. After 1 month, the patient suffered a second episode of blunt trauma with a tennis ball in the same eye. A retinal dialysis was treated successfully with laser photocoagulation. There was persistent hypotony, however, and he was referred to The New York Eye and Ear Infirmary for further evaluation and management.

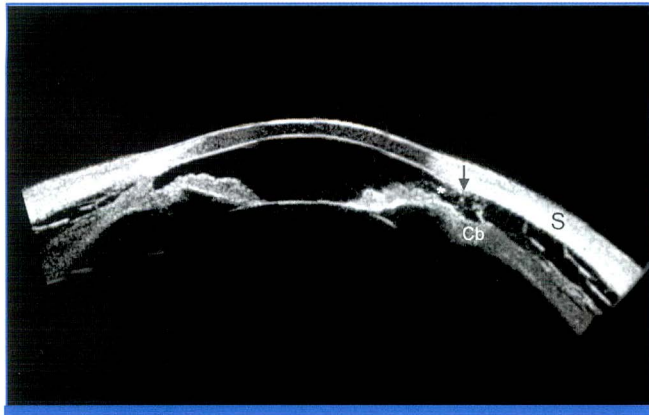
On examination, pinhole visual acuity OS was 20/100 and IOP was 2 mm Hg by applanation tonometry. The cornea was clear and the anterior chamber was deep with 2+ cells and flare. Gonioscopy identified a cyclodialysis cleft at the 3 o'clock to 4 o'clock position and a 360° angle recession. Ultrasound biomicroscopy confirmed gonioscopic findings and identified a 360° ciliochoroidal detachment (Figure 1). Indirect ophthalmoscopy showed the presence of temporal laser scars and macular folds, but no retinal detachment. The cyclodialysis cleft was repaired surgically with a modified Demeler procedure.<sup>1-3</sup> The postoperative course was unremarkable. Ultrasound biomicroscopy showed closure of the cleft (Figure 2). The IOP returned to normal values and vision slowly improved to 20/30.



Table 1. Aetiology of ocular hypotony.

Post-trauma	Postoperative	Bilateral	Miscellaneous
1. Iridocyclitis	1. Wound leak	1. Osmotic dehydration	1. Vascular occlusive disease
2. Retinal detachment	2. Overfiltration	a. Diabetic coma	a. Carotid occlusion
3. Cyclodialysis cleft	3. Iridocyclitis	b. Uraemia	b. Temporal arteritis
4. Scleral rupture	4. Retinal detachment	2. Myotonic dystrophy	c. Central retinal artery or vein occlusion
5. Ciliochoroidal detachment	5. Cyclodialysis		2. Pre-phthisis
	6. Scleral perforation		

**Figure 1.** Ultrasound biomicroscopy of a cyclodialysis cleft from 9 o'clock to 3 o'clock showing separation of the ciliary body (Cb) from the scleral spur (arrow) and the underlying sclera (S). Also shown is the open communication between the anterior chamber and the supraciliary space.



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## Discussion

In 1900, Fuchs recognised the correlation between cyclodialysis and ocular hypotony.<sup>4</sup> Bulk flow of aqueous humor into the supraciliary space and reduced aqueous production may result in chronic hypotony, shallow anterior chamber, choroidal effusion, induced hyperopia, cataract, hypotony maculopathy, and reduced vision.<sup>5</sup> Ocular hypotony can ensue even when the extent of a cyclodialysis cleft is minimal.<sup>6</sup> Cyclodialysis most commonly occurs following blunt ocular trauma, but may also occur after penetrating trauma or inadvertently during surgery involving iris manipulation.<sup>7</sup> Intentional surgical cyclodialysis was first

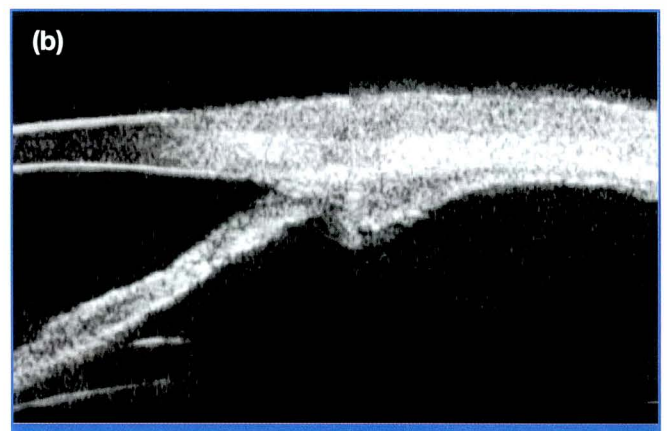
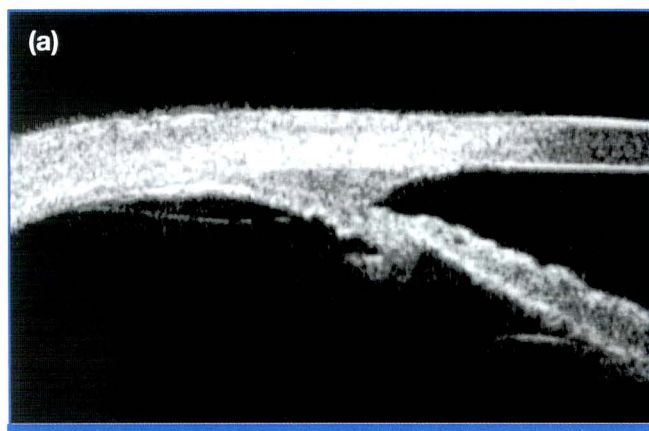
reported by Heine in 1905 and became one of the most popular operations for glaucoma,<sup>8</sup> but fell into disfavour because of unpredictable results with a high rate of intraoperative haemorrhage and the development of phthisis. Careful gonioscopic examination of the anterior chamber angle is an important element in the diagnosis of iatrogenic or traumatic cyclodialysis clefts. The displacement of aqueous into the angle recess during indentation gonioscopy can aid in exposing clefts when the peripheral anterior chamber is flat. However, associated pronounced anterior chamber shallowing may obscure the gonioscopic view of the chamber angle and cleft. Hazy media or abnormal anterior segment architecture can prevent or limit adequate visualisation during gonioscopy.

In the past, invasive techniques have been described to help in localising cyclodialysis clefts. Chandler and Maumenee obtained ciliochoroidal fluid through a scleral incision behind the limbus and

retrieved fluorescein injected into the anterior chamber.<sup>6</sup> Anterior chamber filling with balanced salt solution was shown to increase IOP, deepen the chamber, and allow a better gonioscopic examination during surgery.<sup>9</sup> Viscoelastics may be used to reform the anterior chamber.<sup>7,10,11</sup>

Ultrasound biomicroscopy (Paradigm Medical Industries, Inc., Salt Lake City, Utah) is a useful, non-invasive method for differentiating cyclodialysis, angle recession, and ciliary body detachment.<sup>12</sup> Operating at frequencies of 50 MHz, UBM can achieve a tissue resolution of approximately 50  $\mu\text{m}$  and a tissue penetration of 5 mm. The UBM appearance of cyclodialysis typically shows disinsertion of the ciliary body from the scleral spur with posterior displacement of the ciliary body and iris. UBM permits imaging of a cyclodialysis cleft along its entire longitudinal and circumferential extent, with an accurate assessment of its location and size, regardless of gonioscopic visibility or patent cleft aperture.<sup>13,14</sup> While gonioscopy allows evaluation only from the anterior face of the ciliary cleft, UBM provides cross sectional information of the iridocorneal angle. Moreover, UBM can easily image a cyclodialysis when a direct communication between the anterior chamber and supraciliary space is present because of contrasting reflectivities of the aqueous and adjacent tissue.

**Figure 2.** Postoperative ultrasound biomicroscopy of a repaired cyclodialysis cleft showing close approximation of the ciliary body and the sclera. No residual clefts are detected. (a) 9 o'clock; (b) 3 o'clock.



In 1994, Karwatowski and Weinreb reported the UBM features of inadvertent postoperative cyclodialysis cleft following cataract surgery with posterior chamber intraocular lens implantation through a scleral tunnel incision.<sup>15</sup> Gentile et al found that UBM successfully diagnosed traumatic cyclodialyses not evident on clinical examination in 6 eyes.<sup>13</sup> Berenstein et al confirmed that UBM is safe and effective for the clinical assessment and management of ocular trauma.<sup>12</sup> These authors clearly imaged eyes with angle recession, iridodialysis, cyclodialysis, hyphaema, intraocular foreign body, scleral laceration, and subluxed lens. However, when there is strong clinical suspicion of globe rupture or high risk of infection, UBM is not recommended.<sup>12</sup> Other recent studies have confirmed the effective use of UBM for cyclodialysis clefts in different situations: after ball bullet injury,<sup>16</sup> after air bag injury,<sup>17</sup> after surgical cyclodialysis,<sup>18,19</sup> and after trabeculectomy.<sup>20</sup>

Other non-invasive techniques for diagnosing cyclodialysis clefts have been suggested. Magnetic resonance imaging has been reported, but the inconvenience and risk associated with intravenous injection of gadolinium and the fact that acute inflammation could lead to leakage of the contrast limits this methodology.<sup>21</sup> Jewelewicz et al described a method to localise the extent of a cyclodialysis cleft with scleral transillumination.<sup>22</sup> It is rapid, requires minimal equipment, and can be used during slit lamp examination or intraoperatively. Others have detected large clefts with conventional and immersion B-scan ultrasonography,<sup>23</sup> but the assessment was based on a high index of clinical suspicion and an idea of the possible site of the lesion by gonioscopy.

Authoritative experience in the management of hypotony caused by cyclodialysis clefts is difficult to obtain because of their rarity.<sup>7</sup> Numerous surgical procedures have been proposed to close cyclodialysis clefts. Vannas and Björkenheim placed a suture

through the cleft and ciliary body, anchoring it anatomically to the sclera.<sup>24</sup> Chandler and Maumenee proposed walling off the cleft with the application of penetrating diathermy lesions to the sclera in the area surrounding it.<sup>6</sup> Following diathermy, drainage of the suprachoroidal fluid would allow anatomic reattachment of the ciliary body and subsequent restoration of normal aqueous production and drainage dynamics. Maumenee and Stark described a method involving the injection of a dilute solution of fluorescein and balanced salt solution into the anterior chamber, followed by sclerotomy and drainage of the suprachoroidal fluid with recovery of the fluorescein, proving the connection between the anterior chamber and the suprachoroidal space.<sup>9</sup> After that, penetrating diathermy in an arc surrounding the area of the cyclodialysis cleft was done. Portney and Purcell used an anteriorly placed silicone sponge buckle for reattachment of the ciliary body and closure of the cleft.<sup>25</sup> Sugar reported surgical incarceration of the iris and of ciliary body in a limbal incision.<sup>26</sup>

Non-invasive use of argon laser photocoagulation has been described by Joondeph<sup>27</sup> and Harbin.<sup>28</sup> Partamian suggested using a Zeiss 4-mirror gonioscopy lens in the presence of a shallow anterior chamber for better exposure of the cleft during laser application.<sup>10</sup> Ormerod et al reported good results with the adjunctive use of intracameral sodium hyaluronate in patients in whom adequate gonioscopy during a laser procedure was prevented by shallowing of the anterior chamber.<sup>29</sup> The power recommended for laser treatment was 2 to 3 W to sclera to generate gas-bubble formation, and 1 W to the uveal surface of the cleft to cause marked blanching at the burn site. Brooks et al used transcleral Nd:YAG laser cyclophotocoagulation for traumatic cyclodialysis.<sup>30</sup> One report demonstrated a good result with contact transcleral diode laser therapy.<sup>31</sup>

An ophthalmic laser microendoscope was suggested for treatment of cyclodialysis cleft,<sup>32</sup> but the risks of this procedure involve cataract formation and trauma to the iris and angle structures.<sup>33</sup> Another method with cryotherapy alone was not successful in closing the cleft.<sup>34</sup> Pars plana vitrectomy, gas tamponade, and cryotherapy was also reported, but its indication is limited to patients with additional posterior segment problems.<sup>35</sup> Some authors agree that for patients with traumatic cyclodialysis of less than 3 clock hours of the circumference, non-invasive methods should be attempted first,<sup>36</sup> but for greater than this size their value is limited and direct surgical reattachment is required.<sup>35,37</sup>

Different suture techniques have been proposed for refixation of the ciliary body to the sclera. Techniques of directly suturing the ciliary body to the scleral spur were first described by Hager<sup>38</sup> and Mackensen and Custodis,<sup>39</sup> who performed a full-thickness scleral incision and directly sutured the ciliary body to the scleral spur, and by Best and Hartwig,<sup>40</sup> who prepared 2 scleral flaps over the detached ciliary body and directly reattached the disinserted ciliary muscle to the scleral spur. Naumann and Volcker<sup>41</sup> dissected a scleral lamella over the area of the cleft. After the dissection, an incision was made in the bed of the flap behind and parallel to the scleral spur and the ciliary muscle directly sutured to the scleral spur using 10-0 nylon sutures. Success was achieved in all 27 patients who underwent this procedure.<sup>42</sup> The disadvantage of this technique occurs when dealing with large clefts, requiring large scleral dissection, which could affect the vascular supply to the anterior segment.<sup>35</sup> Demeler reported good results in 10 eyes with direct refixation of the ciliary muscle to the scleral spur with many 10.0 nylon sutures placed close to each other.<sup>2</sup> Wiechens and Rochels described a technique to circumferentially refixate the ciliary body ab interno as an

alternative method in aphakic or pseudo-phakic eyes.<sup>43</sup> Most authors agree that for the first 6 weeks, a medical approach with the use of topical cycloplegic therapy with atropine to relax the ciliary body, allowing it to reappose to the sclera, and promote spontaneous healing of the cleft is required.<sup>7,35</sup> Avoidance of corticosteroids is also indicated in an attempt to promote spontaneous cleft closure.<sup>29</sup> After that time, spontaneous closure of the cleft is unlikely. Surgical intervention is not required if a hypotonous globe with a cleft without retinopathy is present. The presence of hypotonous maculopathy with disc oedema, macular folds, choroidal detachment, or corneal oedema associated with worsening of vision requires treatment. A delay in intervention may cause irreversible damage. Ormerod et al invariably observed visual recovery when the hypotony was reversed, even after several years duration, but the data suggested that early correction achieved the best results.<sup>7</sup>

As in any surgical procedure, post-surgical follow up is as important as the preoperative assessment and the surgical procedure itself. In these instances, UBM may be used to assess closure of the cyclodialysis cleft as well as to detect the presence of any residual clefts. After successful closure or consolidation of hypotonous cyclodialysis clefts, a self-limited episode of ocular hypertension is common in the early postoperative period.<sup>7</sup> Patients with post-traumatic cyclodialysis clefts are likely to have considerable damage to the iridocorneal angle and this will likely remain after closure of the cleft.<sup>30</sup> Intraocular pressure must then be regularly monitored.

## Acknowledgement

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## SEAGIG 2002 — Glaucoma: Global & Southeast Asian Perspectives 2nd Biennial Meeting of the South East Asian Glaucoma Interest Group (SEAGIG)

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# World Health Organization Project to Prevent Blindness in Children

Every minute, 1 child goes blind somewhere in the world. Half of these cases could be avoided, meaning that it is possible to save 250,000 children from darkness every year. The World Health Organization (WHO) has announced the launch of a project for the prevention of blindness in children. The project is financially supported by the Lions Clubs International Foundation, under the auspices of its Lions SightFirst Programme. Lions US\$3.75 million donation represents a major first step towards achieving the global elimination of avoidable blindness in children

Of the half million children who go blind every year, 3 in 5 die either from the causes that led to blindness or from other deprivations. An estimated 1.5 million children currently live with blindness. In terms of

absolute numbers, visual loss in the older population takes a heavier toll. However, in terms of 'years of blindness', the burden of blindness in childhood is only second to that from cataract, which is the most important cause of global blindness.

Blindness and severe visual impairment have far reaching social, economic, and personal implications. When it occurs in children, it also poses serious barriers to the development of the child at a formative stage. Primary health care approaches such as immunisation against measles and rubella, better nutrition, especially with regard to vitamin A, timely prophylaxis against eye infections in the new-born from diseases such as gonococcal infection, and the avoidance of harmful eye medicines, could all contribute to minimising childhood blindness.

Surgical interventions are necessary for conditions such as cataract, corneal opacities and glaucoma in childhood. Besides specialised training needed to equip surgeons to treat these conditions, early detection and increased access to treatment are essential to prevent irreparable damage to the eyes of children. The correction of refractive errors and the provision of low vision care are additional activities to be addressed. Teamwork at all levels becomes a key element for success.

The 5-year project will focus on training of health personnel for prevention, early detection, and treatment in 30 countries in WHO regions. It will also establish child friendly 'Centres for Sight of Children' in these countries. While the project will be executed by the WHO, member governments, members of the Lions Clubs International at all levels, and other non-governmental organisations, will participate in project activities.

Source: Press Release WHO/48.18 June 2002.

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## Abstracts of Asian research published in the international literature

### **National Blindness and Low Vision Prevalence Survey of Bangladesh**



This paper describes the research design and eye examination protocol of The National Blindness and Low Vision Prevalence Survey of Bangladesh and presents the main results of the rural pilot study. A thorough description of the sampling strategy, eye examination protocol, and operational definitions are presented.

Multi-stage stratified (rural/urban) cluster random sampling, with probability proportional-to-size procedures, will be used for selection of a cross-sectional, nationally representative sample (12,900 subjects) of the population.

Each individual will be tested for visual acuity, auto-refracted and undergo optic disc examination. Those with <6/12 visual acuity in either eye will be re-tested with their refractive correction, dilated and examined for anterior and posterior segment disease. A preliminary, separate rural pilot survey sample was conducted according to the eye examination procedures.

204 of 279 eligible participants (73.1%) were examined for the rural pilot study. Forty eight persons had presenting visual acuity worse than 6/12 in either eye. Cataract was the main cause of visual acuity of less than 6/12, followed by refractive error, and age-related macular degeneration.

The pilot survey demonstrated that the proposed examination process for the main survey was both feasible and appropriate for the purposes of this study. The pilot study reveals the burden of cataract and refractive error, which are 2 of the 5 diseases specifically targeted by the WHO global blindness initiative 'Vision 2020'.

Bourne RR, Dineen B, Modasser Ali S, et al.

The National Blindness and Low Vision Prevalence Survey of Bangladesh: research design, eye examination methodology and results of the pilot study. *Ophthalmic Epidemiol* 2002;9:119-132.

### **Novel Mutations Causing Familial Primary Congenital Glaucoma in India**



To determine the possible molecular genetic defect underlying primary congenital glaucoma (PCG) in India and to identify the pathogenic mutations causing this childhood blindness 22 members of 5 clinically well-characterised consanguineous families were studied. The primary candidate gene CYP1B1 was amplified from genomic DNA, sequenced, and analysed in control subjects and patients to identify the disease-causing mutations.

Five distinct mutations were identified in the coding region of CYP1B1 in 8 patients of 5 PCG-affected families, of which 3 mutations are novel. These include a novel homozygous frameshift, compound heterozygous missense, and other known mutations. One family showed pseudodominance, whereas others were autosomal recessive with full penetrance.

In contrast to all known CYP1B1 mutations, the newly identified frameshift is of special significance, because all functional motifs are missing. This, therefore, represents a rare example of a natural functional CYP1B1 knockout, resulting in a null allele (both patients are blind).

The molecular mechanism leading to the development of PCG is unknown. Because CYP1B1 knockout mice did not show a glaucoma phenotype, the functional knockout identified in this study has important implications in elucidating the pathogenesis

of PCG. Further understanding of how this molecular defect leads to PCG could influence the development of specific therapies. This is the first study to describe the molecular basis of PCG from the Indian subcontinent and has profound and multiple clinical implications in diagnosis, genetic counselling, genotype-phenotype correlations, and prognosis. Hence, it is a step forward in preventing this devastating childhood blindness.

Panicker SG, Reddy AB, Mandal AK, et al. Identification of novel mutations causing familial primary congenital glaucoma in Indian pedigrees. *Invest Ophthalmol Vis Sci* 2002;43:1358-1366.

### **Differential Occurrence of Mutations in Eye Diseases in Hong Kong**



Ethnic differences and geographic variations affect the frequencies and nature of human mutations. In the literature, descriptions of causative mutations of eye diseases in the Chinese population are few. In this paper, an attempt was made to reveal molecular information on genetic eye diseases involving Chinese patients from published and unpublished works. Studies of candidate genes of eye diseases in the Chinese population in Hong Kong include MYOC and TISR for primary open angle glaucoma, RHO and RP1 for retinitis pigmentosa, ABCA4 and APOE for age-related macular degeneration, RB1 for retinoblastoma, APC for familial adenomatous polyposis with congenital hypertrophy of retinal pigment epithelium, BIGH3/TGFBI for corneal dystrophies, PAX6 for aniridia and Reiger syndrome, CRYAA and CRYBB2 for cataracts, and mtDNA for Leber hereditary optic neuropathy.

Novel mutations have been revealed in most of these genes, and in RHO, RP1, RB1, BIGH3, and PAX6 mutations that contribute to better understanding of the functions and properties of the respective gene products

have been reported. Absence of MYOC does not necessarily cause glaucoma. No disease causative mutations have been identified in MYOC or ABCA4. There are similarities in the patterns of sequence alterations and phenotype-genotype associations in comparison with other ethnic groups, while the MYOC, RB1, APC, and PAX6 genes have more Chinese-specific sequence alterations. Establishment of a mutation database specific for the Chinese population is essential for identification of genetic markers with diagnostic, prognostic, or pharmacological values.

Pang CP, Lam DS. Differential occurrence of mutations causative of eye diseases in the Chinese population. *Hum Mutat* 2002;19:189-208.

## Population-based Eye Survey in South India

The survey was performed to assess the prevalence of vision impairment, blindness, and cataract surgery and to evaluate visual acuity outcomes after cataract surgery in a South Indian population. Cluster sampling was used to randomly select a cross sectional sample of people aged  $\geq 50$  years living in the Tirunelveli district of south India. Eligible subjects in 28 clusters were enumerated through a door-to-door household survey. Visual acuity measurements and ocular examinations were performed at a selected site within each of the clusters. The principal cause of visual impairment was identified for eyes with presenting visual acuity  $< 6/18$ . Independent replicate testing for quality assurance monitoring was performed for subjects with reduced vision and in a sample of those with normal vision for 6 of the study clusters.

5795 people in 3986 households were enumerated and 5411 (93.37%) were examined. The prevalence of presenting and best corrected visual acuity  $\geq 6/18$  in both eyes was 59.4% and 75.7%, respectively. Presenting vision  $< 6/60$  in both eyes (the

definition of blindness in India) was found in 11.0%, and in 4.6% with best correction. Presenting blindness was associated with older age, female sex, and illiteracy. Cataract was the principal cause of blindness in at least one eye in 70.6% of blind people. The prevalence of cataract surgery was 11.8% — with an estimated 56.5% of the cataract blind already operated on. Surgical coverage was inversely associated with illiteracy and with female sex in rural areas. Within the cataract operated sample, 31.7% had presenting visual acuity  $\geq 6/18$  in both eyes and 11.8% were  $< 6/60$ ; 40% were bilaterally operated on, with 63% pseudophakic. Presenting vision was  $< 6/60$  in 40.7% of aphakic eyes and in 5.1% of pseudophakic eyes; with best correction the percentages were 17.6% and 3.7%, respectively. Refractive error, including uncorrected aphakia, was the main cause of visual impairment in cataract operated eyes. Vision  $< 6/18$  was associated with cataract surgery in government, as opposed to that in non-governmental/private facilities. Age, sex, literacy, and area of residence were not predictors of visual outcomes.

Treatable blindness, particularly that associated with cataract and refractive error, remains a significant problem among older adults in south Indian populations, especially in females, the illiterate, and those living in rural areas. Further study is needed to better understand why a significant proportion of the cataract blind are not taking advantage of free of charge eye care services offered by the Aravind Eye Hospital and others in the district. While continuing to increase cataract surgical volume to reduce blindness, emphasis must also be placed on improving postoperative visual acuity outcomes.

Nirmalan PK, Thulasiraj RD, Maneksha V, et al. A population based eye survey of older adults in Tirunelveli district of south India: blindness, cataract surgery, and visual outcomes. *Br J Ophthalmol* 2002 May;86(5):505-512.

## Visual Function After Cataract Surgery in Singapore

A study was performed at the Singapore National Eye Center to identify the predictors of visual outcomes (visual acuity and visual function) in cataract surgery patients in Singapore and compare the visual outcomes of phaco-emulsification and extracapsular cataract extraction (ECCE). The visual function was measured by the VF-14 and visual acuity in the operated and the better eye in 460 systematically sampled cataract surgery patients preoperatively and 3 months after surgery. Several patient- and surgery-related predictive factors were recorded.

After cataract surgery, 85.1% of patients reported improved visual acuity in the operated eye and 77.6% reported improved visual function. Patients with poorer visual acuity and visual function at baseline reported greater improvements in visual acuity and visual function. Patients who had phaco-emulsification had better final visual function ( $p = 0.006$ ) and better final visual acuity ( $p < 0.001$ ) scores. In multiple linear regression models, final visual function was better in patients without pre-existing eye disease and with better baseline visual function, and final visual acuity in the operated eye was better in patients who were younger, were better educated, had no pre-existing conditions or postoperative complications, and had a better baseline visual acuity.

Patients with poorer baseline visual acuity or who had no pre-existing eye disease reported more improvement in visual acuity in the operated eye. Several factors including no pre-existing eye disease were associated with better final visual acuity and visual function scores.

Saw SM, Tseng P, Chan WK, et al. Visual function and outcomes after cataract surgery in a Singapore population. *J Cataract Refract Surg* 2002;28:445-453.

## Moderate Visual Impairment in India

The aim of this study was to assess the prevalence and demographic associations of moderate visual impairment in the population of the southern Indian state of Andhra Pradesh. 11,786 people of all ages were sampled using a stratified, random, cluster, systematic sampling strategy from 94 clusters in 1 urban and 3 rural areas of Andhra Pradesh. The eligible people were invited for interview and detailed dilated eye examination by trained professionals. Moderate visual impairment was defined as presenting distance visual acuity less than 6/18 to 6/60 or equivalent visual field loss in the better eye.

Of those people in the sample, 10,293 (87.3%) participated in the study. In addition to the previously reported 1.84% prevalence of blindness (presenting distance visual acuity <6/60 or central visual field <20° in the better eye) in this sample, 1237 people had moderate visual impairment, an adjusted prevalence of 8.09% (95% confidence interval, 6.89-9.30%). The majority of this moderate visual impairment was caused by refractive error (45.8%) and cataract (39.9%). Increasing age, female sex, decreasing socioeconomic status, and rural area of residence had the highest odds of being associated with moderate visual impairment.

These data suggest that there is a significant burden of moderate visual impairment in this population in addition to blindness. Extrapolation of these data to the population of India suggests that there were 82 million people with moderate visual impairment in the year 2000, and this number is likely to be 139 million by the year 2020 if the current trend continues. This impending large burden of moderate visual impairment, the majority of which is due to relatively easily treatable refractive error and cataract, would have to be taken into account while estimating the eye care needs in India, in addition to dealing with blindness. Specific

strategies targeting the elderly population, people with low socioeconomic status, those living in the rural areas, and females would have to be implemented in the long term to reduce moderate visual impairment.

Dandona R, Dandona L, Srinivas M, et al. Moderate visual impairment in India: the Andhra Pradesh Eye Disease Study. *Br J Ophthalmol* 2002;**86**:373-377.

## Age-related Macular Degeneration: What's New?

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in the developed western world, accounting for approximately 50% of all cases of registered blindness. The rising prevalence of this disease in Asia seems to parallel the same trend in the developed world. Because of the socio-economic impact of this disorder, much attention has been paid to elucidating the underlying pathogenic mechanisms, as well as seeking alternative forms of treatment. This review discusses the latest advances in AMD diagnosis, treatment, and prophylaxis. A Medline search with emphasis on randomised controlled clinical trials and large case-control series was performed. Only articles cited in Index Medicus were included in the review.

Recent advances in the diagnosis and treatment of AMD include conventional argon laser photocoagulation, photodynamic therapy (PDT), radiation therapy, surgical options, and gene therapy. The introduction of new modalities such as PDT has revolutionised the approach to treatment. However, there has been no breakthrough in achieving satisfactory outcomes with the available techniques for treating occult neovascular lesions.

As results of large prospective randomised clinical trials evaluating new treatment alternatives become available, a treatment algorithm for neovascular

AMD will emerge that best minimises visual loss and may even result in visual improvement.

Koh AH, Ang CL. Age-related macular degeneration: what's new. *Ann Acad Med Singapore* 2002;**31**:399-404.

## Near-work Activity, Night-lights, and Myopia in the Singapore-China Study

This study was performed to investigate the relationship among near-work activity, night-lights, and myopia in schoolchildren in Singapore and Xiamen, China. The refractive error and ocular dimensions of 957 Chinese schoolchildren aged 7 to 9 years in Singapore and Xiamen were determined using cycloplegic autorefractometry and A-scan ultrasound biometry. Information on near-work activity (number of books read per week, reading in hours per day) and night-light use before the age of 2 years was obtained.

The prevalence rate of myopia was 36.7% (95% confidence interval [CI], 33.0%-40.3%) in Singapore and 18.5% (95% CI, 14.0%-23.1%) in Xiamen. The crude odds ratio (OR) of higher myopia (at least -3.0 diopters) for children who read more than 2 books per week was 3.50 (95% CI, 2.15-5.70). In a multivariate logistic regression model, the OR of higher myopia for children who read more was 2.81 (95% CI, 1.69-4.69), adjusted for age, night-light use, parental myopia, and country, whereas there was no association between night-light use before the age of 2 years and higher myopia (OR, 1.54; 95% CI, 0.92-2.58), after controlling for age, books read per week, parental myopia, and country. Reading may be associated with higher myopia in Chinese schoolchildren. However, night-light use does not seem to be related to higher myopia.

Saw SM, Zhang MZ, Hong RZ, et al. Near-work activity, night-lights, and myopia in the Singapore-China study. *Arch Ophthalmol* 2002;**120**: 620-627.



## AUGUST

3-5

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### United Kingdom and Ireland Society of Cataract and Refractive Surgeons Annual Meeting

Chester, England, UK

Contact: United Kingdom and Ireland Society of Cataract and Refractive Surgeons Secretariat, c/o ENTER, North Riding Infirmary, Newport Road, Middlesbrough, TS1 5JE, UK

Tel: (44 164) 285 4054

Fax: (44 164) 223 1154

E-mail: ukiscrs@oxynet.co.uk

27-28

### SEAGIG 2002 — Glaucoma: Global & Southeast Asian Perspectives 2nd Biennial Meeting of the South East Asian Glaucoma Interest Group Manila, The Philippines

Contact: The South East Asian Glaucoma Interest Group Manila Secretariat, c/o OmniEssence Company, Suite 1014 Shaw Tower, Shaw Blvd, Corner St Francis Street, Greenhills East, Mandaluyong City 1550, The Philippines

Tel: (632) 636 7655

Fax: (632) 636 7656

E-mail: OmniEssence@usa.net

29-2 October

### The 20th Annual Vitreous Society Meeting and the 35th Annual Retina Society Meeting

San Francisco, CA, USA

Contact: Medical Conference Planners, Inc, 1251 Post Road, Scarsdale, NY 10583, USA

Tel: (1 914) 722 0664

Fax: (1 914) 722 0465

E-mail: medconfs@aol.com

## OCTOBER

6-11

### 15th Congress of the International Society for Eye Research Geneva, Switzerland

Contact: Kenes International, 17 Rue du Cendrier, P.O. Box 1726, CH - 2111 Geneva 1, Switzerland

Tel: (41 22) 908 0488

Fax: (44 845) 127 5678

E-mail: icer@kenes.com

20-24

### Annual Meeting of the American Academy of Ophthalmology Orlando, Florida, USA

Contact: American Academy of Ophthalmology

Tel: (1 415) 561 8500

Fax: (1 415) 561 8533

E-mail: meetings@aaoo.org

26-27

### Update in Neuro-ophthalmology Chennai, Tamil Nadu, India

Contact: Dr Satya Karna

Tel: (91 44) 827 1616

Fax: (91 44) 825 4180

E-mail: neurocme@lycos.com

27-30

### Bascom Palmer Eye Institute XXIV International American Course in Clinical Ophthalmology Miami, FL, USA

Contact: Rosa Bondar

Tel: (1 305) 326 6110

Fax: (1 305) 326 6417

E-mail: rbondar@bpei.med.miami.edu

## NOVEMBER

14-16

### Australasian Society of Cataract and Refractive Surgeons 2002 Congress

Canberra, Australia

Contact: Jenny Boden

Tel: (61 3) 5977 0240

Fax: (61 3) 5977 0260

17-21

### 34th Annual Scientific Congress of the Royal Australia & New Zealand College of Ophthalmologists

Canberra, Australia

Contact: Congress Organizer

Tel: (61 2) 9690 1001

## MARCH 2003

19-23

### 4th International Glaucoma Symposium Barcelona, Spain

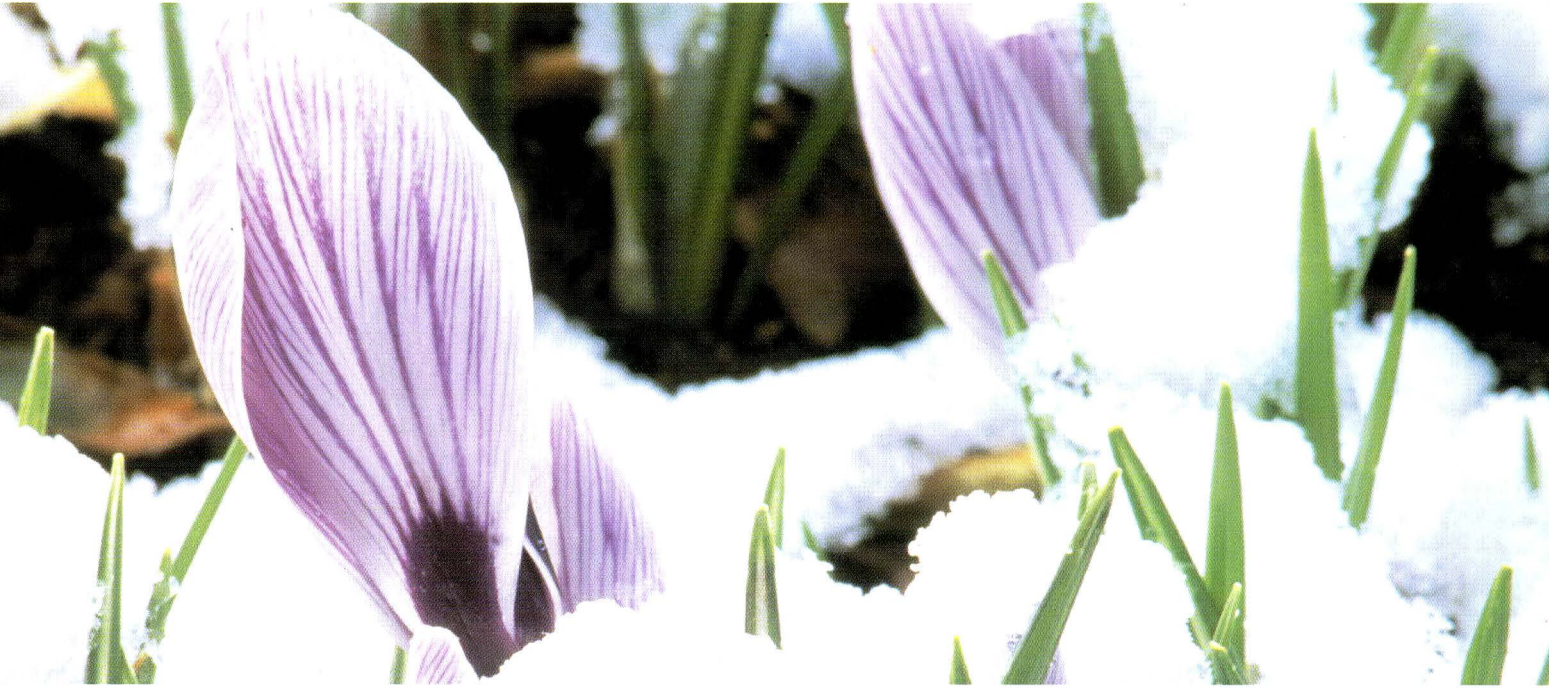
Contact: Kenes International, PO Box 1726, CH-1211 Geneva 1, Switzerland

Tel: (41 22) 908 0488

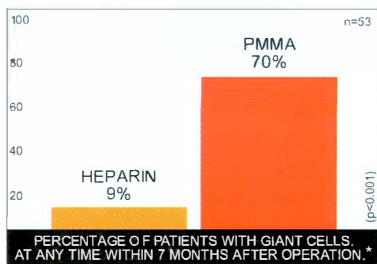
Fax: (44 845) 127 5687

E-mail: glaucoma@kenes.com

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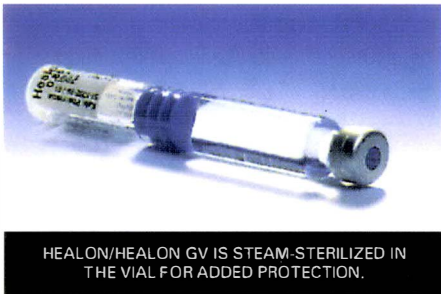
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