RECENT ADVANCES IN GLAUCOMA MANAGEMENT

Dr VKY Yong, Dr PTK Chew

INTRODUCTION

Definition

Glaucoma describes a group of heterogenous disorders in which progressive damage to the optic nerve head and loss of visual field are usually associated with increased intraocular pressure (IOP).

Prevalence

In Singapore, the age-standardised prevalence of glaucoma is 3.2% in the 40 years and older population. In a study by Foster *et al,* primary open angle glaucoma (POAG) was 1.6 times more common than primary acute angle closure glaucoma (PACG). Looking at glaucoma-related blindness, PACG constituted 50% of the cases and POAG constituted 27%[1]. PACG is more common locally than in the Caucasian population and the elderly are also more at risk of an attack of PACG.

Global problem

Glaucoma constitutes one of the top three causes of world-wide blindness. As the population ages, the incidence of glaucoma will rise. Also known as the "silent thief of sight", glaucoma blindness is irreversible and permanent. Hence, it is imperative that adequate screening measures be undertaken to alleviate this growing problem.

VKY YONG, MBBS, FRCS(Edin)
Registrar, Department of Ophthalmology, National University Hospital

PTK CHEW, MBBS, FRCS(Edin), MMed(Ophth), FRCOphth
Senior Consultant and Chief
Deputy Director and Head, Glaucoma Service
The Eye Institute, National Healthcare Group, Tan Tock Seng Hospital

CLASSIFICATION OF GLAUCOMA

- Primary Open Angle Glaucoma (POAG)
- Primary Angle Closure Glaucoma (PACG)
  - acute
  - chronic
- Other causes of glaucoma (secondary glaucoma)

PHYSIOLOGY AND ANATOMY (Figure 1)

Aqueous Secretion

Active secretion is via the ciliary body. This constitutes 80% of aqueous production.

Passive secretion is by processes such as ultrafiltration and diffusion. This contributes the remaining 20% of aqueous secretion.

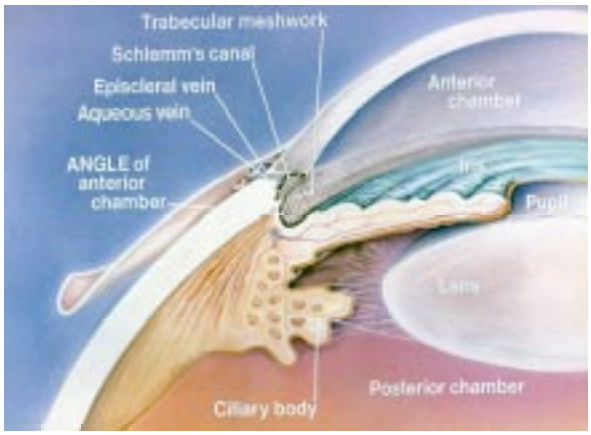

Figure 1: Normal angle structures.

Aqueous Outflow

The trabeculum (trabecular meshwork) is a sieve-like structure through which aqueous humour leaves the eye.

Schlemm's canal is a circumferential channel bridged by septa.

The collector channels leave Schlemm's canal at oblique angles and connect either directly or indirectly with episcleral veins.

Aqueous flows from the posterior chamber into the anterior chamber through the pupil and is drained by the following routes :

1. The trabecular (conventional) route, accounting for almost 90% of aqueous outflow, is through the trabeculum into Schlemm's canal. It is then drained away by the episcleral veins.
2. The uveoscleral (unconventional) route accounts for the remaining 10%. The aqueous passes across the ciliary body into the suprachoroidal space and is drained by the venous circulation in the ciliary body, choroid and sclera. Facilitation of aqueous outflow via the uveoscleral route is the basis for the newer generation of anti-glaucoma medications.

PRIMARY OPEN ANGLE GLAUCOMA (POAG)

This form of glaucoma is aptly referred to as the "silent thief of sight" due to its ability to result in blindness in an insiduous manner. It is generally asymptomatic until it has caused a significant loss of the visual field. It affects both sexes equally and is the most prevalent of all the forms of glaucoma. It is also frequently inherited.

Ocular Risk Factors

1. POAG in the fellow eye
2. Family history of POAG
3. High myopia
4. Central Retinal Vein Occlusion

Systemic Risk Factors

1. Age
2. Diabetes mellitus
3. Hypertension
4. Prolonged steroid use

Clinical Features

1. Visual field changes
   - In glaucoma, the visual field loss begins in the periphery and moves centrally. In advanced visual field loss due to glaucoma, there is the characteristic "tunnel vision" where the patient only has a small central area of his visual field remaining.
   - In the clinic, this can be tested grossly by confrontational visual field testing. However, this method is very gross and by the time visual field defects are picked up in this manner, glaucoma field loss will be very advanced. The test of choice is a computerised automated visual field analyser eg. Humphrey visual field analyser (elaborated later).
   - early visual field changes can be detected by analysers like the frequency doubling threshold (FDT) and the short-wave automated perimetry (SWAP).

2. Optic disc head changes
   - enlarged cup : disc ratio (Figure 2)
   - assymmetry of the cup : disc ratio of both eyes
   - increasing cup : disc ratio over time
   - hemorrhage at the optic disc
   - notching of the optic disc
   - nasalisation of the blood vessels at the optic nerve head
   - progression of optic nerve head changes can now be quantified by an optic nerve head imaging system eg. Heidelberg Retina Tomograph II (HRT II)

3. Raised intraocular pressure (IOP)
   – this is measured most accurately by the Goldman applanation tonometer, which is attached to the slit-lamp
   – if this is not available, an air-puff tonometer or a tonopen is acceptable
   – bi-manual palpation of the eye is also possible but is a subjective test
   – presenting IOP is usually 25-35 mmHg

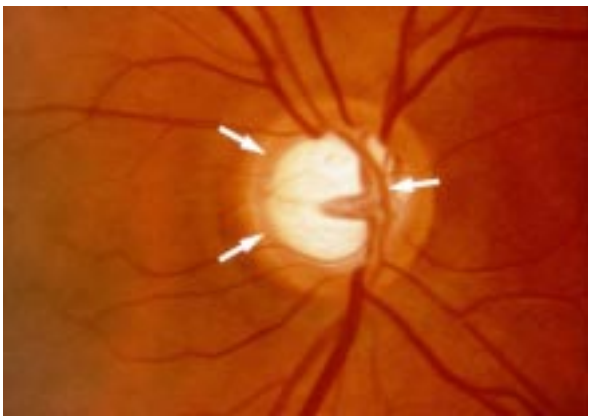

Figure 2: Arrows showing extent of cup.
The cup : disc ratio in this case is 0.7.

Table 1

DRUG	PHARMACODYNAMICS
Newer Drugs *Main advantage is that these drugs have less side effects but are more costly*	
Brimonidine (Alphagan) (bd dosage)	a_2-agonist Decreases aqueous secretion Increases uveo-scleral outflow
Dorzolamide (Trusopt) Brinzolamide (Azopt) (bd dosage)	Carbonic anhydrase inhibitor
Latanoprost (Xalatan) (on dosage)	PGF2a agonist Increases uveo-scleral outflow
Standard Drugs *These drugs are effective but have more side effects*	
Timolol 0.5% (bd dosage)	b-blocker Decreases aqueous secretion
Betaxalol (Betoptic) (bd dosage)	b-blocker Decreases aqueous secretion Cardio-selective b_1-blocker => safer than timolol in patients with pulmonary disease
Pilocarpine 2% & 4% (qds dosage)	Enhances aqueous outflow by producing changes to the trabeculum

MANAGEMENT

Medical

The aim of medical therapy is to lower the IOP by about 30% from the presenting IOP. This is the "target pressure", which is the pressure below which minimal further damage will occur to the patient's optic nerve head.

The mainstay of medical therapy is topical eyedrops. A list of the common anti-glaucoma topical eyedrops, together with their mechanism of action, is shown in Table 1.

Surgical

The aim of surgical intervention is to lower IOP by formation of a fistula eg. trabeculectomy. This is indicated in cases where, despite maximal medical therapy, the IOP is at a level where the optic nerve head is still susceptible to damage, as shown by worsening of the visual fields.

PRIMARY ACUTE ANGLE CLOSURE GLAUCOMA (PACG) (Figure 2)

In this condition, aqueous outflow is obstructed at the pupil margin. This is known as "pupil block" and results in the closure of the angle by the peripheral iris. It occurs in anatomically predisposed eyes and is frequently bilateral. The obstruction to aqueous outflow causes the IOP to build up rapidly over a short period of time. This is an ocular emergency.

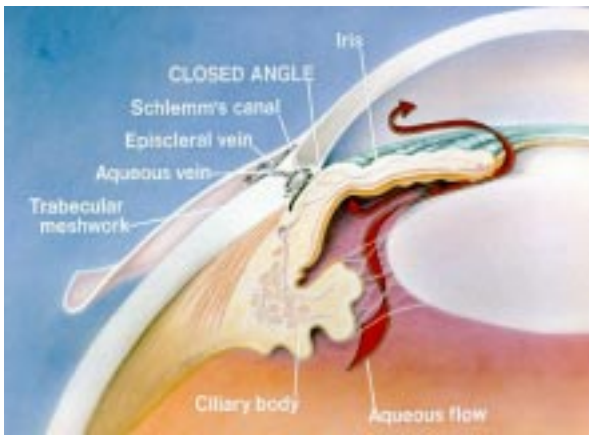

Figure 3: Anatomy of a closed angle.

An island-wide survey conducted in 1997 by Seah *et al* found the incidence of PACG in Singapore to be 12.2 per 100,000 per year[2]. Major risk factors identified in the survey were female, of Chinese ethnic origin and aged 60 years or older. Attacks were more frequent on hotter days as well.

Symptoms

1. Unilateral headache
2. Nausea
3. Vomiting
4. Blur vision
5. Seeing haloes

Signs

1. Hazy cornea (Figure 4)
2. Mid-dilated and unreactive pupil (Figure 4)
3. Ciliary injection (Figure 4)
4. Shallow anterior chamber (Figure 5)
   - this can easily be assessed in the clinic using a pen-torch
   - a pen-torch is shone from the temporal aspect of the eye. In eyes with shallow anterior chambers, an elliptical shadow is seen over the nasal part of the iris, this shadow being cast by the central iris which is bowed forward. This is known as the "eclipse sign"
   - in eyes with normal anterior chamber depths, the whole iris surface will be illuminated uniformly
5. Hard eye
   - on bimanual palpation, the affected eye can be felt to be almost rock-hard, compared with the fellow eye. Presenting IOP is usually in the range of 50-70 mmHg.

Management

The aim of management is to lower the IOP rapidly through systemic medication. At the same

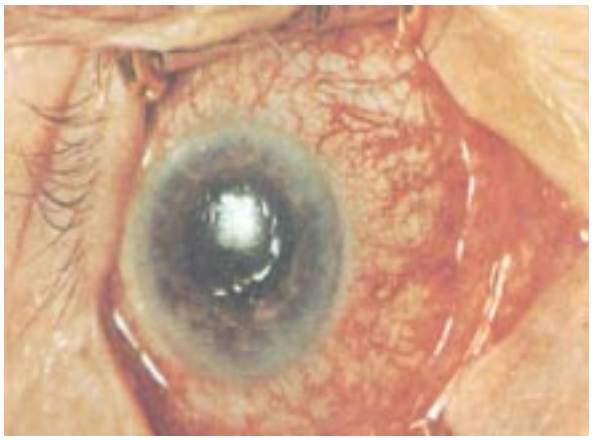

Figure 4: An eye with PACG.

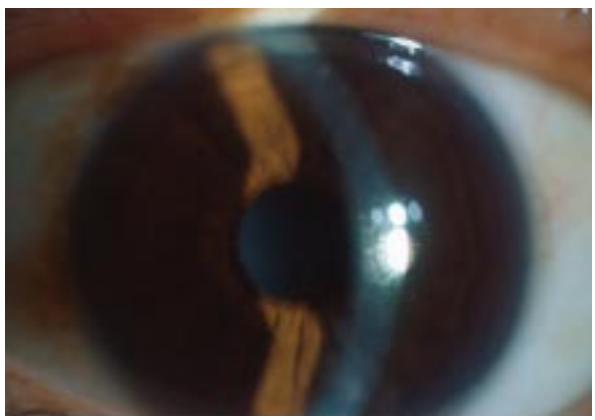

Figure 5: Slit-lamp photograph of an eye with a shallow anterior chamber.

time, topical miotic therapy is instituted to pull the peripheral iris away from the angle, thereby re-opening the channel for outflow of aqueous. As the presenting IOP is usually very high, the aim is for rapid reduction of IOP.

Systemic medication

In the acute setting, the patient with PACG is given intravenous acetazolamide 500mg stat followed by oral acetazolamide 250mg, 4 times a day. If after 4 hours the IOP is not sufficiently reduced, intravenous mannitol 1-2g/kg body weight may be instituted.

Topical medication

Besides systemic medication, topical medication is also started immediately. Miotics e.g. pilocarpine 4% are given every 15 minutes to the affected eye for 1 hour, after which the dosage is reduced to 4 times a day. A topical beta-blocker eg. timolol is also given twice a day. In addition, a topical steroid eg. prednisolone acetate is instilled every 3 hourly.

It is also important to treat the fellow eye with prophylactic topical pilocarpine 2% 4 times a day to prevent a similar attack in that eye.

The patient must be referred to an ophthalmologist immediately.

LASER PERIPHERAL IRIDOTOMY (Figure 6)

This is the definitive treatment for eyes with PACG. An argon laser (Figure 7) is used to create an opening in the peripheral iris. This opening provides an alternative route for the passage of aqueous from the posterior chamber to the anterior chamber of the eye, bypassing the pupil and hence, preventing pupil block from occurring.

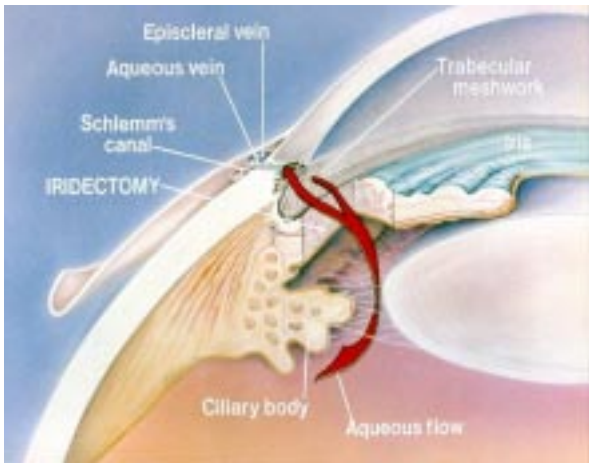

Figure 6a: A schematic diagram showing how a peripheral iridectomy provides an alternative route for aqueous flow.

Figure 6b: Slit-lamp photograph of a peripheral iridectomy (left) and a peripheral iridotomy (right).

Figure 7: Laser procedure in progress.

Surgery

In cases unresponsive to medical and laser therapy, surgical intervention may be necessary.

CHRONIC ANGLE CLOSURE GLAUCOMA (CACG)

As the name suggests, CACG presents insiduously and asymptomatically, much like patients with POAG. Although the anterior chamber angles are closed (like in PACG), the closure occurs gradually, unlike the sudden closure in PACG. Hence, the IOP rises gradually over time and the patient is usually symptom-free till late into the disease.

The management of CACG includes lowering the IOP by topical anti-glaucoma medications as well as performing a laser peripheral iridotomy. If these measures are unsuccessful in reducing the IOP, surgery is considered.

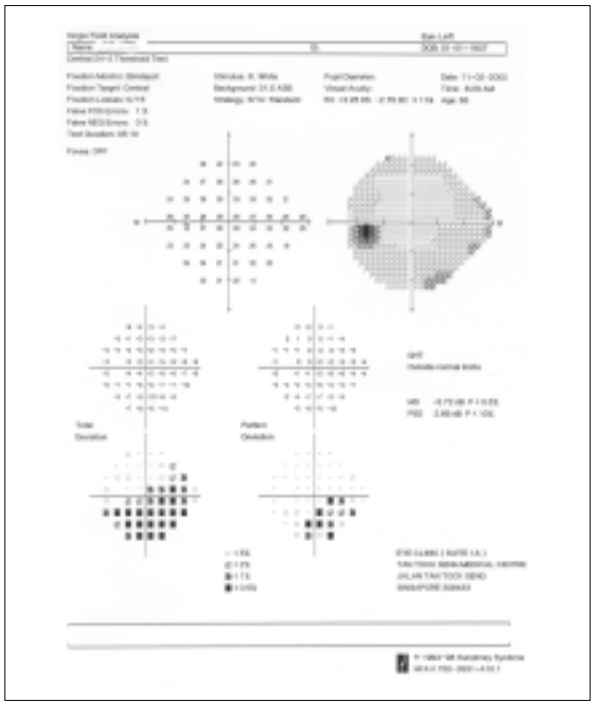

Figure 8: A sample printout of a Humphrey visual field.

INVESTIGATIONS IN GLAUCOMA MANAGEMENT

The ophthalmologist has a full armamentarium of investigations at his disposal. The aim of these investigations is to obtain a baseline level at the point of diagnosis for future comparisons to be made as well as for follow-up purposes, looking for progression of the disease.

Common investigations

1. Humphrey Visual Field (HVF) (Figure 8)
   The most common and important investigation in glaucoma, the HVF is a form of automated perimetry. It evaluates the visual field of the patient and is an important tool in the follow-up of glaucoma patients. Many management decisions are based on the results of the HVF.
2. Stereo disc photos
   This is a method of obtaining an objective assessment of the optic discs. It eliminates inter-observer bias. It is also useful in providing an objective comparison for the assessment of progression of the cup/disc ratio.

Newer investigations

1. Heidelberg Retina Tomograph II (HRT II) (Figure 9)
   This is a confocal laser scanning system for acquisition and analysis of three-dimensional images of the posterior segment of the eye. It

Figure 9: The HRT machine.

is superior to the HVF in that it provides objective and quantitative evidence for diagnosing and following up glaucoma patients.

2. Ultrasound Biomicrosopy (UBM) (Figure 10) Used for diagnosis in the anterior segment of the eye. UBM has a very high resolution (20-60 microns) compared to conventional ultrasound (300-600 microns). This allows us to study anterior segment structures (Figure 11) as if we are looking at a pathological specimen in vivo through a low power microscope. This is of particular importance in conditions like PACG and plateau iris syndrome, where the structure of the peripheral angle and iris is very well evaluated by the UBM. An ultrasound is also non-invasive and is not associated with any pain or side effects.

Figure 10: A UBM machine.

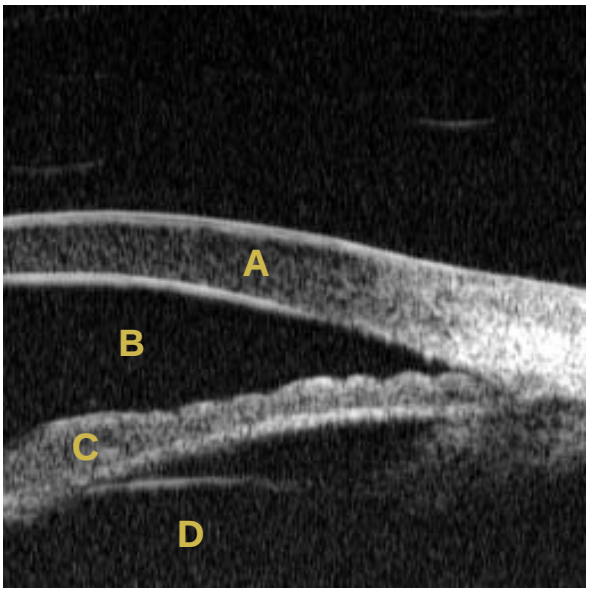

Figure 11: A typical UBM image of the anterior segment
A represents the cornea
B represents the anterior chamber
C represents the iris
D represents the lens

SURGICAL OPTIONS IN GLAUCOMA MANAGEMENT

Surgery is indicated when the IOP is at a level where there is still optic nerve head damage and visual field progression despite maximal medical therapy. Other factors to consider are whether the patient is intolerant or non-compliant to the medications.

A trabeculectomy is the standard filtering operation to treat glaucoma. It creates a fistula between the anterior chamber and the subconjunctival space. Aqueous thus leaves the anterior chamber via a sclerostomy (small opening in the sclera) and travels to the subconjunctival space, where it is absorbed by the conjunctival vessels. As such, the maintenance of the subconjunctival space is essential for success of the operation. If the conjunctival space closes eg. due to scarring, the trabeculectomy will fail.

In recent years, the use of anti-metabolites as an adjunct to trabeculectomy has risen. Anti-metabolites such as mitomycin-C and 5-fluorouracil act to inhibit fibroblast activity at the site of the conjunctiva, preventing scarring and hence, maintaining the subconjunctival space. A review by Wong *et al* found that survival of trabeculectomy surgery was improved significantly with intra-operative use of 5-fluorouracil[3].

With the advent of small-incision cataract surgery by phacoemulsification, there has been a recent trend to perform a combined cataract extraction, implantation of intraocular lens and a

trabeculectomy in a single procedure. This combined procedure is beneficial to the patient as it saves the patient from a second operation.

CONCLUSION

The Singapore population is ageing. According to the Ministry of Health, the percentage of the population aged 65 years and older is increasing with 6.9% in 1998, 7.1% in 1999 and 7.3% in the year 2000. Furthermore, there is also a general increase in the life expectancy for both males and females[4]. This is indeed a worrying trend as many eye diseases, including glaucoma, affect the older population.

The diagnosis of PACG is not difficult as the patient presents in a dramatic fashion. The difficulty lies in detecting cases of POAG and CACG, which are largely asymptomatic and present insiduously. The situation is made worse by the fact that in a survey of Chinese residents in Singapore by Foster *et al*, POAG was 1.6 times more common than PACG[1].

The answer to preventing blindness from glaucoma is early detection. Screening programmes can detect glaucoma in its early stages, making treatment easier and improving the prognosis of those affected. Public education also plays a vital role. Singapore needs an early detection programme for glaucoma. The ideal method for early detection is, however, not known yet. This is a matter of importance for ophthalmologists in the immediate future.

REFERENCES

1. Foster PJ, Oen FT, Machin D, Ng TP, Devereux JG, Johnson GJ, Khaw PT, Seah SK. The prevalence of glaucoma in Chinese residents of Singapore: a cross-sectional population survey of the Tanjong Pagar district. Arch Ophthalmol 2000;118(8):1105-11.
2. Seah SK, Foster PJ, Chew PT, Jap A, Oen F, Fam HB, Lim AS. Incidence of acute primary angle-closure glaucoma in Singapore. An island-wide survey. Arch Opthalmol 1997;115(11):1436-40.
3. Wong JS, Yip L, Tan C, Chew P. Trabeculectomy survival with and without intra-operative 5-fluorouracil application in an Asian population. Aust N Z J Ophthalmol 1998;26(4):283-8.
4. Population and vital statistics. Ministry of Health, Singapore. Health Facts website.