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Can we prevent angle-closure glaucoma?

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Abstract

Purpose **Glaucoma is the second cause, after cataract, of world blindness. Approximately half is thought to be primary angle-closure glaucoma (ACG). This review asks whether ACG can be prevented on a population basis.**
Methods and populations **Review of published information from the Inuit of Greenland, Canada and Alaska, and descriptions of recent studies in Asian populations in Mongolia, China and South-East Asia.**
Results **The Greenland Inuit have the shallowest anterior chamber depths (ACDs) so far recorded. The proportion of blindness due to ACG was reduced from 64% to 9% over 37 years by systematic optical measurement of central ACD and the van Herick test in the older Inuit, followed by gonioscopy and prophylactic iridectomy or laser iridotomy when indicated. In Mongolia, ultrasound measurement of central ACD had good sensitivity and specificity as a screening test. A randomized controlled trial of screening and prophylactic laser is being completed. In China and South-East Asia, the mechanism of angle closure appears to be more varied and complex and its detection may require more elaborate imaging.**
Conclusions **The mechanism of angle closure and potential for prevention by screening are likely to have to be determined specifically for each population at risk.**
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Keywords: glaucoma; angle closure; epidemiology; blindness; biometry

Introduction

This question is important because glaucoma is second only to cataract as a cause of blindness worldwide.[1] Of the estimated 6.7 million people blind from primary glaucoma in 2000, calculated using Quigley's statistical model, half are thought to be primary angle-closure glaucoma (PACG).[2]

It is a particular problem in people of Asian origin. By extrapolating from surveys in nearby countries, we estimated that there may be 1.7 million people blind from glaucoma in China—mostly PACG—and that there are 28 million with occludable angles[3] probably deserving prophylactic intervention.[4]

It is widely believed that PACG can be prevented in individual eyes or individual patients. For example, after an acute attack of angle closure, iridotomy or iridectomy in the fellow eye appears to prevent similar symptomatic episodes in many cases and pressure rises occur in only 12% in the medium term.[5,6] Consequently, prophylactic iridectomy or laser iridotomy has become standard practice.[7] Similarly, on routine clinical examination, evidence of primary angle closure (PAC) may be found, for example, by peripheral anterior synechiae. In these cases, there is strong circumstantial evidence that, if detected early enough, prophylactic laser iridotomy probably prevents progression to glaucoma in the majority of cases. Iridotomy results in a substantial widening of the drainage angle in most cases.[8,9]

However, from the public health point of view, and for the purposes of the Global Initiative to Eliminate Avoidable Blindness (Vision 2020), we need to examine the case for and against prophylactic treatment on the population level.

The Inuit of Greenland, Canada, and Alaska

The native population of North and South America is derived from Asia, around that region which is now Mongolia. They are thought to have come across the Bering Strait in three main waves of migration. The third, possibly as recently as 9000 years ago, became the Inuit (or Eskimos). They were restricted to

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Table 1 Prevalence of established ACG in Inuit (Eskimos) aged 40 years and over

Alaska	Arkell *et al*[12]	*(1987)*	*2.65%*
Canadian arctic	Drance[9]	(1973)	2.9%
Labrador	Johnson *et al*[11]	(1984)	3.0%
W. Greenland	Alsbirk[10]	(1973)	4.8%

the high arctic and moved eastwards as far as the east coast of Greenland, where there are still two isolated settlements.

The high prevalence of primary ACG in the Inuit has been documented in population surveys (Table 1). Drance reported the results of a survey of ocular disease in a collaboration between the Department of Health and Welfare and the universities of Canada.[10] A total of 2800 people were examined in many communities. The prevalence of primary ACG in those aged 40 years and over was 2.9%. Alsbirk found a higher prevalence in the total population of Umanak in west Greenland.[11] Similar prevalences were documented in Labrador[12] and in Alaska.[13] The surveys in Table 1 are arranged geographically from west to east. Although the studies may not be completely compatible, there is the suggestion of a trend from west to east. Whether this is significant or not, Greenland does appear to have the highest prevalence so far recorded.

We owe much of our understanding of ACG to Danish ophthalmologists who have studied and served the Inuit of Greenland over many years. Travelling by dog-sled from community to community, Clemmesen and Skydsgaard completed the first blindness survey in 1962.[14] Almost two-thirds (64%) of all blindness in these Inuit was due, at that time, to glaucoma.

Viggo Clemmesen inspired Poul-Helge Alsbirk, who was the general doctor at the Umanak hospital, to systematically research the characteristics of the Inuit eye. Using a Koeppe lens and a hand-held portable microscope for gonioscopy, they found that 88% of the prevalent glaucoma was angle closure.[15] The preponderance of ACG, compared with open-angle glaucoma (OAG), in the Greenland Inuit was remarkable. In all, 93% of the registered blind due to glaucoma in 1972 were people with ACG, the great majority being female, often with no perception of light.

Alsbirk measured the anterior chamber depth (ACD) and other parameters of the shape of the eyes in whole populations. The mean ACD in 843 Inuit in Umanak *after* excluding the known cases of ACG and their families,[11] are shallower than similar measurements in Caucasians—in this case from Sweden, after Tornquist. At each age, the ACDs are shallower in females than males. For the 60 cases of ACG already known, the mean ACD was 1.8 mm.

Corneal diameters[16] and, to a lesser extent, the axial lengths were correlated with ACD. In other words, those at greatest risk of ACG had the smallest anterior chamber volumes. The Inuit have become superbly adapted to a way of life in the extreme environment in which they live. Alsbirk has suggested that the small volume of the anterior chamber is an adaptation to reduce the risk of freezing of the cornea, and gives examples of this occurring at these latitudes.[17]

Applying this information to the shape of the anterior chamber, the Danish ophthalmologists have systematically examined the older Inuit, on their clinic tours two or three times a year, for both central ACD and the configuration of the limbal chamber depth by the van Herick method.[18] Those judged to have occludable angles on subsequent gonioscopy then received surgical peripheral iridectomies and—after 1991—YAG laser iridotomies.

The proportion of blindness due to glaucoma has been brought down from 64% in 1962 to 9% in the registration figures for both 1999 and 2003.[19] A few late cases still occur in Greenland, undetected or with delayed intervention, because of geographic isolation, but primary ACG is now considered a relatively minor cause of new blindness. So the short answer to the question 'Can ACG be prevented?' is 'Yes—in this specific population, and with sufficient resources'.

Experience in Mongolia

Mongolia, in the general area of Asia from which the Inuit are thought to have migrated, also has an extreme climate, with winter temperatures down to −50°C. An initial population-based survey of the prevalence and causes of blindness in 1991 and 1992, in three representative provinces, showed that 35% of blindness was due to glaucoma, equal to that caused by cataract.[20] This was not 64%, as in Greenland, but was nevertheless very high compared with surveys in any other country. A research programme over the past 10 years has aimed to characterize this glaucoma, with the long-term purpose of preventing blindness from this cause. We studied a representative population sample of 1000 individuals aged 40 years and over in the northern province of Hovsgol.[21] Although OAG occurred, the predominant type of glaucoma was angle closure, and with a pupil-block mechanism as in Greenland. However, although some people had experienced symptomatic angle closure, the presentation was typically asymptomatic (ie 'chronic'). This is true of Asia in general.

We asked what practical and relatively simple tests might be easy to administer for screening in this population, acceptable to the people, and relatively

inexpensive for each person tested. The tests considered were (1) the oblique flashlight test; (2) limbal ACD estimation (the van Herick test); and (3) A-scan ultrasound. These tests were evaluated by Foster and Devereux on the combined data after a further population-based glaucoma survey in the southern-most province of Omnigobi by Devereux.

In the oblique flashlight, or side-light, test, a small light source is shined from the temporal limbus. The depth of the anterior chamber and the degree of curvature of the iris are estimated by the extent of the shadow on the nasal side. Although Chinese workers have claimed good sensitivity and specificity for this test, this could not be confirmed in the Mongolian studies (unpublished). It is possible that the validity of this test could be improved by standardization of the size of the light source and the tangential direction of the light in relation to the plane of the iris, possibly by fixation against the temporal rim of the orbit.

Foster and Alsbirk refined van Herick's original description of estimation of the ACD at the limbus by expressing the extent of the slit-lamp beam visible between the endothelium and the anterior surface of the iris as a percentage of the corneal thickness.[22] This gave excellent sensitivity and specificity in detecting occludable angles, PAC, and primary ACG. However, it requires a stable, high-quality slit lamp and considerable experience to obtain consistent results. It is unlikely to be a satisfactory screening test in the hands of nonophthalmologists.

Foster measured the axial ACDs on the whole population sample of Hovsgol and an additional sample aged under 40 years by the optical method, using the Haag–Streit attachments, and also by a Humphrey A-scan ultrasound.[23] The mean ACDs at each age were again very shallow, but not quite as shallow as in the Inuit (Figure 1). The Caucasian curve in this figure is from Belgian data. A northern Chinese population gave values very similar to the Mongolians. By contrast, Japanese eyes seem to have evolved in a different way, with deep anterior chambers.

Figure 2 is an array of the data for the optical ACDs for the entire Hovsgol sample aged 40 years and over, plotted against age.[24] If a horizontal line was drawn across at, say, 2.3 mm, it can be seen that such a cutoff would detect almost every case of primary ACG, PAC, and suspects. This method could probably be further refined in practice as a screening test by deciding different cutoff points for each gender and for specific age groups.

We wanted to find a screening test that could be applied in remote communities in Mongolia by technicians who were not trained ophthalmologists. As part of his survey in the southern province, Devereux

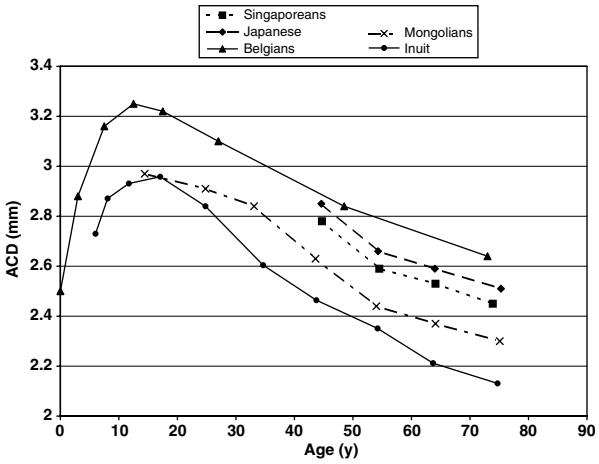

Figure 1 Variation of mean ACD with age in five ethnic groups. All studies employed Haag–Streit optical pachymetry and calculated ACD by subtracting corneal thickness (from Foster PJ. The epidemiology of primary angle-closure and associated glaucomatous optic neuropathy. *Semin Ophthalmol* 2002; **17**: 50–58).

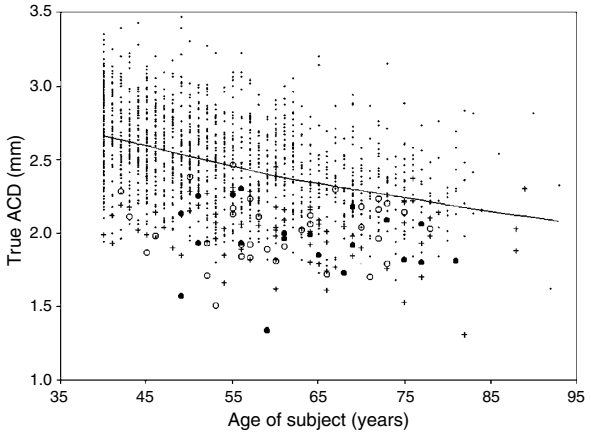

Figure 2 Distribution of true optical ACD by age. Solid line represents mean age-specific ACD as estimated by lowest curve. Crosses are cases of suspected PAC; open circles, PAC; and closed circles PACG. Small dots represent the rest of the study population with ACD measurement (from Devereux *et al*[24]).

also tested the use of the ultrasound probe held in the hand when applied to the cornea. One way of displaying the validity of a screening test is as a receiver operating characteristic, or ROC, curve, in which sensitivity and specificity are plotted on the same graph (Figure 3). The greater the area under the curve, the better the test. The optical method of measuring axial ACD gave the best results. The ultrasound probe mounted in the applanation attachment on the slit lamp was almost as good. The hand-held ultrasound probe was, disappointingly, less good. Therefore, for the screening

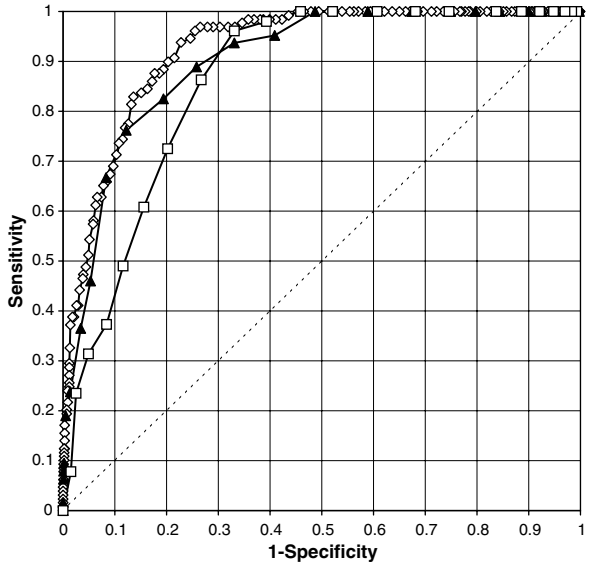

Figure 3 ROC curve comparing optical pachymetry (diamonds) and slit-lamp mounted (triangles) and hand-held (squares) ultrasound tests in the detection of suspected PAC (occludable angles) (Devereux *et al*[24]).

Table 2 Outcome of YAG laser iridotomy for PAC in Asia[8]

- 164 eyes of 98 subjects followed at 1–3 years
- 157/160 (98.1%) remained patent
- Angle width increased median 2 Shaffer grades
- PAC: iridotomy alone sufficient in 97%
- PACG: iridotomy alone sufficient in 53%
- Four eyes required glaucoma surgery

trial described below, the practical screening test adopted was ultrasound, with the headrest of a slit lamp but without the microscope, and with the ultrasound probe mounted on a carriage, which could be moved gently forwards into contact with the cornea.

Before considering a screening programme for any condition, it is necessary to demonstrate that there is a treatment that works. Nolan followed up every person who could be found who had received a YAG laser peripheral iridotomy in the previous two surveys.[25] The results, summarized in Table 2, were even better than hoped. In this population, YAG peripheral iridotomy was effective in preventing progression of PAC. Almost half of those with established PACG required no further treatment to control the intraocular pressure.

On the basis of this previous work, a randomized controlled trial of screening for angle closure was started $5\frac{1}{2}$ years ago by Nolan and Mongolian colleagues.[26] Over 4700 people aged 50 years and over were randomized to a screening arm or a control arm. Existing glaucoma was detected and all optic discs were photographed before the two arms continued. In the intervention arm, 685 subjects who were screened out by measurement of ACD then progressed to a full ophthalmic examination with gonioscopy. Of these, 156 received laser iridotomy. The follow-up is expected to start at the end of 2004. The result of this trial will determine if ACG can be prevented and whether a nationwide screening programme of the older population for angle closure should be recommended for Mongolia.

China and South-East Asia

Until now, we have been considering two populations in which the mechanism of angle closure is thought to be predominantly pupil block. The typical picture of this mechanism, as viewed, for example, by ultrasound biomicroscopy (UBM), is that after the peripheral iridotomy, the iris of an eye with occludable angle flattens out and the angle opens up. However, as you go further south in China or into South-East Asia, the situation appears to be more complex. In southern China, a nonpupil-block mechanism may account for a considerable proportion of angle closure. Wang *et al*[27] stated that 55% of all angle-closure in China is caused by multiple mechanisms, with only 38% attributable to pure pupil block. In 1979, Hung and Chou reported that the dark-prone provocative test was positive in 60% of Taiwanese Chinese eyes after iridectomy, compared with 12.5% in normal eyes.

UBM has been used in Guangzhou to investigate the variations in angle structure in this population.[28] Wide variations have been found in the thickness of the main body of the iris, the thickness of the iris insertion, whether the iris insertion is regular or angulated, and the position of the iris insertion with respect to the ciliary body. Some types of 'plateau iris' are associated with forward rotation of the ciliary body, but in Chinese eyes, some are more related to the innate structure of the iris. Another variation is a very thick iris thrown into circumferential folds. Looking at some of these images, it becomes clear that conventional YAG laser iridotomy would not be expected to prevent progression of angle closure. For some of these structural variations, other preventive treatments will need to be devised such as broad surgical iridectomies or laser iridoplasty.

Similarly, for some of these variations, measurement of axial ACD by itself will not be an adequate screening test for angle closure. UBM technology, the Scheimpflug principle, or Optical Coherence Tomography (OCT) are increasingly being used to give an accurate picture of the anterior chamber architecture. It may be possible to adapt these methods as screening tools for large numbers. Kashiwagi and colleagues in Japan have recently described a rapid optical system.[27] Half of the

anterior chamber is scanned in 0.5 s to create 21 slit-lamp images, which are assembled by computer to describe the configuration of the chamber and angle.

Even less information has been published about the mechanism of angle closure in other Asian countries. An observer with intensive experience in Cambodia estimated that about half of the angle closure he was seeing was due to non-pupil-block mechanisms (A Pyott, personal communication).

Long-term follow-up studies of the effectiveness of prophylactic YAG laser are needed for these populations. Can we predict which angles will remain occludable? The assumptions about the value of peripheral iridotomy are dependent on it being carried out adequately, and safely, without complications.

Conclusion

All ethnic groups are not going to behave in the same way. The mechanisms of angle closure will have to be studied for each specific population in which ACG is a common public health problem. ACG is thought to be preventable, but the policies, screening tools, and prophylactic treatments are likely to vary from population to population.

We are optimistic that PACG can be prevented and therefore we must determine what priority a programme of prevention should have in relation to those already being implemented for cataract and trachoma.

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