

Angle-Closure Glaucoma: Concepts and Epidemiology

Anatomy alone cannot account for who develops this disease and who does not.

BY HARRY A. QUIGLEY, MD

When considered together, open-angle glaucoma (OAG) and angle-closure glaucoma (ACG) are the second leading cause of blindness worldwide. ACG affects 16 million people, and almost 4 million are bilaterally blind.¹⁻³ Although three times more people have OAG than ACG worldwide, the greater morbidity of ACG means that the absolute number blind is similar to that of OAG. In the developing world, more than 90% of individuals with glaucoma are undiagnosed and untreated. Even in developed countries, clinicians presently identify only half of the people with glaucoma.

The World Health Organization's Vision 2020 program strives to carry out more cataract surgery in every country where surgical rates are inadequate. In contrast, international public health efforts to attack glaucoma, particularly ACG, have not yet been advocated, because there are no effective screening methods for the disease and surgeons do not know which persons with narrow angles require iridotomy. The mechanisms behind ACG remain mysterious, but research is beginning to reveal some clues.

OVERVIEW

Physicians' understanding of ACG was enhanced when Curran⁴ found that iridectomy relieved pupillary block, Barkan popularized gonioscopy,⁵ and Rosengren demonstrated⁶ that glaucoma could be divided into cases involving small eyes (later found to be ACG) and large eyes (OAG). Alsbirk expanded the risk factors for ACG⁷ by documenting its high prevalence in Greenland and confirming its association with small eyes. Population-based studies⁸⁻¹¹ indicate that the incidence of ACG increases with age, is more common in women, and has a greater prevalence in Asians and East Indians than in Europeans and Africans. ACG is equally prevalent in individuals of

African as European origin. Acute, symptomatic attacks of angle closure occur in only 20% to 30% of those with angle closure and ACG,¹² with the rest having an asymptomatic course. Twin studies support a genetic influence in ACG,¹³ but no specific gene has been isolated. As with other diseases, many genes will eventually be associated with ACG as well as gene/environment interactions.

DEFINITION

Until recently, research on ACG was hampered by the lack of consistent diagnostic criteria. A definition of ACG by consensus¹⁴ now allows comparisons among studies, and the word *glaucoma* is used only when there is disc and field loss. The gonioscopic definition for angle closure is coverage of more than one-half of the pigmented meshwork without indentation. Terms such as *chronic*, *intermittent*, and *subacute* ACG have been eliminated. Recently, the disc and field changes were found to be so similar between ACG and OAG^{15,16} that the same general criteria can be applied.

ANATOMY AND IRIDOTOMY

Although ACG occurs more commonly in short eyes, anatomic risk factors do not explain why many people with small eyes and narrow angles never develop the disease. Chinese persons have a fivefold higher incidence of ACG than Europeans, yet the proportion of small eyes among Chinese is not greater than among Europeans or Africans.¹⁷ Cross-sectional evidence among Chinese persons¹⁸ shows greater shallowing of the anterior chamber with age than in Europeans or Africans. Gonioscopy and even ultrasound biomicroscopy (UBM), however, do not separate the many patients with benign narrow angles from those who will develop ACG.^{19,20} If the Chinese have the same proportion of small eyes, then something other

than anatomy explains the high prevalence of ACG in this population.

There are 10 narrow angle suspects for every person who will develop ACG. Surgeons should avoid performing iridotomy needlessly, as it may speed the development of cataract.²¹ At present, they perform iridotomy on most suspects with narrow angles.²² If the relative proportion of persons with narrow angles to those with ACG is 10 to 1, then iridotomy would appear to have a 90% cure rate, even if it were totally worthless. The other side of this problem is that half of the individuals being treated for “glaucoma” in the United States have no gonioscopy recorded in their chart.²³ To minimize unneeded iridotomy in the developed world and to direct limited resources in developing countries, physicians must move beyond static, anatomic measurements (which ignore how much the eye changes from moment to moment) to develop new, physiological risk factors.

PHYSIOLOGY

The Iris

UBM videos show dramatic changes in the angle as the pupil enlarges and constricts. Recent quantitative measurements of the iris and angle with anterior segment optical coherence tomography that took the pupil's size into account showed that the angle's narrowing on dilation is partially due to changes in iris volume.²⁴ As the pupil constricts, the iris gets fatter, swelling with more aqueous humor water, and then loses volume on dilation, much like a sponge. Eyes with ACG lose less iris volume on dilation, making angle closure more likely. This physiological risk factor may vary ethnically, providing one explanation for racial differences in ACG. Current provocative tests for ACG do not predict who will develop the disease,²⁵ but dynamic physiological tests might.

Other mechanisms may contribute to ACG. A hole in the iris eliminates the pupillary block mechanism, but one-third of eyes are gonioscopically narrow after iridotomy (plateau iris configuration). Very few of these develop high IOP with pupillary dilation.²⁶ Some surgeons claim that these eyes will undergo a “creeping” closure and advocate laser iridoplasty,²⁷ but there is no controlled evidence for this treatment.²⁸ Prospective studies fail to show that any large proportion of eyes with documented angle closure undergo progressive angle closure with years of follow-up after iridotomy.²⁹ Rarely, eyes with plateau iris configuration develop high IOP with pupillary dilation after iridotomy (plateau iris syndrome). In addition to developing pupillary block, these eyes may lose less iris volume upon the pupil's dilation. Alternatively, the peripheral iris attachment to

the ciliary body may allow obstruction of the trabecular meshwork.³⁰

Choroidal Expansion

Another dynamic, physiological risk factor in ACG is choroidal expansion. Anterior segment surgeons noted that some eyes exhibit positive pressure when they create the cataract incision, such that the iris prolapses and the lens moves toward the cornea. This phenomenon is associated with serous fluid in the suprachoroidal space.^{31,32} I proposed that eyes with ACG have a greater tendency for this choroidal expansion,³³ as evidenced by their greater tendency for a flat chamber after trabeculectomy.³⁴ Nanophthalmos is the extreme example, but this phenomenon is probably common to eyes with primary ACG. In small eyes predisposed to angle closure, an expansion in choroidal volume would increase resistance in the iris/lens channel, thereby intensifying pupillary block by moving the lens forward. There are many known situations in which choroidal expansion causes secondary angle closure (eg, choroidal hemorrhage, topiramate-induced,³⁵ or Valsalva³⁶), but recent research has found choroidal expansion (referred to as *effusion*) in eyes with primary ACG.^{37,38}

Choroidal expansion is five times more common in asymptomatic ACG eyes than in controls. A 20% choroidal expansion would dramatically increase IOP to 60 mm Hg yet would be invisible clinically. The tendency for choroidal expansion must vary among eyes, depending upon choroidal elasticity and vascular permeability. This physiological response could present another opportunity for new provocative testing.

Malignant Glaucoma

Malignant glaucoma^{39,40} illustrates an additional physiological contribution to ACG, although aqueous misdirection is not its mechanism. Acute choroidal expansion causes an elevation in IOP and increased aqueous outflow, thereby producing a posterior-to-anterior IOP gradient. Water must move from the posterior vitreous cavity toward the posterior and anterior chambers. Fluid from behind the posteriorly detached vitreous (still attached at the vitreous base) must pass through the vitreous gel to equalize this difference. If vitreous resistance to fluid movement were minimal, water would pass through easily, thus eliminating the pressure differential. Vitreous limits water's passage, however, and as pressure across it increases, flow decreases.⁴¹

I propose that eyes with malignant glaucoma have poor vitreous fluid conductivity, which produces a vicious circle in the behavior of the vitreous gel, but without a one-way valve or aqueous misdirection. With the

vitreal unable to equalize the posterior-to-anterior IOP difference, the gel compresses, moves toward the cornea, and presses the iris and lens forward to flatten the chamber, as shown in vitro by Epstein et al.⁴² In eyes with ACG, the lens' forward movement increases resistance in the iris/lens channel and thus contributes to typical angle closure. Iridotomy in eyes with extremely poor vitreal fluid flow removes the pupillary block, but the vitreal collapse continues, which explains their malignant glaucoma.

The idea that malignant glaucoma results from misdirected aqueous cannot be correct; if aqueous could move from the ciliary body posteriorly through the vitreal gel, it would flow in the opposite direction just as easily. The "misdirection" requires a mythical one-way valve for posterior aqueous movement, which does not exist and is not needed if one understands the vitreal-collapse phenomenon. Choroidal expansion has been observed with UBM in eyes with malignant glaucoma⁴³ and could be the initiator for vitreal collapse.

CONCLUSION

Clinicians previously thought that ACG had only the pupillary block mechanism and that other entities had their own unique mechanisms (plateau iris, malignant glaucoma, nanophthalmos). These other mechanisms are dominant in some entities, but they contribute as physiological risk factors for primary ACG. Research into the multiple dynamic features of ACG may explain its risk factors and lead to better diagnosis. Women may be more prone to choroidal expansion, or Asians may have different iris fluid exchange. These hypotheses should be tested in longitudinal studies of individuals at risk for ACG. □

Harry A. Quigley, MD, is the director of glaucoma services for The Wilmer Eye Institute at Johns Hopkins University in Baltimore. Dr. Quigley may be reached at (410) 955-2777; hquigley@jhmi.edu.



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