### A CONSTRUCT FOR UNDERSTANDING ANGLE-CLOSURE GLAUCOMA

### The Role of Ultrasound Biomicroscopy

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In order to approach the treatment of different disorders leading to angle-closure glaucoma most effectively, it is necessary to understand the differences between them and the anatomic and pathophysiologic mechanisms by which they develop. A disease has a specific cause, mode of onset, pathophysiology, and course, or natural history. Intervention can potentially occur at a number of different stages, from prevention, intervention to limit progression and cure, to reversal of damage caused by the disease.

Just as open-angle glaucoma is becoming realized to consist of a group of disorders of diverse causes related by a final common pathway, angle-closure glaucoma needs to be appreciated within a similar framework. Angle-closure "glaucoma" is not a single entity, but a number of different disorders related by a final common pathway, the first step of which is iris apposition to the trabecular meshwork. These diseases are characterized by abnormal relationships of anterior segment structures, which in turn stem from abnormalities of size or position of structures, themselves in turn caused by underlying etiologic factors

Supported in part by the Department of Ophthalmology Research Fund of the New York Eye and Ear Infirmary or initiating events. The resulting physical barrier to aqueous humor outflow acutely or gradually leads to elevated intraocular pressure (IOP).

Angle-closure may be caused by abnormalities in the *relative* sizes or positions of anterior segment structures, abnormalities in the *absolute* sizes or positions of anterior segment structures, abnormal *forces* in the posterior segment that alter the anatomy of the anterior segment, or any combination thereof. Because the terminology for many of these disorders was developed years ago and has been used inconsistently, it is not ideal for describing angle-closure as it is understood today. Therefore, it is easier to classify the angle-closure glaucomas in terms of the underlying mechanism causing the angle-closure (Table 1).<sup>41, 42</sup>

Approximately 90% of patients with angle-closure have relative pupillary block as the underlying mechanism. Laser iridotomy provides the definitive treatment. The other 10% of patients with angle-closure have either a mechanism or combination of mechanisms other than or in addition to pupillary block. Only in the last decade or so have these other mechanisms been so well recognized. Some patients' conditions can worsen by routine

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#### Table I. MECHANISMS OF ANGLE-CLOSURE GLAUCOMA

I. Pupillary block

A. Relative pupillary block (primary angle-closure)

B. Miotic induced angle-closure

- C. Posterior synechiae
  - 1. Crystalline lens
  - Intraocular lens
     Anterior hyaloid face

II. Plateau iris

A. True plateau iris

B. Pseudoplateau iris-iris and ciliary body cysts

III. Lens-induced angle-closure

- A. Intumescent lens (phakomorphic)
- B. Anterior lens subluxation

1. Trauma

- 2. Exfoliation syndrome
- 3. Hereditary disorders
- C. Drug sensitivity, e.g., sulfonamides
- IV. Malignant (ciliary block) glaucoma

A. Primary

- 1. Phakic
- 2. Pseudophakic
- 3. Aphakic

B. Secondary

- 1. After panretinal photocoagulation
- 2. After scleral buckling procedures
- 3. After central retinal vein occlusion
- 4. Intraocular tumors
- 5. Posterior scleritis
- 6. Retrolenticular tissue contracture
  - a. Retinopathy of prematurity
  - b. PHPV
- 7. Uveal effusion from adjacent inflammation
  - a. Posterior scleritis
  - b. AIDS

treatment for angle-closure. This statement applies particularly to the use of miotics in patients with intumescent or anteriorly subluxed lenses or malignant glaucoma who respond paradoxically.

The ability to recognize these other causes of angle-closure and to diagnose them in clinical situations is crucial to choosing the optimal treatment for any patient. Understanding of the anatomic and pathophysiologic mechanisms involved in the cause of angle-closure glaucoma assists in the making of the diagnosis and in optimizing treatment. Until recently, the development of an encompassing schema has been hindered by the inability to visualize the entire anterior segment, which prevents a detailed understanding of the underlying anatomic abnormalities. Although slit lamp biomicroscopy and gonioscopy allows the anterior chamber to be viewed, the posterior chamber, iris-lens relationship, and ciliary body, have, for the most part, remained hidden. Indentation gonioscopy provides accurate information as to the extent of angle closure and presence of synechiae but only permits inferential data regarding the structures posterior to the iris.

With high frequency, high resolution, anterior segment ultrasound biomicroscopy (UBM), it is possible to image the structures surrounding the posterior chamber, examination of which has been limited previously to histopathologic examination.<sup>24,26</sup> It has already proven useful in elucidating important features of various types of glaucoma.<sup>13,21–23,25,28,45</sup> UBM is ideally suited to the study of angle-closure because of its ability to simultaneously image the ciliary body, posterior chamber, irislens relationship, and angle structures. In this article, we will illustrate how UBM has improved our understanding of angle-closure glaucoma and is helping to elucidate new approaches to therapy.

### RELATIVE ABNORMALITIES OF ANTERIOR SEGMENT RELATIONSHIPS

### Relative Pupillary Block

Terminologically, angle-closure glaucoma has been divided into primary and secondary forms. Primary angle-closure glaucoma, by far the most common cause of angle-closure, results from relative pupillary block, an impedance to the flow of aqueous humor between the lens and iris from the posterior chamber to the anterior chamber. The reduced aqueous flow causes pressure in the posterior chamber to become higher than that in the anterior chamber. This disparity of pressures results in anterior bowing or convexity of the iris, narrowing of the angle, and, depending on the presence or absence of other incompletely understood factors, acute or chronic angleclosure glaucoma.

Relative pupillary block typically occurs in hyperopic eyes, which have a shorter than average axial length, a more shallow anterior chamber, a thicker lens, a more anterior lens position, and a smaller radius of corneal curvature. 4, 10, 14, 17, 46 Aside from crowding, the anterior segment structures and their anatomic relationships appear normal (Fig. 1). When pupillary block develops, the iris assumes a bombé configuration, creating an angle that is narrow throughout its approach. Indentation gonioscopy forces the entire iris posteriorly,

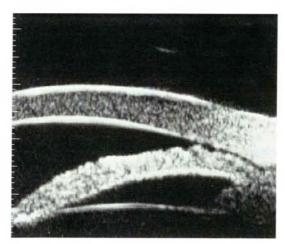


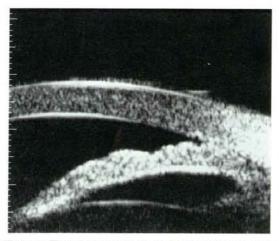
Figure 4. Ultrasound biomicroscopy (UBM) of an eye with relative pupillary block and a very narrow angle inlet when the eye is scanned with room lights on.

dark conditions, and the resultant appearances of the angle can be shown to the patient with graphic explanations (Figs. 4 and 5).

## ABNORMALITIES OF IRIS AND CILIARY BODY

### Plateau Iris

Plateau iris configuration refers to an angle appearance in which the iris root angulates forward and then centrally.<sup>47</sup> In many cases, the iris root is short and inserted anteriorly on



**Figure 5.** The same eye scanned with room lights out. The angle has closed. These photographs can be shown to the patient to serve as an excellent explanation of the potential for future angle-closure and the necessity for laser iridotomy.

the ciliary face so that the angle is shallow and narrow, with a sharp drop-off of the peripheral iris at the inner aspect of the angle. The iris surface appears flat, and the anterior chamber is of relatively normal depth, clinically.

Plateau iris syndrome refers to the development of angle-closure, either spontaneously or after pupillary dilation, in an eye with plateau iris configuration, despite the presence of a patent iridectomy or iridotomy. Some patients may develop acute angle-closure glaucoma.<sup>8, 15, 16, 50</sup>

In plateau iris, an anteriorly postioned ciliary body narrows the angle by physically supporting the iris root (Figs. 6 and 7).<sup>25, 33</sup> The level of the iris stroma with respect to the angle structures, or the "height" to which the plateau rises, determines whether or not the angle will close up completely to the level of Schwalbe's line or only partially, leaving the upper meshwork free of obstruction and leading to chronic angle-closure, a much more common situation in these patients than acute angle-closure (Fig. 8).<sup>18</sup>

Patients with plateau iris tend to be female, young (from 30 to 50 years of age), less hyperopic than those with relative pupillary block, and often have a family history of angleclosure glaucoma. When indentation gonioscopy is performed in such an eye, the ciliary processes prevent posterior movement of the peripheral iris. As a result, a sinuous configu-

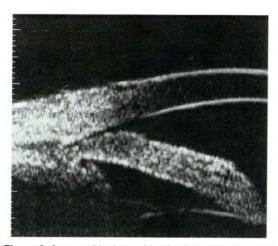
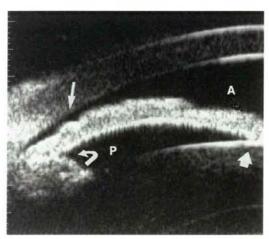


Figure 6. An eye with plateau iris after laser iridotomy (not shown in this photograph) scanned with room lights on. The anterior chamber is moderately deep, the iris and iris root are comparatively thick, and the iris surface is planar. The ciliary processes are positioned anteriorly, and the ciliary sulcus, although present, is minimally defined. The approach to the angle is relatively wide until the point at which the iris root angulates posteriorly, where the angle suddenly becomes extremely narrow.



**Figure 1.** Typical appearance of an eye with relative pupillary block. The peripheral anterior chamber (*A*) is shallow because of the presence of iris bombé, caused by increased pressure in the posterior chamber (*P*). The entire iris approach and angle inlet are narrowed (*straight arrow*). The ciliary sulcus (*curved arrow*) is normal. The arrowhead indicates the site of iridolenticular apposition.

opening the angle. If synechiae are absent, the angle opens widely.

Laser iridotomy is the definitive treatment for pupillary block angle-closure glaucoma, providing an alternative pathway for aqueous from the posterior chamber to reach the anterior chamber, thus eliminating the pressure gradient between the two chambers and allowing the iris to assume a planar configuration (Fig. 2). Plugging of the iridotomy by pigment or regrowth of the iris pigment epithelium (Fig. 3) can once again produce pupillary block.

When assessing a patient with a narrow angle for occludability, it is important to perform gonioscopy in a completely darkened room, using the smallest square of light for a slit beam to avoid stimulating the pupillary light reflex. With the lights on or the beam elongated, the quadrant of the angle to be assessed is first examined with the Zeiss fourmirror lens with no pressure on the cornea and with the patient looking sufficiently far in the direction of the mirror so that the examiner can see as deeply into the angle as possible. The beam is then squared so the pupil is not illuminated and the angle is observed while the pupil dilates in the dark. The narrowest quadrant, usually the superior angle (inferior mirror) is the one to observe. At least 2 minutes in total darkness should be allowed for the angle to close before assuming that it is not spontaneously occludable. If the angle closes under these conditions, opening the door of the exam room, turning on the light, or increasing the size of the slit beam will allow the pupil to constrict once again, so that the angle configuration in any quadrant can be compared in a light-dark-light situation. Patients often receive conflicting opinions from ophthalmologists and are both anxious about the possibility of developing angle-closure and confused about the necessity for iridotomy. UBM is extremely useful in these circumstances in explaining the situation to the patient. The eye is scanned both in light and

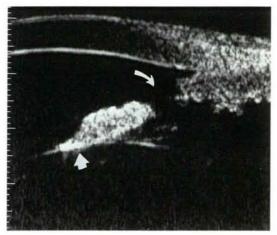
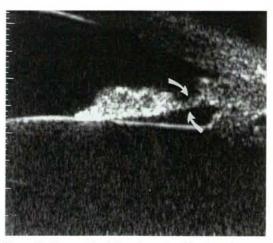


Figure 2. After laser iridotomy (*curved arrow*), iris configuration becomes planar. Iridolenticular apposition (*arrow*) is not eliminated by iridotomy.



**Figure 3.** Regrowth of iris pigment epithelium (between arrows) bridging an iridotomy. Iris bombé has not developed yet in this eye because there is still a small opening in the center of the regrowing pigment epithelium.



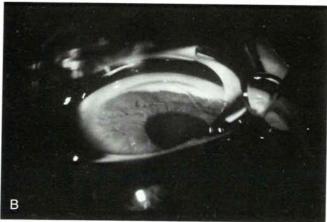


Figure 9. A 36-year-old man with a high plateau. *A*, Gonioscopy after laser iridotomy shows the angle to be closed up to the level of Schwalbe's line. *B*, With indentation, the deepest point of depression of the iris surface occurs approximately two thirds of the distance between the center of the pupil and the periphery. The iris then rose over the ciliary processes, and the angle barely opens, even with firm pressure. (*From* Ritch R: Plateau iris is caused by abnormally positioned ciliary processes. Journal of Glaucoma 1:23–26, 1992, with permission.)

### Iris and Ciliary Body Cysts

Iris and or ciliary body cysts can produce either acute or chronic angle-closure glaucoma.<sup>3</sup> These are usually easily diagnosed, as the angle is closed either in one quadrant or, if cysts are multiple, intermittently. However, when angle-closure mimicking pupillary block occurs, a high index of suspicion and careful gonioscopic evaluation are required.<sup>49</sup> UBM is extremely helpful in making the diagnosis in these patients (Figs. 13 and 14).

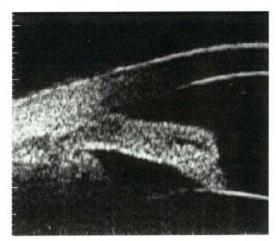
# ABNORMALITIES OF THE LENS AND ZONULES

Swelling of the lens may precipitate acute angle-closure glaucoma (phakomorphic glaucoma; Figs. 15 and 16). Again, some element of pupillary block may also be present in such patients. Phacomorphic glaucoma is often unresponsive to medical therapy, and paradoxical reactions to pilocarpine are common. Pilocarpine, even in elderly patients, increases

axial lens thickness and causes further shallowing of the anterior chamber.<sup>1</sup>

Peripheral iridoplasty is effective in breaking attacks of phakomorphic angle-closure.31 Very often, the eye is severely inflamed, as these patients have usually been referred after being treated unsuccessfully for a few days. Breaking the attack with iridoplasty allows 2 to 3 weeks for the inflammation and folds in Descemet's to clear, permitting cataract extraction under conditions much closer to ideal. Repeat angle-closure during the waiting time has not recurred in our experience; because the lens is stationary, any pilocarpine is immediately discontinued at the time of iridoplasty. Any element of pupillary block is treated as soon as possible (usually within 2 to 3 days) after breaking the attack.

In cases of anterior lens subluxation due to trauma or such hereditary disorders as Weill-Marchesani syndrome, peripheral iridoplasty is less successful because the pressure of the normal-sized lens against the iris continues, with or without an iridotomy, as long as the underlying cause is present. Cycloplegics are



**Figure 7.** The same eye in Fig. 6 scanned with room lights out. The pupil has dilated and the angle has closed. Argon laser peripheral iridoplasty can open the angle in such an eye by compressing and thinning the peripheral iris stroma.

ration results (sine wave sign), in which the iris follows the curvature of the lens, reaches its deepest point at the lens equator, then rises again over the ciliary processes before dropping peripherally. Much more force is needed during gonioscopy to open the angle than in

pupillary block because the ciliary processes must be displaced, and the angle does not open as widely (Figs. 9 and 10).

Except in rare younger patients (from ages 20 to 30), some element of pupillary block is also present. As a general rule, the older the patient, the less prominent the angulation of the peripheral iris and the greater the element of pupillary block. Iridotomy is successful at opening the angle when a component of pupillary block is present but periodic gonioscopy remains indicated; the angle can further narrow with age due to enlargement of the lens.

Continued appositional angle-closure in the presence of a patent iridotomy is an indication for argon laser peripheral iridoplasty. This procedure consists of placing a ring of contraction burns (500 µm spot size, 0.5 sec duration, 200-400 mW power) circumferentially on the peripheral iris in order to contract the iris stroma between the site of the burn and the angle, thus widening the angle itself (Figs. 11 and 12). 31, 32, 34, 37, 52 Histopathologic examination suggests that the short-term effect is related to heat shrinkage of collagen and the long-term effect secondary to contraction of a fibroblastic membrane in the region of the laser application. 39

Figure 8. Schematic representation of plateau iris. The angle is occludable when the pupil is dilated, but it is at the height of plateau (the extent to which the iris stroma protrudes anteriorly), which determines the level of the angle wall that will be occluded and whether the IOP will rise. A, Complete plateau iris syndrome. The iris will occlude the trabecular meshwork up to Schwalbe's line and IOP will rise. B and C, Incomplete plateau iris syndrome.The iris will occlude the angle to the level of the midmeshwork. The lower the level of meshwork that the iris reaches, the less likely a rise in IOP will occur. D. Low plateau. The angle will close only to the top of the scleral spur. (From Lowe RF, Ritch R: Angle-Closure glaucoma: Clinical types. In Ritch R, Shields MB, Krupin T (eds): The Glaucomas. St. Louis, CV Mosby Co, 1989, pp 839-853; with permission.)

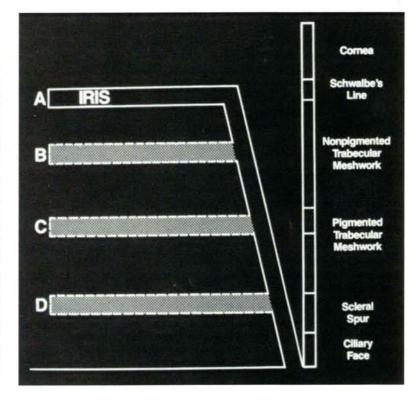






Figure 10. A 30-year-old woman with a midlevel plateau. A, Before indentation, the angle is closed to midtrabecular meshwork. The iris assumes a characteristically flat approach to the angle. B, With indentation, the deepest displacement of the iris occurs at the lens equator. More angle structures are seen in this patient compared with the patient in Figure 9 because the plateau is lower and the ciliary processes are not as prominent, so that there is less resistance to the pressure of indentation. The angle opens only with difficulty and remains narrow (sine wave sign). (From Ritch R: Plateau iris is caused by abnormally positioned ciliary processes. Journal of Glaucoma 1:23-26, 1992; with permission.)

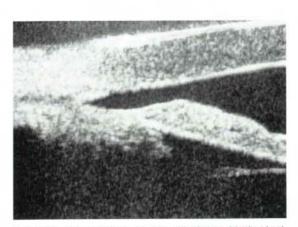


Figure 11. An angle from an eye with plateau iris that had continued appositional angle-closure after laser iridotomy underwent argon laser peripheral iridoplasty. The iridoplasty burn has compressed and thinned the peripheral iris stroma, and thereby "scooped out" the peripheral iris to create a space between iris root and trabecular meshwork, thus opening the angle. Note that the position of the ciliary processes, in this case extending quite anteriorly, is unchanged.

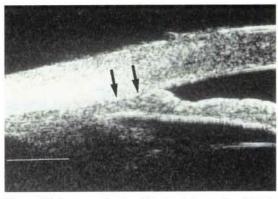


Figure 12. An example of an iridoplasty burn placed insufficiently peripheral on the iris surface. The compaction of iris stroma does not affect the angle, which remains closed (arrows).

useful if the zonules are intact, but these may not always be so.<sup>38</sup> A more complete discussion of this subject can be found in the literature.<sup>12, 36</sup> If not treated in time, forward lens movement can lead to malignant glaucoma.

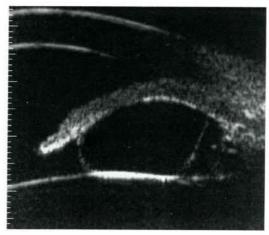
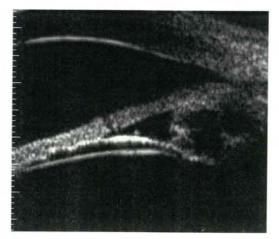


Figure 13. A large intraepithelial iris cyst causing angleclosure.



**Figure 14.** The same eye in Figure 13 after laser iridotomy. Smaller, peripheral iris-anterior ciliary epithelial cysts are still present.

## ABNORMALITIES POSTERIOR TO THE LENS

### Malignant Glaucoma

Malignant (ciliary block) glaucoma remains the most challenging cause of angle-closure glaucoma. It is a multifactorial disease in which many components may play varying roles:

- previous acute or chronic angle-closure glaucoma
- 2. shallowness of the anterior chamber
- 3. forward movement of the lens
- 4. pupillary block by the lens or vitreous
- 5. slackness of the zonules
- anterior rotation and/or swelling of the ciliary body
- thickening of the anterior hyaloid membrane
- 8. expansion of the vitreous
- posterior aqueous displacement into or behind the vitreous.<sup>5, 11, 40, 43, 44, 51</sup>

Analogous to pupillary block, in which the angle is occluded by iris because of a pressure differential between the posterior and anterior

chambers, a pressure differential is created posterior to the lens by aqueous diversion into the vitreous in ciliary block.

Primary malignant glaucoma has been regarded as a phenomenon resulting from expansion of the vitreous volume by posterior aqueous diversion, the basic cause of which remains unknown, and may occur in phakic, pseudophakic, and aphakic eyes. Anterior rotation of the ciliary body may or may not be present. Swelling or anterior rotation of the ciliary body with forward rotation of the lensiris diaphragm and relaxation of the zonular apparatus causes anterior lens displacement favoring direct angle-closure (Fig. 17).27 Accurate diagnosis and treatment are often more difficult when the initiating event is posterior to the lens-iris diaphragm. Secondary malignant glaucoma occurs when expansion of other posterior segment structures pushes the vitreous and the lens anteriorly, as may happen with intraocular tumors. Malignant glaucoma can also occur when a wound leak or overfiltration leads to a shallow anterior chamber with forward lens movement, blocking aqueous access to the anterior chamber.

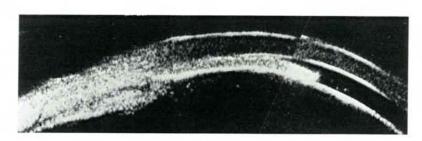


Figure 15. Composite UBM of an eye with phakomorphic glaucoma. The anterior chamber is extremely shallow and the lens wedges the iris into the angle and against the cornea. The pars plicata and pars plana can both be seen.

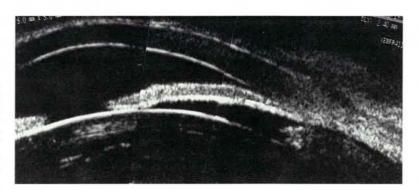
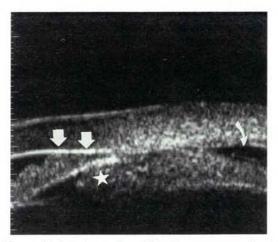


Figure 16. Composite UBM of an eye with pupillary block for comparison. Iridolenticular apposition occurs only in the sphincter region, and the central anterior chamber is of moderate depth. The ciliary sulcus can be seen between the tips of the ciliary processes and the iris root.

In predisposed eyes, miotic therapy can have a pronounced effect on lens position and trigger malignant glaucoma. <sup>9, 11, 20, 30</sup> Unequal anterior chamber depths, a progressive increase in myopia, or progressive shallowing of the anterior chamber are clues to the correct diagnosis.

Malignant glaucoma may occur following cataract surgery with posterior chamber intraocular lens implantation (Figs. 18 and 19).<sup>2, 6, 7, 19, 29, 45, 48</sup> The differential diagnosis includes pupillary block, choroidal hemorrhage, and ciliochoroidal effusion with anterior rotation of the ciliary body and secondary angle closure. Shallowing of the central anterior chamber occurs in pseudophakic malignant glaucoma but not in pupillary block (Fig. 20). Rupture of the anterior hyaloid face is usually curative and allows aqueous to move into the anterior segment. We have examined several patients with presumed aqueous midirection in whom an annular ciliary body de-



**Figure 17.** Anterior rotation of the ciliary processes (*star*) has forced the peripheral iris against the trabecular meshwork (*arrows*). A shallow retrociliary effusion is present. (*curved arrow*).

tachment had caused anterior movement of the ciliary body. Whether a posterior diversion of aqueous flow is present in these disorders is unknown.

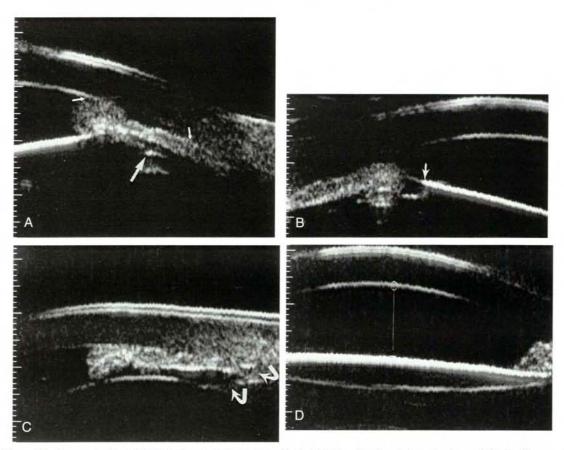
UBM images are consistent with accepted concepts regarding the posterior diversion of aqueous into the vitreous (see Figs. 18 and 19). Anterior rotation of the ciliary body is present and is compatible with an abnormality of the vitreociliary anatomic relationship leading to aqueous misdirection. The marked forward displacement of the posterior chamber lens and ciliary body reflects enlargement of the vitreous cavity due to admixture of aqueous and vitreous. Nd:YAG hyaloidectomy eliminates the blockage of access of aqueous to the anterior chamber, allowing the structures to move posteriorly, deepen the anterior chamber, and open the angle.

### SYNECHIAL ANGLE CLOSURE

Closure of the angle by peripheral anterior synechiae can be easily imaged by UBM and both the position and the extent of the synechiae determined (Figs. 21 and 22).

### CONCLUSION

High resolution, high frequency, anterior segment UBM is still in its infancy. It is enhancing our understanding of the underlying mechanisms involved in both open-angle and angle-closure glaucomas. UBM helps to differentiate the various disorders causing angle-closure glaucoma. It is proving to be useful in the understanding of both phakic and pseudophakic malignant glaucoma and synechial angle-closure. Other imaging modalities for the cornea, anterior segment, and posterior segment have been and are currently being (Text continued on page 292)



**Figure 18.** Pseudophakic malignant glaucoma in an eye with a posterior chamber intraocular lens. *A*, In the temporal angle, peripheral iridocorneal apposition is present (*small arrows*). The haptic is visible beneath the iris (*large arrow*). *B*, The nasal portion of the optic (*arrow*) is anterior to the iris. *C*, Anterior rotation of the ciliary body (*arrows*) in apposition to the peripheral iris. *D*, The central anterior chamber is shallow. (*From* Tello C, Chi T, Shepps G, et al: Ultrasound biomicroscopy in pseudoaphakic malignant glaucoma. Ophthalmology 100:1330–1334, 1993; with permission.)

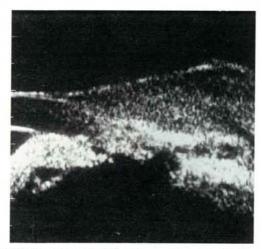


Figure 22. An eye that had undergone trabeculectomy and that, on gonioscopy, appeared to have the ostium occluded by iris. UMB, however, shows the iris to by synechially opposed to the anterior meshwork, whereas the ostium posterior to it is open and leads into a channel created by the scleral flap. The bleb is diffusely edematous without cyst formation.

developed. The next decade should prove to be to ocular imaging what the 1980s was to the development and use of the laser.

### ACKNOWLEDGMENT

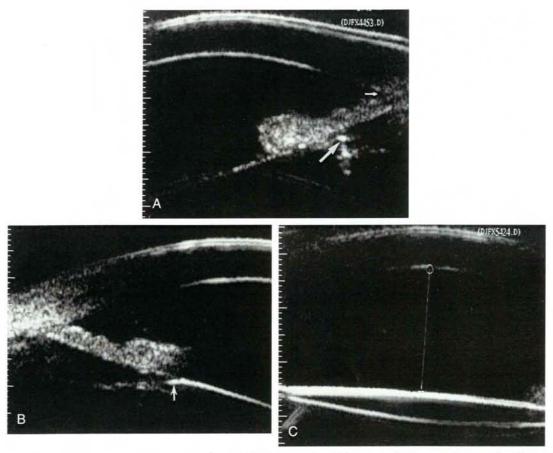
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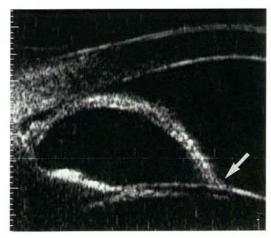
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**Figure 19.** The same eye as in Figure 19, after Nd: YAG anterior hyaloidectomy. *A*, The angle is open (*small arrow*) and the haptic has moved posteriorly (*large arrow*). *B*, The nasal portion of the optic (*arrow*) is posterior to the iris. *C*, The central anterior chamber is deep. (*From* Tello C, Chi T, Shepps G, et al: Ultrasound biomicroscopy in pseudoaphakic malignant glaucoma. Ophthalmology 100:1330–1334, 1993; with permission.)



**Figure 20.** Pseudophakic pupillary block. Posterior synechiae to the lens optic (*arrow*) led to extreme iris bombé. The anterior chamber is deep.

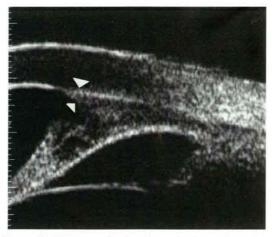


Figure 21. This eye with chronic angle-closure is seen to be synechially sealed. The sharp edge of the synechia is demarcated by the arrowheads.

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