

Glaucoma Surgery and Aqueous Outflow

How Does Nonpenetrating Glaucoma Surgery Work?

BLEBS. SHALLOW CHAMBERS. Bleb leaks. Flat chambers. Dellen. Blebitis. No bleb. Late failure. Hypotony. Choroidal effusions. Maculopathy. Is there a better way? If the problem is in the meshwork, why do we cut a hole in the eye?

Viscocanalostomy and deep sclerectomy are surgical procedures for glaucoma that have been designed to avoid some of the complications of conventional glaucoma surgery.^{1,2} The concept of nonpenetrating glaucoma surgery was first introduced in 1962, and variations have been described since then.^{3,4} Viscocanalostomy is reported to lower intraocular pressure (IOP) without creating a filtering bleb.¹ Deep sclerectomy, a nonperforating filtration procedure, is reported to avoid shallow anterior chambers and the other early postoperative problems of conventional filtering surgery and also produce lower, more diffuse blebs.^{2,5-7} Both procedures involve fashioning a partial-thickness scleral flap and then removing a second layer of sclera deep to the initial flap. This unroofs Schlemm's canal and exposes Descemet's membrane. The resulting trabeculo-Descemet membrane acts as a semipermeable layer of tissue, allowing aqueous to percolate through it. In viscocanalostomy, after removal of the deep scleral layer, Schlemm's canal is cannulated and expanded with a viscoelastic material. Viscoelastic material is also injected into the region of excised sclera, or "scleral lake," to prevent healing.

By never entering the anterior chamber or removing the trabecular meshwork, hypotony, hyphema, and other complications are said to be avoided.^{1,2,6} Variations of these procedures include (1) removing the inner wall of Schlemm's canal and adjacent meshwork but leaving the inner meshwork intact and (2) placing a collagen implant in the filtration bed to prevent episcleral fibrosis.²

Do these procedures relieve the specific pathological problem of primary open-angle glaucoma (POAG)? Or do they function as simply another way to make a hole in the eye?

AQUEOUS OUTFLOW

Before discussing the potential IOP-lowering mechanism of nonpenetrating glaucoma surgery, a brief review of traditional thought on the mechanisms of aqueous outflow is worthwhile. Most aqueous humor from the anterior chamber leaves the eye through the "conventional" outflow pathway—the anterior chamber to the trabecular meshwork, Schlemm's canal, and collector

channels—before entering the systemic venous circulation in the episcleral veins. While this pathway accounts for most aqueous outflow, up to 30% may leave the eye through the uveoscleral, or "unconventional," outflow pathways.⁸ Although use of prostaglandin-like medications can dramatically increase the amount of aqueous traversing the uveoscleral pathways, the abnormal resistance to aqueous outflow in open-angle glaucoma is found in the trabecular meshwork. The increased IOP found in glaucoma is caused by an increase in aqueous outflow resistance within the drainage pathways and not by excess secretion of aqueous humor.^{9,10}

The Normal Eye

Resistance of the trabecular meshwork to aqueous outflow in the normal eye was assessed by Grant¹⁰ nearly 4 decades ago. In a now classic experiment, a modified scalpel was used to incise the trabecular meshwork of enucleated normal eyes, measuring outflow resistance before and after each cut. The trabecular meshwork consists of 3 layers of tissue: nearest the anterior chamber is the uveal meshwork, which resembles a network of collagen cords; next is the corneoscleral meshwork, which is a series of flat lamellae or sheets; and finally is the juxtacanalicular tissue (JCT) adjacent to Schlemm's canal. Grant found that incision of the inner layers of the meshwork—the uveal and proximal corneoscleral layers—did not affect outflow resistance. A deeper incision through the entire meshwork and into Schlemm's canal, however, eliminated 75% of the normal outflow resistance.¹⁰

Juxtacanalicular Tissue. The deeper meshwork incised by Grant¹⁰ included the JCT near Schlemm's canal and the endothelial cell lining of the canal itself. The JCT contains a mixture of cells, extracellular matrix, and aqueous pathways that appear as empty space under electron microscopy. The extracellular matrix contains basement membrane material, proteoglycans, and glycosaminoglycans. With its small openings and tortuous flow pathways, the JCT is expected to be the principal site of outflow resistance,^{10,11} although this opinion is not universally shared. Despite the small and tortuous aqueous flow pathways in the JCT, theoretical calculations suggest that it contains too much optically empty space to account for the measured outflow resistance of the eye.¹¹ If, however, the JCT were filled with an extracellular matrix gel such as glycosaminoglycans and proteoglycans, sufficient outflow resistance would be created to match that measured in the eye.¹¹

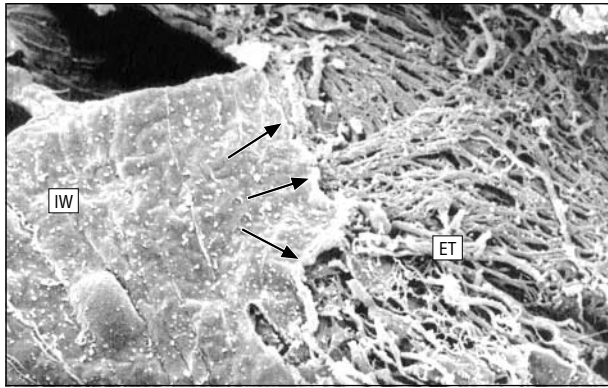


Figure 1. Scanning electron microscopic image of the inner wall of Schlemm's canal and underlying juxtacanalicular tissue. Schlemm's canal has been unroofed by removing the outer wall of the canal. Inadvertent damage occurred to some inner wall cells, removing them and exposing the elastic tendons of the juxtacanalicular tissue. The boundary of the damaged cell layer is indicated by arrows. IW indicates inner wall cells; ET, elastic tendons (original magnification $\times 1800$). Reprinted with permission from A. Mermoud and T. Shaarawy, eds. *Non-Penetrating Glaucoma Surgery*. London, England: Martin Dunitz Ltd; 2001:38.

Schlemm's Canal. Although the JCT contains large areas of optically empty space, as seen with electron microscopy, a continuous anatomic barrier to aqueous outflow does exist. This barrier is the endothelial lining of Schlemm's canal. Of interest is the "leakiness" of this cellular lining: it has the highest hydraulic conductivity of any endothelium in the body. This is probably because of the numerous micron-sized transcellular pores in the endothelial lining and the giant vacuoles with which they are often associated.¹²⁻¹⁷

Schlemm's canal is large enough that in its normal expanded state it should not generate appreciable outflow resistance. As IOP increases, the trabecular meshwork expands into the lumen of the canal, causing a concomitant narrowing of the lumen,¹⁷ raising the possibility that this collapse might cause a significant increase in outflow resistance. Throughout the canal, however, are collagenous septae between the inner and outer walls. The proximity of the septae to collector channels suggests that they would prevent collapse of the canal and occlusion of collector channels as IOP is increased.^{17,18} Although outflow resistance is indeed elevated by collapse of the canal, resistance levels at high IOPs are not as high as those found in glaucoma. In normal eyes, facility of outflow decreases from 0.40 $\mu\text{L}/\text{min}/\text{mm Hg}$ at 10 mm Hg to 0.28 at 50 mm Hg.¹⁹ In comparison, the facility of eyes with POAG is usually less than 0.13.^{18,19} Thus, collapse of Schlemm's canal is probably not the primary cause of glaucoma, but if it occurs it could make the problem worse.

The Glaucomatous Eye

Grant¹⁰ also studied a series of 8 enucleated glaucomatous eyes and found that an incision through the meshwork into Schlemm's canal eliminated all of the abnormal glaucomatous outflow resistance. The remaining scleral resistance was similar to that found in normal eyes.¹⁰ This finding of the abnormal outflow resistance residing in the trabecular meshwork is supported by the

success of laser and surgical procedures on the meshwork in glaucomatous eyes: laser trabeculoplasty, trabeculotomy, goniotomy, and direct removal of the trabecular meshwork (goniocyrtage) in adults with POAG.²⁰⁻²⁴ Surprisingly, despite the laboratory and clinical evidence, histologic examination of the meshwork of glaucomatous eyes does not reveal specific abnormalities or enough filling in of the aqueous pathways to account for the elevation in IOP.²⁵⁻²⁸ The few changes found seem to be an exaggeration of aging changes found in the normal eye. Studies²⁹⁻³³ have examined glycosaminoglycans and proteoglycans, phagocytosis by trabecular cells, and the size of Schlemm's canal yet have not found the "plug" that must occur in the meshwork in glaucoma. Elucidation of the pathophysiologic mechanism of POAG remains an area of intense research.

HOW DOES NONPENETRATING SURGERY WORK?

An examination of viscocanalostomy and deep sclerectomy reveals several features common to both of these nonpenetrating procedures. Analysis of each step in light of what is known about aqueous outflow resistance can lead to an understanding of how the procedures lower IOP. Both procedures share 2 major steps: fashioning a routine scleral trabeculectomy flap and then unroofing Schlemm's canal. Variations include creating a scleral lake after removing a layer of sclera deep to the initial trabeculectomy flap, removing the inner wall of Schlemm's canal, and expanding the size of Schlemm's canal by injecting viscoelastic material.

Unroofing Schlemm's Canal

Removal of the outer wall can cause damage to the inner wall of the canal (**Figure 1**).^{12,33,34} The septae, which bridge the inner and outer walls, can easily damage the inner wall when they are pulled away during the unroofing procedure (Figure 2). Such damage to the inner wall and adjacent JCT region effectively removes these regions and allows aqueous humor access to the canal.

Creation of Descemet's Window

Excising a deep layer of sclera and exposing Descemet's membrane may create a route for aqueous drainage that bypasses the meshwork. Descemet's membrane, however, is not permeable enough to relieve the elevated pressure of glaucoma.^{35,36} A window of exposed Descemet's membrane approximately 21×21 mm would be required to lower IOP to the low teens. The relative impermeability of Descemet's membrane is supported by the 41% goniopuncture rate after deep sclerectomy.⁵ If Descemet's membrane is thinned or partially removed during the procedure, however, its permeability would increase. When considered in conjunction with the meshwork, the permeability of the trabeculo-Descemet membrane is probably due to properties of the meshwork remaining after the unroofing of Schlemm's canal and not to the exposure of Descemet's membrane.

Scleral Lake

Removal of the inner layer of sclera creates an aqueous space, which in some cases may be the site for placement of a collagen implant. Creation of this scleral lake underneath the outer scleral flap has no theoretic effect on the abnormal outflow resistance found in glaucoma. Ultrasonic measurements of the area of the lake found no relationship to IOP in a series of human eyes.³⁷

Injection of Viscoelastic Material

Injection of viscoelastic material into the ends of Schlemm's canal is designed to enlarge the canal and lower IOP.¹ There is no theoretic basis, however, for relieving elevated IOP by expanding the lumen of Schlemm's canal. Injection of viscoelastic material will certainly dilate the canal lumen, but the viscoelastic material itself will probably not remain in the canal long enough to prevent healing of the cut ends of the canal. A more likely explanation is that expansion of the canal ruptures both the inner and outer endothelial walls of the canal, as demonstrated in the human eye (**Figure 2**) and in the monkey eye.³⁴ These ruptures extend into the juxtacanalicular connective tissue and may also rupture some of the meshwork itself.

Viscocanalostomy and deep sclerectomy likely function as "gentle" trabeculotomies, allowing aqueous to bypass the site of abnormal outflow resistance, the JCT. Aqueous probably enters the canal through inadvertent ruptures in the JCT and the inner wall of the canal and also through the unroofed outer wall. If the ruptured regions of the JCT and canal heal with time, surgery may fail in eyes that did not develop filtration blebs. This problem is starting to be seen in the increasing failure rates of deep sclerectomy with time. The failure rate has increased from 3% at 6 months after surgery to 29% at 24 months and 55% at 36 months if medications were not added.^{2,5} With medication, however, the success rates are higher.⁵

FUTURE GOALS

Our understanding of aqueous outflow mechanisms is incomplete, especially in understanding the pathogenesis of POAG. The ideal surgical procedure would address the as yet unknown pathological site of glaucoma and leave the eye otherwise intact. Direct removal of the trabecular meshwork or the abnormal portion of it makes the most theoretical sense, allowing aqueous to bypass the plugged juxtacanalicular region and gain direct access to Schlemm's canal and collector channels. This would normalize IOP and avoid creation of filtration blebs. Goniotomy and trabeculotomy are current surgical procedures that come close to this goal but are thwarted by healing and scarring of the incision in the meshwork in adults.^{2,21,38,39} Healing also occurs with nonpenetrating surgery, as reflected in the increased failure rates with time.^{2,5}

In practice, however, any procedure that is effective in lowering IOP, has minimal complications and adverse effects, and provides long-term success in pressure control would be helpful in the management of glaucoma. The current practice of filtration surgery, es-

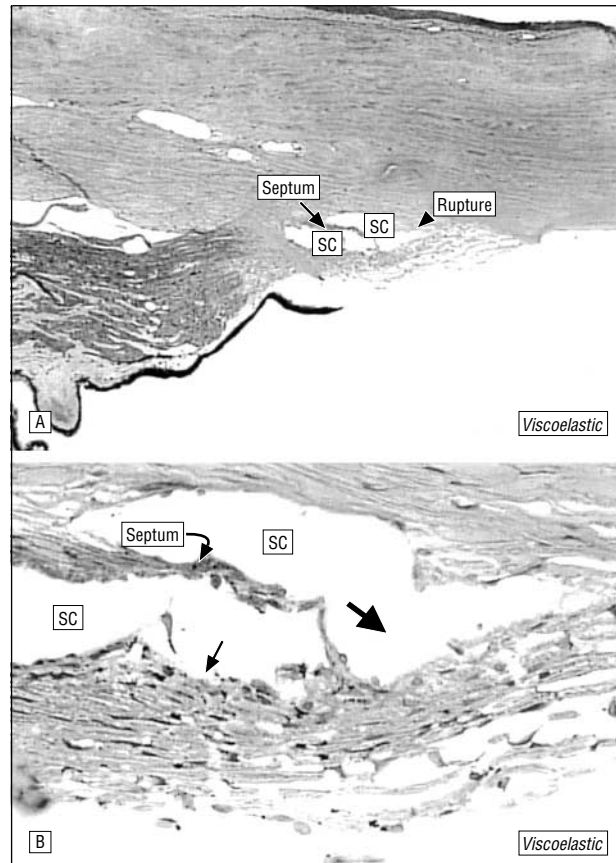


Figure 2. Viscocanalostomy in an autopsy eye. Schlemm's canal (SC) was dilated with viscoelastic material. Note the septum within the lumen of the canal. A, Dilatation of the canal, with rupture of the anterior portion of the canal wall, is apparent (arrowhead). The septum bridging the inner and outer walls of the canal is seen (arrow) (toluidine blue, original magnification $\times 40$). B, Higher magnification of Figure 2A. Rupture of the anterior wall of Schlemm's canal is seen (large arrow). Disruption of the inner wall of the canal is also apparent because of displacement of the septum (small arrow). Note the sharp kink in the septum (toluidine blue, original magnification $\times 400$). Reprinted with permission from A. Mermoud and T. Shaarawy, eds. *Non-Penetrating Glaucoma Surgery*. London, England: Martin Dunitz Ltd; 2001:46.

pecially with the use of antifibrotic agents such as mitomycin C, creates eyes that can develop conjunctival leaks, infection, and problems from filtration blebs. Nonpenetrating surgery may avoid these problems but will be subject to long-term failures as the eye continues its long-term healing and wound remodeling over the years. We look forward to improvements in the surgical control of pressure in the new millennium.

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Supported in part by research grant EY 07065 from the National Institutes of Health, Bethesda, Md (Dr D. H. Johnson); Research to Prevent Blindness Inc, New York, NY (Dr D. H. Johnson); Mayo Foundation, Rochester, Minn (Dr D. H.

Johnson); and research grant EY 09699 from the National Institutes of Health (Dr M. Johnson).

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A look at the past...

Santos Fernandez (Havana): Amblyopia Due to Peripheral Neuritis of the Optic Nerve Resulting From Intestinal Auto-Intoxication

In the late war, Santos Fernandez saw a number of cases of central scotoma with fundus changes like those seen in tobacco amblyopia, without other evidences of the abuse of tobacco or alcohol. In all the patients there were digestive disturbances with severe, long-continued diarrhea. Besides auto-intoxication, the great debilitation of the patients due to overexertion, worry and the like, played a role.

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