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Symposium: Microsurgery of the Outflow Channels

CLINICAL RESEARCH

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ADVANCES in microsurgical techniques and increased understanding of the pathogenesis of primary open-angle glaucoma have prompted the development of a variety of new glaucoma operations. All of them have tended to fractionate the filtering procedure so as to specifically bypass or eliminate the presumed sites responsible for the increased resistance to aqueous outflow.

Exposing Schlemm's canal directly to the anterior chamber aqueous may have been accomplished by trabeculo-canalectomy[1-3] or by trabeculotomy.[4-7] The trabecular meshwork has been classically accepted as the major site of resistance. Experimental evidence obtained in vitro showed that in normal human and rhesus monkey eyes, excision of the perilimbal sclera down to Schlemm's canal had little effect on outflow facility[8,9] (G. R. Keskey, MD, and B. Becker, MD, unpublished data). However, ab interno trabeculotomy in vitro increased outflow facility significantly, eliminating 75% to 90% of the resistance.[10,11] In vivo ab externo trabeculotomy in human eyes with primary open-angle glaucoma improved outflow facility and lowered intraocular pressure[12,13] (B. Becker, MD, unpublished data). Unfortunately, most observers found that the increased outflow facility was temporary. This may have been a consequence of regeneration, healing over, and scarring of the trabecular opening or of damage to the outer wall of Schlemm's canal.

In most of the in vivo series for which successful results have been reported, the trabeculotomy or trabeculo-canalectomy has been done by an ab externo approach. Therefore, questions about damage to the outer wall of Schlemm's canal and even through-and-through filtration have been difficult to resolve. In rhesus monkeys, the increase in outflow facility after ab externo trabeculotomy appeared to be only temporary, with evidence indicating regeneration or healing of the meshwork incisions.[14,15] Excised specimens from patients with primary open-angle glaucoma successfully controlled by trabeculo-canalectomy showed absence of filtration tissue or closed ends of Schlemm's canal. In addition, many of

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This investigation was supported in part by grants EY00004 and EY00336 from the National Eye Institute.

Presented at the Seventy-sixth Annual Meeting of the American Academy of Ophthalmology and Otolaryngology, Las Vegas, Nev, Sept 20-24, 1971.

the long-term trabeculo-canalectomy successes failed to show improved outflow facility. These findings offered evidence against the proposed basis for the operative procedures and also raised questions about the sites of resistance to outflow.

Dvorak-Theobold and Kirk,[16] as well as Krasnov and associates,[17] suggested that in many eyes with primary open-angle glaucoma, intrascleral pathways were obstructed peripheral to Schlemm's canal. Sinusotomy, or externalization of the canal to the sub-Tenon or subconjunctival spaces, was utilized to obviate these sites of resistance. Khasanova and his co-workers[18] demonstrated a decrease in resistance to aqueous outflow after sinusotomy in eyes with primary open-angle glaucoma. However, as Krasnov[17] and others emphasized, one could not rule out microscopic damage to the inner wall of Schlemm's canal. In addition, sinusotomy in the living eye might well eliminate or decrease that portion of the resistance to outflow of aqueous humor influenced by episcleral venous pressure. This could result in as much as an 8 to 10 mm Hg fall in intraocular pressure. In human eyes enucleated at autopsy, large sinusotomies increased outflow facility, but here again the questions of alterations or bulging of the inner wall have not been resolved.

To clarify the major sites of resistance in primary open-angle glaucoma, we made repeated quantitative measurements of outflow facility during each stage of trabeculo-canalectomy and other ab externo procedures in human eyes with uncontrolled primary open-angle glaucoma. A manometric constant pressure perfusion system was utilized (Fig 1). The anterior chamber was cannulated at the beginning of the operative procedure. Done with care, this presented no significant risk to the patient and only minimal inconvenience to the surgeon. The rate of flow of fluid into the anterior chamber divided by the differences between the perfusion pressure and intraocular pressure represented the outflow facility (microliters per minute per millimeters of mercury). For example, at various stages of the trabeculo-canalectomy procedure (conjunctival reflection, cutdown through episcleral tissue, raising the scleral flap, entrance of Schlemm's canal, and opening into the anterior chamber), outflow facility was measured. As might be expected, all resistance was lost when the anterior chamber was opened. However, the cannula permitted instant re-formation of the anterior chamber at any time during the procedure. In particular, the eye with a cannulated anterior chamber and constant pressure perfusion afforded a continuous flow of aqueous humor from Schlemm's canal throughout the procedure. This occurred in spite of retrobulbar injections, hyposecretion, and manipulative compression and softening of the globe. It permitted more ready identification of outflow channels during the operation. In the seven consecutive eyes with uncontrolled primary open-angle glaucoma tested to date, outflow facility did not increase through the stage of presumptive entrance into the canal of Schlemm. Admittedly, it is difficult to be certain one has entered the canal. However, the excised specimen from at least one of these eyes showed external opening of Schlemm's canal quite clearly (Fig 2). Therefore, in all of our patients so far tested, it appeared most unlikely that the site of maximum resistance was external to Schlemm's canal.

Using Schiøtz tonography on 18 eyes before and five minutes after removing a scleral strip almost to Schlemm's canal, Nesterov[19] noted no significant increases in outflow facility. In his series, increases in outflow facility were found, however, when Schlemm's canal was un-

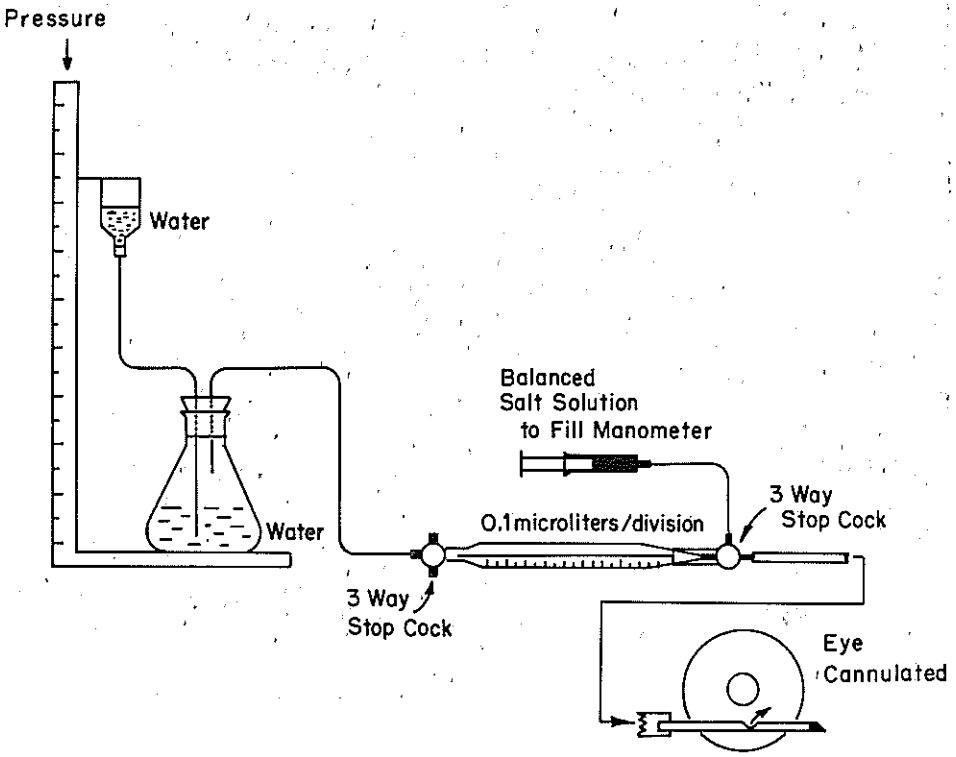

FIG 1—Constant pressure perfusion system for measuring outflow facility by determining amount of fluid entering cannulated eye per minute per millimeters of mercury of pressure head.

roofed. As in successful in vitro sinusotomies in eyes enucleated at autopsy, the Nesterov procedure involved large openings (8 to 14 mm long) in Schlemm's canal. In our in vivo experiments where no increase in outflow facility was noted, Schlemm's canal was never opened more than 2 to 3 mm. Microscopic damage to the trabecular meshwork or bulging and leakage of the inner wall of Schlemm's canal would be more apt to occur with the larger openings in Schlemm's canal both in vitro and in vivo.

More difficult to investigate was the possibility that collapse or compression of Schlemm's canal was an important pathophysiologic mechanism in primary open-angle glaucoma.[19-24] Recent evidence for this view stemmed from the decrease in outflow facility in vitro associated with raising perfusion intraocular pressure,[21] the increase in outflow facility induced by increasing episcleral venous pressure,[20] and the old observation of absence of reflux of blood into Schlemm's canal in primary open-angle glaucoma.[22,24,25] Wide externalization of the canal of Schlemm as in sinusotomy might well decrease the resistance to outflow by eliminating compression of the trabecular meshwork against the outer wall of the canal. In our manometric experiments with small entry into the canal, such an effect might not be noted.

Of considerable interest to us was one eye with primary open-angle glaucoma in which a suture was introduced

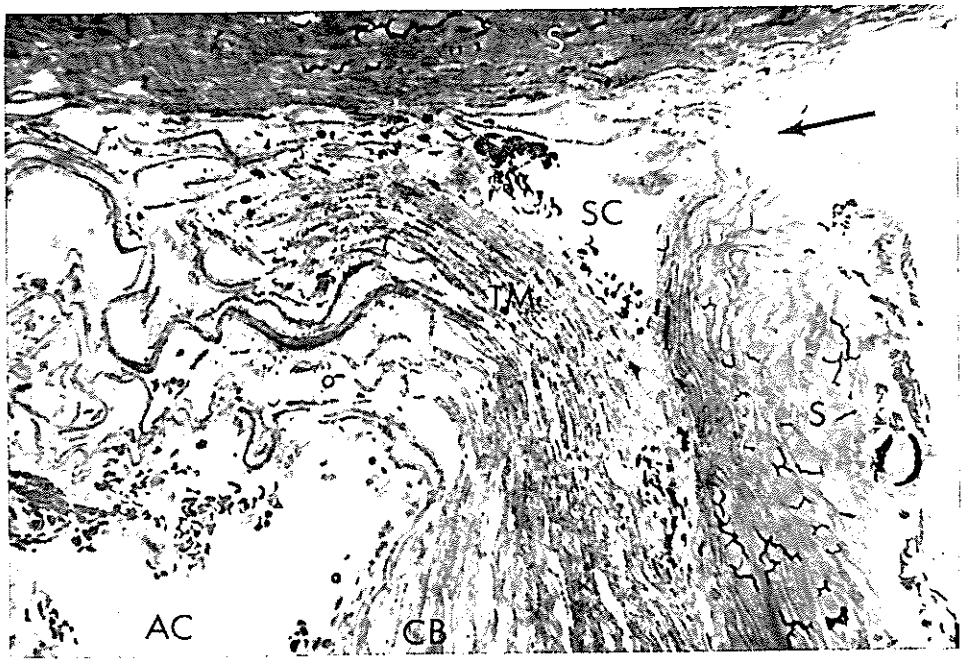

FIG 2—Excised trabeculo-canalectomy specimen illustrating incision through sclera (*S*) into (*arrow*) Schlemm's canal (*SC*). Note relationship of trabecular meshwork (*TM*), ciliary body (*CB*), and anterior chamber (*AC*) (toluidine blue, ×295).

into the canal in an effort to hold it open. In this patient the initial outflow facility, measured manometrically on the operating room table, was 0.02μl/min/mm Hg. After the canal of Schlemm was entered, the outflow facility was still 0.02μl/min/mm Hg, but after suture insertion, a facility of 0.09 μl/min/mm Hg was recorded. This returned to 0.02μl/min/mm Hg again on suture removal. More work must be done with respect to cannulation of the canal of Schlemm during surgery on patients with primary open-angle glaucoma in order to confirm or deny such facility changes. The information so obtained could be of enormous interest not only in regard to the "collapse" theory of impaired outflow facility but also in respect to its practical therapeutic applications.

Reflux of blood into the canal of Schlemm has been demonstrated readily in normal eyes but rarely in eyes with ocular hypertension or glaucoma.[22-25] These observations could be used as an argument for the collapse of Schlemm's canal in primary open-angle glaucoma. To explore this phenomenon further, we used a standard suction gonioprism device to demonstrate reflux of blood into Schlemm's canal. We selected normotensive corticosteroid-responsive individuals whose eyes showed reflux filling of Schlemm's canal with blood when their outflow facilities and intraocular pressure were normal. Subjecting these eyes to topical corticosteroids resulted in the expected marked decrease in outflow facility and rise in intraocular pressure. However, in 12 out of 18 patients tested to date, the elevated intraocular pressure did not prevent the complete backfilling of Schlemm's canal with blood. Thus, these were examples of decreased outflow facility and elevated in-

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