

Highlights From the Innovative Glaucoma Surgery Symposium

A summary of the main points of discussion.

BY GILLIAN McDERMOTT, MA, AND RICHARD A. LEWIS, MD

In early March 2009, *Glaucoma Today* convened the first Innovative Glaucoma Surgery Symposium. Attendance was by invitation only and included clinicians, scientists, and members of industry. The goal was to use educational, cutting-edge presentations as a starting point for lively discussion among the attendees and panelists. Dr. Lewis and Iqbal Iqbal Ahmed, MD, FRCSC, served as the course directors.

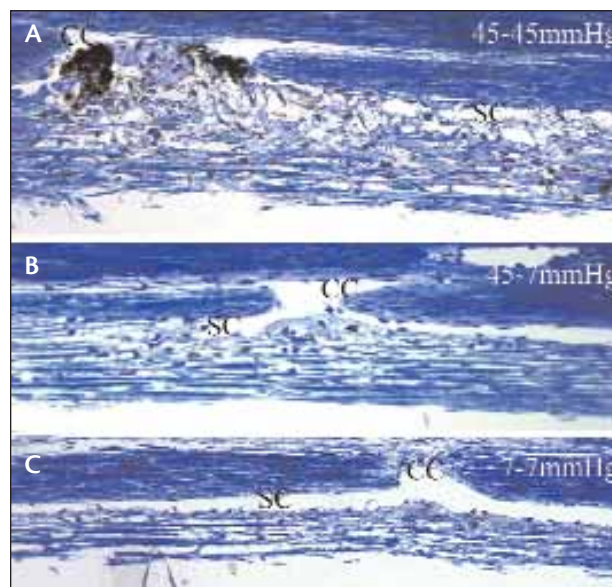
Held over the course of 1.5 days, the educational program focused on Schlemm's canal and suprachoroidal outflow as well as the relationship between innovation in the field of glaucoma, regulatory agencies, and financial investors. This article provides an overview of the discussion.

THE PHYSIOLOGY OF SCHLEMM'S CANAL AND SUPRACHOROIDAL OUTFLOW

During his introductory remarks, moderator M. Bruce Shields, MD, commented that glaucoma surgery has lagged behind corneal, retinal, and cataract surgery in terms of advances. He also stated that the problem with conventional glaucoma surgery is that it does not enhance the physiological route of aqueous outflow.

In his presentation, Murray Johnstone, MD, stated that surgeons must look at the aqueous vein in order to determine whether a procedure has achieved the desired effect. The ocular pulse serves as a pump with the trabecular meshwork as a mediator. He also raised questions about the effects of retained devices in the canal space.¹

Haiyan Gong, MD, PhD, reported that she and her fellow researchers have been studying normal autopsy eyes and those with primary open-angle glaucoma (POAG). They found the collapse of Schlemm's canal and herniation into the collector channel ostia to be common among the eyes with POAG, even when the eye was fixed at zero pressure. The longer the IOP remains high, Dr. Gong said, the less pli-



(Courtesy of Haiyan Gong, MD.)

Figure 1. Light microscopy images (20X) of the collector channel ostia regions of normal human eyes after an acute elevation in IOP. When the eye was continually perfused at 45 mm Hg, Schlemm's canal was collapsed, and the trabecular meshwork was herniated into the collector channel ostium (A) compared with the eyes perfused at other pressures (images B and C). When the eye was first perfused at 45 mm Hg and then the IOP was reduced to 7 mm Hg, the herniation into the collector channel ostia seen at 45 mm Hg in image A was reversed; only deformation of the trabecular meshwork was seen facing the collector channel ostium region. Schlemm's canal was wider in this eye (B) than in the one perfused continually at 45 mm Hg. When the eye was continually perfused at 7 mm Hg, Schlemm's canal was open, and no herniation was visible (C). Abbreviations: SC, Schlemm's canal; CC, collector channel.

(Courtesy of Carol B. Toris, PhD.)

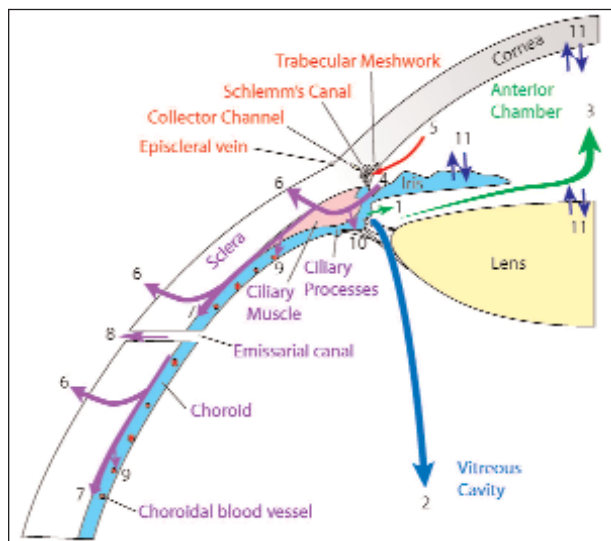


Figure 2. Aqueous humor is produced by the ciliary processes of the ciliary body and is secreted into the posterior chamber (1). Some of this fluid will move posteriorly through the vitreous cavity (2). The rest flows through the pupil into the anterior chamber (3). This fluid drains through the anterior chamber angle via one of two drainage pathways, the ill-defined uveoscleral outflow pathway (4) and the well-defined trabecular outflow pathway (5) through the trabecular meshwork, Schlemm's canal, collector channels, episcleral veins, and other structures not drawn. The uveoscleral outflow pathway starts with the ciliary muscle. From there, fluid can flow in many directions, including across the sclera (6), along the supraciliary and suprachoroidal spaces (7), through emissarial canals (8), into choroidal vessels (9) and vortex veins (not drawn), and into ciliary processes (10), where it is secreted again. Finally, there is some exchange of anterior chamber aqueous humor with the iris, lens, and cornea (11). Adapted by the author from Toris CB. Aqueous humor dynamics I: measurement methods and animal studies. The eye's aqueous humor. In: Civan MM, ed. *Current Topics in Membranes*. Vol. 62. Elsevier, Inc.: San Diego; 2008:193-229.

able the changes in the trabecular meshwork tissue seem to become. The disturbing implication of these findings is that normally reversible morphological changes after an acute elevation in IOP (Figure 1) may become permanent in cases of POAG. Occluded collector channel ostia may explain the variable success of surgical procedures intended to restore outflow into the episcleral venous system via the canal. In addition, Dr. Gong commented on the reflux of blood in the collector system; its presence, when noted in the canal, is an indication of a patent system.²

Carol Toris, PhD, and her colleagues have been studying the circadian rhythms of aqueous humor dynamics in normotensive and hypertensive human eyes (Figure 2). They found that, compared with daytime, IOP decreased at night

when measured while subjects were seated, but it increased when measured while patients were supine. Aqueous flow and outflow facility decreased at night. Dr. Toris reported that uveoscleral outflow appeared not to change during the 24-hour period, but she said that further study is needed to confirm this observation. Dr. Toris stated that the alterations in IOP due to changes in posture are probably related to episcleral venous pressure.³ Determining aqueous flow in vivo would be useful. Subsequent discussion centered on the role of measuring outflow and the use of an "angiogram" of Schlemm's canal to aid in the development of new glaucoma surgical devices and to improve the success of their implementation.

According to John Samples, MD, the number of collector channels is a matter of debate, with the figure ranging from 30 in some textbooks to as low as 15 per some researchers. The quantity of these channels has implications for the surgical devices under development for the treatment of glaucoma. Dr. Samples also predicted an increase over the next 10 years in the number of studies demonstrating the usefulness of stem cells in the treatment of glaucoma. These cells appear to adhere to the trabecular meshwork beams, he said.⁴ Growth in this area of research became more likely on March 9, when President Barack Obama signed an executive order lifting restrictions on the use of federal funding to perform research on human embryonic stem cells.

Dr. Samples also discussed CD44, which is cytotoxic to the trabecular meshwork and retinal ganglion cells. Where does CD44 go upon ablation of the trabecular meshwork? That question has implications for laser trabeculoplasty. Because misfolded proteins may be cytotoxic in the outflow system, will surgical procedures bypassing the trabecular meshwork result in a lack of cells that can serve as macrophages?⁴

SURGERY TO ENHANCE SCHLEMM'S CANAL AND SUPRACHOROIDAL OUTFLOW

E. Randy Craven, MD, stated that surgeons may choose to implant more than one iStent (Glaukos Corp., Laguna Hills, CA) for a greater reduction of IOP in a given eye once the FDA approves the device. He acknowledged that placing the iStent is challenging. The limitation is hitting an open area of Schlemm's canal, Dr. Craven said, because of anatomical changes in eyes with glaucoma and elevated IOP. He indicated that the iStent's implantation seems to produce greater IOP lowering when the device is located near a collector channel. He reported that placing more than one of the implants increases the chance of accessing Schlemm's canal and a collector channel.⁵

Ab interno trabeculotomy using the Trabectome (NeoMedix, Inc., Tustin, CA) lowers the IOP to approximately 15 mm Hg, regardless of the preoperative pressure,

reported Brian Francis, MD. Key to a successful procedure, he and another attendee agreed, is to perform the ablation slowly and carefully so as not to tear the tissue at the inner wall of Schlemm's canal. Potential causes for the procedure's failure include synechial closure of the cleft, obstruction of distal outflow, and, hypothetically, the growth of tissue over the cleft.⁶

After identifying Schlemm's canal, a major factor in successful canaloplasty is tensioning the canal, stated Dr. Lewis. In a prospective multicenter study, combined phacoemulsification and canaloplasty decreased IOP 2 mm Hg more on average than canaloplasty alone at 30 months. Comparing canaloplasty with trabeculectomy in his own series, Dr. Lewis cited the value of fewer side effects and less frequent postoperative visits with the former, a nonpenetrating procedure.⁷ The ensuing discussion focused on the idea of developing a formula to account for efficacy, side effects, and the direct and indirect costs of existing and new procedures in order to compare them.^{8,9}

Dr. Ahmed delivered a presentation on suprachoroidal procedures. He reported that the available data are limited. The location of major resistance to uveoscleral outflow is unknown, and there is no consensus on whether an ab interno or ab externo surgical approach is superior.¹⁰

IMAGING

It is possible to measure Doppler signals from Schlemm's canal and the collector channels, Joel Schuman, MD, reported, but the process is currently very difficult and only suitable for a laboratory environment. Researchers are able to confirm pulsations and measure the velocity of aqueous flow through various structures within the eye, he said.¹¹ In response to a question from the audience, Dr. Schuman replied that of great interest would be determining whether Schlemm's canal opens and closes and how aqueous flows through the canal and the collector channels.

Two-photon excitation microscopy—a fluorescence imaging technique that uses a titanium sapphire laser—permits visualization of tissue up to a depth of 1 mm, according to Malik Kahook, MD. The approach's limitations include scleral obstruction, the need for an objective lens, and the great expense of pulsed lasers. To date, two-photon microscopy has produced well-defined images of the cornea but not the trabecular meshwork. The advantage of the technique is its potential to link function and structure simultaneously.¹²

Dr. Ahmed presented a video on channelography, which he used as a means to predict the patency of downstream collector channels and surgical efficacy.¹³

REGULATION AND INVESTMENT

In her discussion of regulation in the specialty of glaucoma, Judy Gordon, DVM, noted that implants used to treat

nonrefractory glaucoma are considered class 3 devices. As such, according to current guidelines, these devices must undergo a randomized comparative trial in approximately 300 implanted patients and complete the FDA's premarket approval process to establish reasonable evidence of the devices' safety and efficacy. She urged glaucoma specialists and ophthalmologic societies to become involved with the International Organization for Standardization/American National Standards Institute committee developing guidance for class 3 devices in order to ensure that the process is effective.¹⁴

Surgical technologies and solutions remain a small piece of the glaucoma market, Bill Link, PhD, told attendees. If surgical solutions are not implemented earlier in the disease process among a greater number of patients, he said, innovation in this area will remain low, because the market will remain too small to support it¹⁵ (see the interview with Dr. Link on page 38). □

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