# **ARVO HIGHLIGHTS**

News from the organization's first meeting outside the state of Florida.

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s in years past, we were invited to share high-lights of this year's meeting of The Association for Research in Vision and Ophthalmology (ARVO), now a traveling meeting held this year in Seattle, Washington. As always, the ARVO abstracts discussed do not necessarily represent the most innovative or exciting research presented at the meeting or even that with the greatest impact. Instead, we elected to showcase projects that interested us.

#### NITRIC OXIDE-DONATING LATANOPROST

Latanoprost forever changed the glaucoma therapeutic landscape nearly 20 years ago. Now, clinical trials are evaluating a novel formulation of the drug coupled with nitric oxide. This gas potentiates cGMP production, which plays a role in aqueous humor dynamics. In a short (29 days) dose-ranging study, nitric oxide-donating latanoprost was found to lower IOP by a statistically significant 1 mm Hg more than regular latanoprost (8-9 mm Hg vs 7-8 mm Hg). Presumably, this greater efficacy is due to the liberation of nitric oxide once the complex enters the eye, with the effects of latanoprost and nitric oxide being at least partly additive.

Major clinical trials have demonstrated that every millimeter of mercury matters. Less clear is whether 1 mm Hg will be considered worth the cost difference between generic latanoprost and a branded product, should this or a similar drug come to market.

#### SELECTIVE LASER TRABECULOPLASTY

One of the reasons surgeons have transitioned from argon to selective laser trabeculoplasty (SLT) is that the latter procedure is much easier to perform and teach. Given the huge spot size of SLT, even residents whose gonioscopy skills are imperfect can usually hit the trabecular meshwork, as confirmed by two ARVO presentations.

The first was a retrospective series of 112 resident-performed SLTs at a Veterans Administration hospital.<sup>2</sup> Through 24 months of follow-up, mean IOP reductions were on the order of 4 mm Hg (22%). As the investigators noted, this amount was comparable to that reported in studies where SLT was performed by attending-level physi-

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cians. In a second retrospective study, researchers directly compared the outcome of 43 SLTs performed by residents versus 68 of the procedures performed by attending surgeons.<sup>3</sup> The reductions in IOP and medication and the rate of posttreatment IOP spikes were statistically equivalent between the groups.

We were also intrigued by the results of a small clinical trial comparing traditional SLT using a goniolens to transscleral SLT delivered to the trabecular meshwork by directly treating the limbus without a goniolens.<sup>4</sup> Both methods produced an equivalent IOP reduction on the order of 25% at 2 months. The latter technique would certainly make the procedure faster and easier, but more study is required to fully explore this novel approach.

### STRUCTURAL VERSUS FUNCTIONAL PROGRESSION

Detecting glaucomatous progression remains a major clinical challenge. A 7-year longitudinal study compared structural and functional progression in a cohort of 60 eyes (from a mixture of glaucoma suspects, patients with established glaucoma, and a few healthy individuals as well). Participants were regularly assessed with both visual field tests (mean of 12 per subject) and optical coherence tomography (OCT; mean of 27 per subject).<sup>5</sup>

Over the follow-up period, 41 eyes (68%) experienced disease progression. Interestingly, progression was detected in 47% of these by OCT alone, in 10% by fields alone, and in 12% by both. Of the seven eyes with glaucomatous progression by both structural and functional criteria, the disease advanced first by OCT in three, by fields in one, and by both simultaneously in the remaining three. This study confirms what other research has suggested: glaucoma advances dif-

ferently among patients, and clinicians must monitor both structure and function to identify disease progression.

#### **CAUTION ON PATIENTS' BREATHING**

It is generally understood that the IOP is higher if patients hold their breath during the measurement than if they breathe normally. A prospective study out of China suggests that breath holding has broader implications for glaucoma.<sup>6</sup> The investigators measured IOP and cerebrospinal fluid pressure before and during a Valsalva maneuver in neurology patients undergoing a scheduled lumbar puncture. The investigators then performed optic nerve imaging with the Heidelberg Retina Tomograph (Heidelberg Engineering GmbH) before and during the Valsalva maneuver in healthy volunteers.

Not surprisingly, the IOP increased by 2 mm Hg during the Valsalva maneuver, and cerebrospinal fluid pressure rose 10 mm Hg as well. Of interest to us was that the Valsalva maneuver also affected the topography of the optic nerve, with statistically significant decreases in optic cup volume, cup-to-disc area, and cup-to-disc diameter ratios as well as increases in neuroretinal rim volume and mean nerve fiber layer thickness. The effect of the Valsalva maneuver essentially improved Heidelberg Retina Tomograph parameters across the board. These findings underscore the importance of instructing patients to breathe normally during optic nerve imaging as well as during IOP measurements.

#### A SWITCH FROM PRESERVED TO PRESERVATIVE-FREE TIMOLOL

The toxic effects of preservatives on the ocular surface are well known, but the matter is particularly relevant to glaucoma patients who are on long-term topical therapy. Tear film dysfunction is a multifactorial process that commonly affects individuals with glaucoma. A group of researchers from Italy and Spain prospectively studied changes to the ocular surface in 132 glaucoma patients switched after 1 to 3 months from preserved to preservative-free timolol.<sup>7</sup>

To evaluate the health of the ocular surface, the investigators performed a complete eye examination with fluorescein staining, tear breakup time, Schirmer testing, and an Ocular Surface Disease Index questionnaire. They found no significant difference in IOP between the preserved and preservative-free  $\beta$ -blockers. In contrast, they found a statistically significant difference for abnormal fluorescein staining, tear breakup time (from 9.38 ±4.7 seconds at baseline to 10.64 ±4.7 seconds after 3 months), and Schirmer testing (from 12.9 ±5.96 mm at baseline to 14.2 ±5.87 mm after 3 months). The Ocular Surface Disease Index questionnaire showed an improvement in reported dryness and foreign body sensation.

## Weigh in on this topic now!



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<ul> <li>1. Did you attend the 2013 annual meeting of The Association for Research in Vision and Ophthalmology?  Yes No</li> </ul>
2. Do you plan to attend in 2014?  Yes  No

#### **DIGITAL IMAGING VERSUS FILM**

Electronic medical records have been widely adopted by US physicians' offices, and digital imaging is becoming standard practice. The advantages of the latter are many, but perhaps the most obvious are convenience and instantaneous feedback on image quality. That said, it remains important to ensure that the interpretation of stereo digital glaucomatous optic nerve features and of film imaging is

A group of researchers from the Universities of Calgary and Alberta imaged the eyes of patients with glaucoma, glaucoma suspects, or healthy patients to produce stereoscopic digital images and film slides.8 Images were graded by each of four glaucoma specialists in a random order using proprietary software (Secure Diagnostic Imaging). Weighted kappa was calculated to identify the reproducibility of digital imaging using film as the gold standard. Sensitivity, specificity, and area under the receiveroperating characteristic curve were also calculated for disc hemorrhage and notching. They evaluated 192 eyes with a weighted kappa (0.781; 95% CI, 0.740-0.823), indicating substantial agreement between digital and film imaging. There was less variability for high cup-to-disc ratios, suggesting better agreement for large vertical cup-to-disc ratios. Digital stereoscopic imaging demonstrates excellent reproducibility compared with stereo film for cup-to-disc ratio, notching, and disc hemorrhages.

#### **ENDOTHELIAL CELL LOSS AFTER** TRABECULECTOMY

Surgeons always discuss the possible harmful effects of glaucoma tube surgery on the cornea, including corneal decompensation, which, when severe, may necessitate a corneal transplant. These same effects are given less consideration before trabeculectomy surgery, but

perhaps that should change.

A group from Peru prospectively studied the changes in endothelial cell density (ECD) in 59 eyes of 53 patients undergoing trabeculectomy with mitomycin C during 1 year. To minimize secondary effects on endothelial cells, intracameral anesthesia was not used, and viscoelastic was injected to maintain the anterior chamber intraoperatively. Central corneal endothelial cells were studied with specular microscopy at baseline and up to 120 days after surgery.

The investigators found that mean ECD decreased 464 cells/mm<sup>2</sup> (17.86%) 30 days and 563 cells/mm<sup>2</sup> (21.67%) 120 days after surgery (P < .001). Greater ECD loss was observed in patients with postsurgical hyphema or a flat anterior chamber compared with patients who did not experience complications (-1,059 vs -456 cells/mm<sup>2</sup>; P < .001). ECD was also reduced in pseudophakic patients compared to those without prior cataract surgery (-571 vs -405 cells/mm<sup>2</sup>; P < .001). These data support the consideration of risk factors for corneal damage when deciding on surgical management for glaucoma.

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