

Journal Highlights

NEW FINDINGS FROM *OPHTHALMOLOGY*, *AJO* AND *ARCHIVES*

Ophthalmology

GS-101 Antisense Oligonucleotide Eyedrops for Corneal Neovascularization

September's *Ophthalmology*

Cursiefen et al. demonstrated that GS-101 antisense oligonucleotide stopped progression of corneal neovascularization and reduced regression of newly outgrowing blood vessels in patients who were previously unresponsive to conventional therapy.

In this double-blind, placebo-controlled phase 2 study, three groups of 10 patients were treated for three months at different doses (twice a day at 43, 86 or 172 µg/day total) and one group of 10 patients received placebo. The 86-µg/day drops proved the most effective, while the low dose tended to stabilize the neovascularization. There was no apparent benefit to the higher dose over the medium dose. In the placebo group, corneal neovascularization progressed in all patients.

The authors conclude that these results support the continuation of phase 2 studies and eventually the start of a phase 3 clinical trial.



Pentacam Used to Explain Hyperopic Shift After DSAEK

September's *Ophthalmology*

Reports have shown that Descemet's stripping automated endothelial keratoplasty (DSAEK) results in a mild postoperative hyperopic shift.

To determine whether changes in posterior corneal curvature are the cause of this shift, Scoria et al. used the Pentacam Scheimpflug imaging system to evaluate 34 eyes of 29 patients with Fuchs' endothelial dystrophy or pseudophakic bullous keratopathy undergoing DSAEK. Seven of these patients also had a cataract and underwent phacoemulsification with posterior chamber IOL implantation. The Pentacam evaluation was done one, three and 12 months postoperatively. The DSAEK grafts were significantly thicker in the periphery and midperiphery than in the center at all times—thickening diminished over time at all locations.

The authors state that this difference in thickness between center and periphery induced a change in posterior corneal curvature and resulted in a mild hyperopic shift. They recommend this shift be taken into account when cataract surgery and DSAEK are performed so as to help improve refractive outcome predictability.

Injection Frequency of Ranibizumab for Exudative Age-Related Macular Degeneration

September's *Ophthalmology*

Determining the optimal dosing schedule of anti-VEGF therapy for exudative age-related macular degeneration remains a challenge. In this retrospective, interventional case series of 131 eyes, Dadgostar et al. studied the effect of intravitreal ranibizumab monotherapy administered on an as-needed basis, and they examined the relationship between injection frequency and visual outcome.

Optical coherence tomography was used to determine the presence of intraretinal fluid, subretinal fluid, intraretinal cysts or increasing pigment epithelial detachment size. Eyes that received more frequent injections (less than a two-month average inter-injection interval) gained more vision (+2.3 lines at six months) than eyes receiving injections less frequently. Yet, resolution of intra- and subretinal fluid on OCT did not correlate with the degree of vision improvement.

The authors conclude that ranibizumab used on an as-needed basis may result in poorer treatment and significantly less visual gain. They call for a prospective study to confirm whether more frequent injections (once every one or two months, for example) result in a greater mean visual acuity improvement.

Wavefront-Guided PRK After RK

September's *Ophthalmology*

Koch et al. conducted a study to determine whether wavefront-guided photorefractive keratectomy (PRK) using prophylactic mitomycin C was a viable treatment alternative for correcting refractive errors in eyes that had undergone radial keratotomy (RK).

In this case series, the authors reviewed the records of 27 patients (32 eyes) with RK who underwent PRK, and they divided the patients into myopic PRK and hyperopic PRK based on their preoperative spherical equivalent.

In the myopic PRK group, uncorrected visual acuity improved by three lines on average, with 55 percent of patients being within 0.5 D and 100 percent of patients being within 1 D of attempted refraction.

In the hyperopic PRK group, uncorrected visual acuity improved by three lines on average, with 57 percent of patients within 0.5 D and 74 percent of patients within 1 D of attempted refraction. Six of the 32 eyes developed mild to moderate haze postoperatively. No eye lost more than two lines of BCVA.

Correcting Myopia With Light-Adjustable Lens Technology

August's *Ophthalmology*

In a pilot study involving 14 eyes of 14 patients undergoing cataract surgery, Chayet et al. demonstrated that residual myopia errors up to -1.5 D can be corrected using a light-adjustable lens (LAL).

LALs are made of a silicone-lens matrix containing photosensitive macromers that allow for postoperative, noninvasive adjustment of refractive power using ultraviolet light. The researchers implanted LALs that would purposely result in myopic errors of up to -1.5 D. They then treated the lens with a digital light device to induce the targeted myopic refractive change. Once this was achieved, the LAL was treated again to lock in the lens power. Of the 14 eyes, 13 eyes (92.9 percent)

achieved 0.25 D of the target refraction the first day after lock-in, with 100 percent of the eyes reaching 0.5 D of the targeted refractive adjustment at a nine-month postoperative follow-up.

The next step for these researchers is to refine nomograms to correct toric refractive error.

Intravitreal Bevacizumab for Refractory Cystoid Macular Edema

August's *Ophthalmology*

Results from a study by Arevalo et al. suggest that intravitreal bevacizumab is well-tolerated in patients with refractory pseudophakic cystoid macular edema (CME) after cataract surgery. At 12 month follow-up, treated eyes showed significant improvement in BCVA and a decrease in central macular thickness measured by optical coherence tomography (OCT).

In this multicenter study, 36 eyes of 31 patients with refractory CME received at least one intravitreal injection of 1.25 mg or 2.5 mg of bevacizumab and were followed for 12 months. The mean number of injections was 2.7, and the interval between injections was 15.1 weeks. Twenty-six eyes (72.2 percent) showed improvement of BVCA, and no eye experienced a deterioration of visual acuity. OCT showed that mean central macular thickness at baseline was 499.9 μm and this measurement decreased to a mean of 286.1 μm at 12 months.

Given these promising initial results, the authors call for further study with longer follow-up and a larger patient population.

High Incidence of Visual Impairment in Barbados Eye Studies

August's *Ophthalmology*

Hennis et al. found that the incidence of visual impairment is exceedingly high in black participants of the Barbados Eye Studies, with cataract, open-angle glaucoma and diabetic retinopathy representing the major causes of blindness.

The Barbados Eye Studies involved a cohort selected by random sampling

(40 to 84 years of age at baseline) who were reexamined after four and nine years. Men experienced a higher nine-year incidence of low vision and blindness, and these conditions were both positively associated with older age at baseline. The principal causes of bilateral blindness were age-related cataract (48.3 percent) and open-angle glaucoma (14.3 percent). Diabetic retinopathy and optic atrophy resulted in blindness in 8.7 percent and 7.1 percent of affected eyes, respectively.

For these populations, the authors call for blindness prevention programs involving education accompanied by screening, early detection and appropriate treatments.

Childhood Uveitis Described in Multicenter Report

August's *Ophthalmology*

Smith et al. conducted a retrospective chart review to better describe the disease characteristics and visual outcome of pediatric uveitis.

The researchers used records from three uveitis centers with different referral patterns and geographic locations to maximize the number and diversity of patients. Results from the 527 pediatric patients revealed a median age of 9.4 years at diagnosis, with idiopathic uveitis, juvenile idiopathic arthritis-associated uveitis and pars planitis constituting the leading diagnoses. Complications were frequent, with cystoid macular edema and hypotony resulting in the most significant visual impact. The prevalence of legal blindness was 9.23 percent at baseline, 6.52 percent at one year, 3.17 percent at three years, 15.15 percent at five years and 7.69 percent at 10 years. Hispanic patients were more likely to experience infectious uveitis and to present with vision loss even with non-infectious uveitis.

The authors conclude that the rate and spectrum of vision-threatening complications associated with pediatric uveitis are significant, and prospective studies are necessary to help determine which children are most at risk for this disease.

American Journal of Ophthalmology**Myopic CNV Treatment Comparison**September's *AJO*

Hayashi et al. studied myopic eyes with choroidal neovascularization treated with intravitreal bevacizumab and compared them with eyes treated with photodynamic therapy (PDT).

Forty-four eyes of 42 consecutive patients with myopic CNV treated with PDT and 43 eyes of 43 consecutive patients with myopic CNV treated with bevacizumab were evaluated. For control, 74 eyes of 71 consecutive patients with untreated myopic CNV were also evaluated. Thirty-nine of the bevacizumab-treated eyes (91 percent) had angiographic closure and 21 (49 percent) had an improvement of more than two lines in BCVA at one year. Bevacizumab-treated patients had significantly better BCVA than PDT-treated and control eyes at one year. The CNV size continued to decrease during the 12-month follow-up in the successfully treated bevacizumab eyes, and the size did not decrease in 65 percent of the successfully treated PDT eyes. Choriorretinal atrophy developed significantly more frequently in PDT-treated than bevacizumab-treated eyes.

The authors conclude that bevacizumab is more effective than PDT for treatment of myopic CNV. The differences in the regression pattern of CNV and the rate of choriorretinal atrophy probably explain the better BCVA in the bevacizumab-treated eyes

Corneal Epithelial Opacity in Dysfunctional Tear SyndromeSeptember's *AJO*

Chen et al. used laser scanning confocal microscopy to evaluate the appearance of the superficial corneal epithelium in patients with dysfunctional tear syndrome (DTS) and compare it with its appearance in an asymptomatic control group. The researchers then determined the correlations between microscopic findings and clinical severity parameters.

Thirty-one patients with newly diagnosed DTS and 21 asymptomatic control subjects were evaluated. Subjects with DTS were classified into four levels of clinical severity (DTS 1 through 4) based on the criteria of the Delphi dry eye panel report. Areas of single or multiple opaque superficial epithelial cells were measured as a percentage of the 400 x 400- μ m field area in four randomly selected confocal images from each eye.

The mean area of opaque superficial corneal epithelial cells was significantly greater in DTS patients than in normal subjects from the control group. Significant differences were observed between the DTS severity groups and the control group—except for the DTS 1 group. The area of opaque cells significantly increased with level of clinical severity. The confocal findings showed significant correlation with clinical severity parameters, including blurred vision symptoms, BCVA, conjunctival lissamine green staining scores, corneal fluorescein staining scores and videokeratoscopic surface regularity index.

The authors conclude that morphologic changes in the superficial corneal epithelium of DTS patients, as detected by laser scanning confocal microscopy, correlates with blurred vision symptoms and objective severity parameters. Objective confocal image analysis of the superficial corneal epithelium may prove useful for classifying DTS severity and for monitoring the efficacy of therapies

High-Speed Fourier-Domain vs. Conventional Time-Domain OCTAugust's *AJO*

Keane et al. compared the sensitivities of high-speed Fourier-domain optical coherence tomography (FD-OCT) with conventional time-domain optical coherence tomography (TD-OCT) for the detection of clinical findings important in the management of common vitreoretinal disorders.

In this study, FD-OCT scans (128 B-scans x 512 A-scans) were obtained in 50 eyes of 28 consecutive patients

undergoing conventional high-resolution TD-OCT scans (6 B-scans x 512 A-scans). The average sensitivity for detection of all features in this study was 94 percent for FD-OCT and 60 percent for TD-OCT. Clinical findings were identical between devices in 18 percent of cases. FD-OCT detected features that were not visible on conventional OCT scans in 78 percent of cases. FD-OCT was also more sensitive than TD-OCT for the detection of multiple findings, including diffuse intraretinal edema, subretinal fluid, large pigment epithelium detachments and subretinal tissue.

The greater sensitivity of FD-OCT systems for the detection of intraretinal and subretinal fluid may be of particular importance for the treatment of patients with neovascular age-related macular edema as well as many other retinal conditions.

Hyperopic Patients Implanted With Multifocal IOLsAugust's *AJO*

Patients with hyperopia have fewer alternatives to surgical refractive correction than patients with myopia. In a prospective, nonrandomized study, Fernandez-Vega et al. assessed the visual quality after bilateral implantation of the Acri.Lisa 366D IOL.

Eighty-five patients in the study had bilateral implantation (170 eyes). Patients were divided into two groups: low to moderate hyperopia (IOL power, 21 to 24.5 D) and high hyperopia (IOL power, 25 to 36 D). The researchers then determined monocular and binocular BCVA, best distance-corrected near visual acuity, binocular best distance-corrected intermediate visual acuity and distance contrast sensitivity under photopic and mesopic conditions.

At the six-month postoperative visit, there were no statistically significant differences between the two groups with regard to monocular and binocular BCVA. Monocular and binocular best distance-corrected near visual acuity were also comparable between groups. The mean binocular

best distance-corrected intermediate visual acuity changed significantly as a function of the distance of the test for both groups, and there were no statistically significant differences between groups at any distance. No differences were found between groups in binocular distance contrast sensitivity under mesopic and photopic conditions.

The authors conclude that bilateral implantation of the Acri.Lisa 366D in patients with high hyperopia provided a satisfactory full-range of vision comparable with that obtained in patients with low to moderate hyperopia.

Archives of Ophthalmology

Progression of RPE Alterations and Choroideremia

July's Archives

Renner et al. report clinical and functional findings in two female carriers of choroideremia who were followed for 11 and 17 years and who showed progression of fundus alterations. Follow-ups included repeated clinical and electrophysiologic examinations and fundus autofluorescence. Molecular analysis of the CHM gene was done by direct sequencing of the coding exons.

The two carriers showed marked pigmentary alterations in the periphery of the retina. In addition, one of the carriers presented with multiple small yellowish flecks in the macula. Both carriers developed subnormal 30-Hz flicker responses on full-field electroretinogram during follow-up, whereas electrooculography was normal. In both carriers, progression of fundus alterations was noted. Fundus autofluorescence showed multiple small flecks with reduced autofluorescence.

The authors conclude that fundus alterations in female carriers of choroideremia can progress over time and a mild cone dysfunction can develop. Multiple yellowish flecks can also exist in the macula. The typical mottled irregularity in fundus autofluorescence is a valuable diagnostic criterion that facilitates specific genetic testing.

Posterior Chamber Phakic ICL for Moderate to High Myopia

July's Archives

Kamiya et al. assessed the long-term clinical outcomes of the Visian implantable collamer lens (Staar Surgical) for moderate to high myopia.

The researchers included 56 eyes of 34 patients with myopic refractive errors of -4 to -15.25 D who underwent implantable collamer lens implantation and routine postoperative examinations. The researchers also assessed the safety, efficacy, predictability, stability and adverse events of the surgery.

LogMAR uncorrected visual acuity and logMAR BCVA were -0.03 ± 0.23 and -0.21 ± 0.09 , respectively, on four-year postoperative exams, and the safety and efficacy indices were 1.19 ± 0.25 and 0.83 ± 0.29 . At four years, 79 and 93 percent of the eyes were within 0.5 and 1 D, respectively, of the targeted correction. Manifest refraction changes of -0.24 ± 0.57 D occurred from one month to four years.

No vision-threatening complications occurred during the observation period.

Prevalence of Dry Eye Disease Among U.S. Men

June's Archives

Schaumburg et al. estimated the prevalence and risk factors for dry eye disease among a survey of U.S. men 50 years of age and older. Men who had a clinical diagnosis of dry eye or severe symptoms were counted as disease cases for the analysis. Prevalence estimates were also determined for the U.S. population and compared with those previously ascertained in a similar cohort of women. Finally, the authors examined associations of possible risk factors for dry eye disease.

There was a statistically significant increase in prevalence of dry eye disease with age, ranging from 3.9 percent among men 50 to 54 years of age to 7.67 percent among men 80 years of age and older. Men who had high blood pressure or benign prostatic hyperplasia were at a 28 and 25 percent

higher risk of dry eye disease, respectively. Men who used antidepressants, antihypertensives and medications to treat benign prostatic hyperplasia also had significantly higher risks of dry eye disease. The prevalence of dry eye disease in the United States was estimated at 4.34 percent, including 1.68 million men 50 years of age and older. This latter figure is expected to increase to over 2.79 million by 2030.

The authors conclude that dry eye disease is a prevalent problem among older men in the United States that is likely to grow. The inclusion of milder cases of dry eye disease would swell prevalence estimates considerably. Hypertension, benign prostatic hyperplasia and use of antidepressants are associated with an increase in the prevalence of dry eye disease among men.

Infliximab Therapy for Refractory Uveitis

June's Archives

Suhler et al. trialed the use of infliximab for patients with vision-threatening noninfectious uveitis who had failed therapy with corticosteroids plus at least one other immunosuppressive drug.

Early results of the study published in 2005 indicated that approximately three-quarters of patients demonstrated initial benefit from infliximab therapy after 10 weeks but that significant toxicity, including drug-related lupus and thromboembolic events, was possible.

The current study extends the results of the initial study to two years. Longer-term study demonstrated continued benefit, with approximately 60 percent of patients maintaining benefit each year in the study, and some patients maintaining benefit out to four years or more.

Ophthalmology summaries are written by Lori Baker Schena and edited by John Kerison, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. Archives of Ophthalmology summaries are written by the lead authors.

ROUNDUP OF OTHER JOURNALS

Identifying High-Risk Uveal Melanoma Through Genomic Profiling

Investigative Ophthalmology & Visual Science

2009;50:2572–2580

In uveal melanoma, 90 percent of cases metastasize to the liver with often lethal results. Even with successful treatment of the primary tumor, the survival rate is only 50 percent at 10 to 15 years. Recently, oncologists and ophthalmologists have looked into the possibility of developing adjuvant systemic treatments for patients who are at high risk for uveal melanoma. But how can the high-risk patient be identified? To answer that question, **Trolet et al.** analyzed genomic profiles in a series of 86 ocular tumors, as well as 66 liver metastases, to identify and design a genome-based classifier for metastatic risk assessment.

The investigators analyzed the series using a comparative genomic hybridization microarray. They performed a clustering—dividing the tumors into subgroups—and were able to observe a subgroup that had a high metastatic rate in the ocular tumors and the liver metastases. They also constructed a prognosis classifier that led to a classification accuracy of 85.9 percent.

The authors conclude that these results can help in the development of a DNA-based genomewide technique to serve as a prognostic tool for identification of high-risk patients in future clinical trials of uveal melanoma that involve adjuvant therapy.

Clinical Features Help Identify High-Risk Unilateral Retinoblastoma

Journal of Pediatric Hematology/Oncology
2009;31:325–329

In unilateral retinoblastoma, adjuvant therapy has been recommended for children at high risk for extraocular relapse following enucleation. While some pathologically defined risk

factors are obvious—such as invasion to the choroid, sclera and the optic nerve—identification of such factors as microscopic tumor residue can be challenging. Imaging tests may not be sensitive enough and resources for an adequate pathology examination may be limited.

Chantada et al. conducted a retrospective study to see whether it is possible to identify clinical features at the time of diagnosis that could possibly predict which patients have microscopically residual disease and other pathology risk factors.

The researchers conducted a retrospective analysis of 182 patients with unilateral retinoblastoma treated with enucleation from 1988 to 2006. Pathology risk factors included postlaminar optic nerve, massive choroidal invasion and scleral involvement, either alone or in combination.

The researchers also separately analyzed a higher-risk cohort within this subgroup. A multivariate analysis demonstrated that high IOP, glaucoma and, more specifically, glaucoma that led to buphthalmia were significantly correlated with the occurrence of both high-risk pathology risk factors and the occurrence of microscopically residual tumors.

These findings may help identify the subgroup of high-risk patients who could perhaps benefit from preoperative chemotherapy.

Partial Coherence Interferometry Provides No Clinical Advantage

Investigative Ophthalmology & Visual Science

2009;50:2547–2552

Does partial coherence interferometry (PCI) increase the accuracy of refractive outcomes after cataract surgery compared with the current generation of applanation ultrasound biometry (AUS)? According to findings from **Raymond et al.**, it does not.

The researchers conducted a controlled trial of 205 patients using the IOLMaster (Carl Zeiss Meditec) or Microscan Model 100A+ (Sonomed). The dependent variable was the mean absolute postoperative refractive error (MAE), while the independent variable was the biometric technique (either PCI or AUS) that was used to determine the IOL power to be implanted in the eye undergoing cataract surgery.

The MAE in patients with implanted PCI-calculated IOLs was 0.40 ± 0.37 D compared with 0.45 ± 0.41 D for patients with implanted AUS-calculated IOLs. Moreover, in an analysis of best possible outcomes, there was no statistically significant difference between MAE in these two groups of patients.

The researchers conclude that while PCI tends to be less time-consuming and more patient-friendly than AUS, the technique has a significant failure rate—this failure is especially significant with patients who have dense cataracts. They predict that studies that report an improvement of PCI over AUS will not be validated in future randomized clinical trials.

Roundup of Other Journals is written by Lori Baker Schena and edited by Deepak P. Edward, MD.

The Year In Review



The editors of the *American Journal of Ophthalmology*, *Archives of Ophthalmology* and *Ophthalmology* invite you to a review of interesting

research published during the year that has immediate clinical relevance to the profession.

The Editors' Choices Symposium

Tuesday, Oct. 27

Time: 8:30 to 10:30 a.m.

Location: West, Room 2002

Fee: No charge