

Journal Highlights

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

Ophthalmology

Intravitreal Bevacizumab Reduces Postvitrectomy Hemorrhage

October's *Ophthalmology*

In a clinical trial involving 68 eyes of 68 patients with proliferative diabetic retinopathy, **Ahmadieh et al.** found that intravitreal bevacizumab (IVB) one week prior to pars plana vitrectomy decreases the incidence of early postvitrectomy hemorrhage. In addition, it may result in resolution of the hemorrhage, preventing the need for surgery.

Thirty-five eyes in the IVB group received 1.25 mg intravitreal bevacizumab, and 33 eyes in the control group had a sham procedure using a topical antiglaucoma medication. The incidence of postvitrectomy hemorrhage one week and one month after surgery was significantly lower in the IVB group. No significant injection-related complications were reported.

While the trial demonstrated the efficacy of IVB in treating these patients, no conclusions can be drawn about the safety of the procedure due to the small number of cases involved.



Intracameral Cefuroxime to Prevent Endophthalmitis

October's *Ophthalmology*

Sharifi et al. utilized a cost-effectiveness model to evaluate different antibiotic options used to prevent endophthalmitis following cataract surgery. The researchers chose intracameral cefuroxime as the base comparator since the antibiotic was the subject of at least two large clinical studies.

They analyzed the threshold efficacy that might be reasonably expected to justify observed cost differences between intracameral cefuroxime and alternative antibiotic choices. The cost-effectiveness ratio for intracameral cefuroxime was \$1,403 per case of postoperative endophthalmitis prevented.

By comparison, the least expensive topical fluoroquinolone in the study, ciprofloxacin, would have to be greater than eight times more effective than intracameral cefuroxime to achieve cost-effective equivalence.

The researchers conclude that intracameral cefuroxime is relatively cost-effective in preventing endophthalmitis following cataract surgery and that this cost-effectiveness model should serve as a framework to help clinicians, patients, hospitals and other health care stakeholders evaluate the relative cost and clinical effectiveness of different treatments.

Natural History Model of Exudative Age-Related Macular Degeneration

October's *Ophthalmology*

Shah and Del Priore used a previously developed natural history model to compare rates of visual loss in untreated eyes with wet AMD classified as predominantly classic, minimally classic and occult with no classic (based on fluorescein angiography).

Their meta-analysis of prior clinical trials involved plotting visual acuity data of untreated control eyes for each study from appropriate subgroups. This was done on a double reciprocal (Lineweaver-Burk) plot of $1/[\text{letters lost}]$ vs. $1/[\text{months}]$. A horizontal translation factor to shift each data subset was introduced to correct for differences in the time of entry into clinical trials. They next established the coefficient of determination before and after adjustments for visual acuity at time of enrollment.

Using this analytic model, the researchers demonstrated a strong correlation for visual acuity as a function of time that is independent of the fluorescein angiographic classification of a lesion.

This finding suggests that initial protocol visual acuity, rather than angiographic classification, represents the major determinant of the behavior of visual acuity as a function of time in exudative AMD.

Older Glaucoma Patients at Risk for Driving Cessation

October's *Ophthalmology*

Ramulu et al. have found that bilateral glaucoma represents a strong risk factor for driving cessation in older individuals. The researchers conducted a cross-sectional analysis of the Salisbury Eye Evaluation (SEE), a cohort study of older residents of the Eastern Shore of Maryland. Participants reported their driving habits during each of four study rounds spanning the course of eight years.

The current study used data from the fourth round of SEE to assess the impact of glaucomatous visual field loss on driving cessation and limitation. Multivariable regression analysis showed that bilateral, but not unilateral, glaucoma patients were more likely to no longer be driving when compared to those without glaucoma. The odds that bilateral glaucoma patients were no longer driving doubled for every 5 dB of visual field worsening in the better eye.

The researchers conclude that these findings indicate a significant social impact caused by glaucomatous visual field loss. Consequently, preventing glaucoma from progressing to more advanced stages could have a major impact on older populations.

American Journal of Ophthalmology

Corneal Powers Obtained From Four Different Devices

October's *AJO*

Ophthalmologists use different devices to measure corneal refractive (as opposed to structural) power in preparation for refractive or cataract surgery. But are they comparable? Shirayama et al. assessed the repeatability and comparability of anterior corneal power values obtained from the Galilei Dual Scheimpflug Analyzer, Humphrey Atlas corneal topographer, IOLMaster and a manual keratometer.

Three sets of corneal power mea-

surements were obtained by a single observer in 20 patients for each of the four devices. The repeatability of the three measurements from each device was evaluated by means of coefficient of variation, standard deviation and intraclass correlation coefficient. An analysis of variance was used to compare the differences in corneal powers among devices.

For each device, the coefficient of variation of repeated measurements was lower than 0.22 percent. The standard deviation of three repeated measurements ranged from 0.042 to 0.096 D. The intraclass correlation coefficients were higher than 0.99 in all devices. Mean central corneal powers were 43.80 D, 43.88 D, 43.92 D and 43.76 D for the Galilei, Atlas, IOLMaster and manual keratometer, respectively. Standard deviations of the differences between devices ranged from 0.07 D for Galilei and IOLMaster to 0.14 D for Galilei and Atlas. For astigmatism, the mean astigmatism values for the Galilei, Atlas, IOLMaster and manual keratometer were 0.54 D at 84 degrees, 0.51 D at 88 degrees, 0.62 D at 88 degrees and 0.52 D at 87 degrees, respectively.

The authors conclude that the corneal power measurements from these four devices were highly reproducible, comparable and correlated.

Azathioprine for Ocular Inflammatory Diseases

October's *AJO*

Alternatives to systemic corticosteroids are frequently required or desirable in treating ocular inflammatory disease. In this cohort study, Pasadhika et al. evaluated the treatment outcomes of azathioprine for noninfectious ocular inflammatory diseases.

They reviewed the medical records of 145 patients starting azathioprine as a sole noncorticosteroid immunosuppressant at four tertiary uveitis services. The main outcome measures included control of ocular inflammation, sustained control after tapering prednisone to less than 10 mg/day and

discontinuation of treatment because of side effects. Among 145 patients (255 eyes) treated with azathioprine, 63 percent had uveitis, 23 percent had mucous membrane pemphigoid, 11 percent had scleritis and 3 percent had other inflammatory diseases. By Kaplan-Meier analysis, 62 percent of patients with active disease initially gained complete inactivity of inflammation sustained over at least 28 days within one year of therapy, while 47 percent of patients tapered systemic corticosteroids to less than 10 mg/day while maintaining control of inflammation within one year of therapy. Treatment success was most common for intermediate uveitis (90 percent with sustained inactivity within one year). Over the median follow-up of 230 days, azathioprine was discontinued at a rate of 0.45 per person-years because of side effects, ineffectiveness, disease remission or unspecified causes.

The authors conclude that azathioprine was moderately effective—especially in intermediate uveitis—as a single corticosteroid-sparing immunosuppressive agent in terms of control of inflammation and corticosteroid-sparing benefits. Treatment, however, required several months to achieve its goals. Treatment-limiting side effects occurred in approximately 25 percent of patients within one year, but these side effects were typically reversible.

Imaging Fundus Autofluorescence in Idiopathic Macular Telangiectasia

October's *AJO*

The etiology of type 2 idiopathic macular telangiectasia (IMT) remains unknown, but newer imaging techniques can help elucidate the pathogenesis. Wong et al. used multiple imaging methods to investigate patients with type 2 IMT at different disease severity stages so as to characterize and categorize disease progression through the full spectrum of disease phenotypes.

In this case series, 12 patients (22 eyes) with type 2 IMT were examined with fundus photography, angiogra-

phy, OCT imaging, fundus autofluorescence (FAF) and microperimetry testing in an institutional setting. Eyes examined by multiple imaging methods were classified into five proposed categories (0 through 4). Category 0 (fellow) eyes had normal results on all imaging methods. Category 1 eyes had increased foveal autofluorescence on FAF imaging as the only imaging abnormality. Category 2 eyes had increased foveal autofluorescence together with funduscopy and angiographic features typical of type 2 IMT. Category 3 eyes had additional evidence of foveal atrophy on OCT. Category 4 eyes had all the above features plus clinically evident pigment clumping. FAF signal increased in intensity in the foveal region from category 0 through category 3, whereas category 4 eyes demonstrated a mixed pattern of increased and decreased FAF signal.

The findings outline a sequence of changes seen with multiple imaging methods in advancing stages of disease. An increase in foveal autofluorescence is an early anatomic change in type 2 IMT that may precede typical clinical and angiographic changes. Loss of macular pigment density in the fovea and a changing composition of fluorophores in the retinal pigment epithelium may underlie these changes on FAF in the fundus.

Fourier-Domain vs. Time-Domain OCT for Glaucoma Detection

October's *AJO*

Newer imaging techniques may provide an earlier diagnosis of glaucoma. In an observational cohort study, **Sehi et al.** compared the ability of Fourier-domain OCT and time-domain OCT to both discriminate between normal and glaucomatous eyes and assess retinal nerve fiber layer (RNFL) thickness.

Normal and glaucomatous eyes underwent complete examination, standard automated perimetry, optic disc photography, TD-OCT (Stratus OCT, Carl Zeiss) and FD-OCT (RTVue, Optovue). One eye per subject was enrolled. Two consecutive scans

were acquired using a 3.46-mm diameter scan with TD-OCT and a 3.45-mm diameter scan with FD-OCT. For each of five RNFL parameters, the area under the receiver operator characteristic curve was calculated to compare the ability of FD-OCT and TD-OCT to discriminate between normal and glaucomatous eyes.

Fifty healthy persons and 50 glaucoma patients were enrolled. Average, superior and inferior RNFL thickness measurements were significantly greater with FD-OCT compared with TD-OCT in normal eyes and glaucomatous eyes. The areas under the receiver operator characteristic curves for RNFL thickness were similar using FD-OCT and TD-OCT.

The authors speculate that the high-resolution scanning provided with FD-OCT may enable better detection of early structural damage as compared with TD-OCT.

Archives of Ophthalmology

Choroidal Nevus: Frequency of Transformation Into Melanoma

August's *Archives*

Shields et al. evaluated the frequency of growth of choroidal nevi into melanoma from an ocular oncology practice in Philadelphia. Choroidal nevi included in this study were a mean of 5 mm in diameter—which is larger than choroidal nevi from the Blue Mountain Eye Study where the diameter has been published at 1.5 mm. Thus, many patients in this group would fit criteria of suspicious choroidal nevus.

In the present analysis, the authors found that nevi grew into melanoma in 2 percent of patients at one year, 9 percent at five years and 13 percent at 10 years. They found that risk factors for growth into melanoma include a nevus thickness of greater than 2 mm, subretinal fluid, orange pigment, tumor margin of 3 mm or less from the optic disc, hollowness on ultrasound and the absence of halo. Nevi exhibiting three or four of these factors had five times greater risk for growth into melanoma

than those with no risk factor. Nevi with all six risk factors had 21 times greater risk.

The authors conclude that eyes with choroidal nevi should be evaluated carefully for the above risk factors and that patients with one or more risk factors should be examined by an ocular oncologist or qualified specialist.

WT1 and Bcl-2 Expression in Melanocytic Lesions of the Conjunctiva

August's *Archives*

Furusato et al. examined WT1 and Bcl-2 expression in a variety of conjunctival melanocytic lesions to evaluate their diagnostic utility compared with other melanocytic markers. Protein expression and localization of WT1 and Bcl-2 were studied by immunolabeling in 123 conjunctival melanocytic lesions and compared to Bcl-2, S-100, HMB45 and Melan A.

WT1 showed a graded increase in expression in lesions with increasing atypia. Higher mean numbers of WT1 positive cells also correlated with increasing atypia in melanocytes, while Bcl-2 expression was more robust than S100, HMB45 and Melan A. WT1 and HMB45 showed diffuse and strong staining in atypical nevi, primary acquired melanosis with atypia and malignant melanoma.

The authors conclude that Bcl-2 is a highly sensitive marker for melanocytic tumors of the conjunctiva, while HMB45 and WT1 staining can distinguish benign from malignant lesions.

Excision of Periocular Basal Cell Carcinoma

August's *Archives*

Levin et al. report their experience with 200 cases (192 patients) of periocular basal cell carcinoma (BCC) treated with an enhanced frozen-section control (FSC) technique using stereoscopic microdissection of the surgical margins. All tumors were excised en bloc with 1 mm beyond the clinically apparent tumor and were examined using an enhanced FSC technique.

The overall recurrence rate was 1 percent with a mean follow-up of four years. In the 93 percent of patients with primary tumors, the recurrence rate was 1.1 percent with a mean follow-up of 3.9 years. There were no recurrences in the secondary tumor group after a mean follow-up of 4.8 years. Of the 200 lesions, 66 percent required a single en bloc resection to achieve tumor-free margins. Of those with positive histological margins, 88 percent required a single additional 1-mm en bloc excision.

The authors conclude that an enhanced FSC technique using stereoscopic microdissection of the surgical margins permits greater conservation of healthy tissue and yields cure rates comparable to those of the standard

FSC technique and Mohs' micrographic surgery.

Wound Healing Response in Mitomycin C–Treated Leaking Blebs

August's *Archives*

Einer et al. characterized histopathologic features of leaking mitomycin C–treated blebs and aberrant wound healing that may lead to persistent conjunctival thinning and leakage.

The authors examined 40 MMC-treated filtering blebs excised for persistent leaks from 40 patients. Ninety percent of the leaking blebs contained epithelial-stromal domes with areas of acellular bands of collagen underlying attenuated epithelium. Seventy-five

percent of the blebs demonstrated varying degrees of fibrovascular repair growing from the bleb margin—either beneath or interdigitating with the acellular zone. A novel observation in 65 percent of specimens was Alcian blue positive myxoid stroma at the interface between the fibrovascular proliferation and the epithelial-stromal dome. The association between the presence of fibrovascular proliferation and Alcian-blue staining myxoid stroma was significant.

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

Intravitreal Ranibizumab to Treat CNV Secondary to Pathologic Myopia

Eye

2009;23:1275–1281

Is intravitreal ranibizumab efficacious and safe for treating choroidal neovascularization (CNV) secondary to pathologic myopia? According to results from a case series by **Monés et al.** involving 23 eyes of 23 patients, the answer is yes. In the study, pathologic myopia is defined as an eye with a minimum refractive error of –5 D and retinal signs such as lacquer cracks and peripapillary chorioretinal atrophy. Following an initial injection, these patients received intravitreal ranibizumab as needed and were followed monthly for 12 months.

Patients received an average of 1.52 injections. Some patients demonstrated a progressive improvement beyond one month after a single injection. No serious ocular complications were reported. At 12 months, the mean visual acuity improved by 9.53 letters with 69 percent of patients increasing at least one line and 34.7 percent increasing three or more lines.

Rose Bengal vs. Lissamine Green in Dry Eye Syndrome

Cornea

2009;28:735–740

In a randomized, comparative, crossover study of 60 eyes of 30 consecutive patients with dry eye syndrome, **Machado et al.** evaluated and compared the corneal staining patterns and patient comfort levels of lissamine green and rose bengal. They also assessed the correlation of disease severity and staining patterns.

Patients were randomly divided into two groups depending on which dye was administered first. The second dye was applied one hour later or after the first drop was washed out—whichever occurred last.

The researchers found that lissamine green offered comparable and similar staining patterns as rose bengal in patients presenting with mild to moderate dry eye syndrome. In addition, lissamine green was better tolerated in terms of patient comfort than rose bengal. The researchers did identify a poor correlation between patient symptoms and signs.

Transpalpebral Tonometer IOP Measurements Compared

Cornea

2009;28:724–727

The TGDc-01 (Ryazan State Instrument-Making Enterprise) is a new digital transpalpebral tonometer designed to measure IOP. Its effectiveness has received mixed reviews in the literature. **Shemesh et al.** conducted a study in patients who had undergone penetrating keratoplasty (PKP) to compare the IOP measurements of this new device with the two methods currently being used to measure IOP: Goldmann tonometry and the Tonopen XL (Reichert).

The study involved 45 eyes of 43 patients. The researchers found that the transcorneal IOP measurements made by Goldmann tonometry agreed more closely with the measurements obtained by the Tonopen XL. In addition, the TGDc-01 readings were lower compared with the other two devices.

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