

# Journal Highlights

## NEW FINDINGS FROM *OPHTHALMOLOGY*, *AJO*, AND *JAMA OPTHALMOLOGY*

### ***Ophthalmology***

#### **Prevalence of Myopia in Europe**

July *Ophthalmology*

As educational levels rise in Europe, is the prevalence of myopia rising as well? **Williams et al.** investigated this question and found that myopia is indeed becoming more common among Europeans. However, higher education seems to be one of several factors contributing to the condition, rather than the sole cause.

For this meta-analysis, the researchers evaluated 15 population-based cross-sectional studies from the European Eye Epidemiology Consortium. The studies were conducted between 1990 and 2013, and data were available for 61,946 participants aged 44 to 78.

The results indicate that myopia is becoming more common across Western and Northern Europe, with a clear trend toward higher prevalence in younger participants. Education had a strong effect: Myopia was twice as common in those who had achieved higher educational levels than in those who left school before they turned 16. However, increasing levels of myopia were not explained by education alone,

and other factors—such as increased computer time and longer school days with less time outside—may play a role, the authors noted.

#### **Kinetics of Geographic Atrophy Progression in AMD**

August *Ophthalmology*

**Lindner et al.** described the directional kinetics of the spread of geographic atrophy (GA) in eyes with age-related macular degeneration (AMD) and foveal sparing. They found a faster centrifugal than centripetal GA spread.

This prospective, noninterventional natural history study involved 47 eyes (36 patients) with foveal sparing in GA. They were examined via fundus autofluorescence and near-infrared reflectance imaging. Areas of foveal sparing and GA were measured by 2 independent readers, and a linear mixed-effect model was used to model GA kinetics over time.

Data analysis revealed a 2.8-fold faster progression of atrophy toward the periphery than toward the fovea during follow-up (range, 5.9-74.6 months). Although the underlying mechanisms for this differential progression remain unclear, the findings may be of use to researchers who are studying strategies to prolong foveal survival in eyes with GA.

#### **Phantom Eye Syndrome**

August *Ophthalmology*

In the largest study to date on the topic, **Hope-Stone et al.** investigated the prevalence and features of phantom eye syndrome (PES) after enucleation for uveal melanoma. They found that a significant number of patients experience PES and suggest that those who are slated for enucleation should be routinely informed about this possibility.

For this cross-sectional study, the researchers evaluated 179 patients with uveal melanoma. Enucleation had taken place 4 to 52 months before this study began. The patients answered a questionnaire that asked about 3 symptoms: pain, visual sensations, and a feeling of seeing through the removed eye. In addition, the participants' mood was assessed using a standard anxiety and depression evaluation scale.

Of the 179 participants, 108 (60.3%) experienced symptoms, with 86 (48%) reporting visual sensations, 50 (28%) reporting a feeling of seeing, 42 (23%) reporting pain, and 14 (7.8%) reporting all 3 symptoms. The researchers also investigated potential triggers of PES; the most common were darkness and fatigue.

Because the symptoms can cause distress, PES should be discussed before surgery, the researchers said. They added that patients who reported post-surgical pain in this study were more likely to be anxious and depressed.



**AMD, Intravitreal Injections, and IOP**September *Ophthalmology*

**F**reund et al. assessed changes in IOP in patients who received intravitreal injections for wet age-related macular degeneration (AMD). They found that, through 96 weeks of treatment, aflibercept was less likely than ranibizumab to cause a rise in IOP.

This study analyzed data on 2,457 patients in the phase 3 VIEW 1 and 2 trials. Participants were randomized to 1 of 4 treatment regimens for 52 weeks; 3 of these groups received aflibercept in different dosing regimens, while the fourth group received 0.5 mg of ranibizumab every 4 weeks. From week 52 through week 96, treatment continued on a variable basis with at least quarterly dosing; interim injections were allowed based on anatomic and visual assessment.

Mean change in IOP from baseline was consistently lower for all 3 aflibercept regimens than for the ranibizumab regimen, the researchers found. Through week 96, 6.4% of those receiving ranibizumab experienced a rise in IOP of 10 mm Hg or more, compared with 2.9% to 3.8% of those receiving aflibercept. Moreover, through week 96, 20.2% of the patients treated with ranibizumab had an IOP of 21 mm Hg or greater, compared with 12.5% to 14.2% of those receiving aflibercept. Notably, a personal history of glaucoma at baseline did not correlate with these outcomes.

The researchers noted that the mechanism underlying these findings was unclear; hypotheses include possible differences in the size of protein aggregates the 2 drugs form in the vitreous, as well as the inflammatory propensity of their source molecules.

**American Journal of Ophthalmology****Ocular Surface Squamous Neoplasia Treatment**August *AJO*

**L**i et al. reported a retrospective interventional case series that evaluated the recurrence rate of

ocular surface squamous neoplasia (OSSN) after excision and cryotherapy and determined factors associated with recurrence.

This study reviewed all cases of OSSN from 1998 through 2013 that were treated with excisional biopsy and adjunctive cryotherapy in a New Jersey health care system. All recurrences of OSSN after excision and cryotherapy were noted and categorized in relation to clinical characteristics, pathologic grade, and margin involvement. A total of 43 cases of OSSN from 42 patients were analyzed with a median follow-up of 29 months; of these, 33% had dysplasia, and 67% had squamous cell carcinoma.

Among the 43 cases of OSSN, there were 3 recurrences, for a recurrence rate of 7.1% after wide excision with cryotherapy. This figure remained the same at 1, 2, and 5 years. All 3 cases that recurred had been incompletely excised. However, the majority of incompletely excised OSSN (25/28) experienced no recurrence, suggesting that minimal recurrence can be achieved with excision and cryotherapy applied to the margins.

**Acupuncture as Treatment for Glaucoma**August *AJO*

**L**aw et al. used a prospective double-masked randomized crossover study to evaluate acupuncture as treatment for glaucoma. They found that acupuncture therapy for glaucoma did not show any overall effect on diurnal IOP reduction or on visual acuity. One eye per patient with primary open-angle glaucoma and stable IOP was randomized to receive 1 acupuncture series consisting of 12 sessions with either eye-related acupoints (eye-points) or non-eye-related acupoints (non-eye-points). Patients then crossed over to receive a series of the other acupoint treatment. Measures evaluated included IOP, blood pressure (BP), heart rate (HR), best-corrected visual acuity (BCVA), visual field (VF), optic disc and peripapillary retinal nerve fiber layer (RNFL) measurements, com-

pliance, and adverse reactions.

Twenty-two patients volunteered and 11 (50%) completed the study; 8 (36%) did not complete treatment owing to changes of health, moving away, lack of transportation, or family crisis; and 3 (14%) were withdrawn because of needle sensitivity or IOP elevation (8 mm Hg) in the contralateral eye.

After an acupuncture session, the researchers found a small, temporary mean IOP increase after using either eye-points (from 12.9 to 13.6 mm Hg) or non-eye-points (from 13.0 to 13.5 mm Hg). HR, diurnal IOP, and BCVA showed no statistically significant changes after 12 sessions of either series. Systolic and diastolic BP were reduced after 12 sessions of the non-eye-points series. Optic disc, RNFL, and VF showed no statistically significant changes.

**Punctal Plug Retention Rates in Treatment of Dry Eye**August *AJO*

**B**risette et al. conducted an interventional randomized double-masked controlled trial to compare retention rates of SuperFlex versus Parasol punctal plugs. The study demonstrated a higher rate of retention at 6 months of the Parasol punctal plug compared with the SuperFlex plug.

The study evaluated 50 eyes from patients with moderate to severe dry eye. Each eye from eligible patients was separately randomized to receive SuperFlex or Parasol punctal plugs. The main outcome measure was plug retention at 6 months. Secondary outcome measures included objective tests of Schirmer I, tear meniscus height, tear breakup time, inferior fluorescein corneal staining, and average lissamine green conjunctival staining.

Punctal plug retention was significantly different between the 2 types at 6 months: 68% of Parasol plugs were retained, compared with 32% of SuperFlex plugs. Mean retention time was 4.7 and 3.4 months for the Parasol and SuperFlex plugs, respectively. Additionally, eyes with Parasol plugs required less frequent artificial tear use

at 6 months. There were no additional significant differences between groups, and no complications were reported.

This study also demonstrated the effectiveness of punctal occlusion for the treatment of moderate to severe dry eye. With both types of plugs, there was a statistically significant improvement in all secondary outcome measures at 6 months, except for conjunctival staining.

### **JAMA Ophthalmology**

#### **Disorganization of Retinal Inner Layers and Vision After DME**

July *JAMA Ophthalmology*

The prognosis and treatment response in center-involved macular edema (ME) may vary according to underlying anatomic abnormalities. Radwan et al. investigated whether variables seen on spectral-domain optical coherence tomography (SD-OCT), particularly disorganization of retinal inner layers (DRIL), are associated with subsequent VA after resolution of edema in diabetic and nondiabetic ME.

This was a retrospective longitudinal cohort study, in which Snellen VA testing and SD-OCT macular imaging were performed at a tertiary referral eye center for retinal diseases. The researchers reviewed the medical records of all patients with ME from Dec. 1, 2010, to Dec. 31, 2012. The date of the last follow-up was June 1, 2013.

Participants included 55 patients (70 eyes) with center-involved ME that had resolved during an 8-month period. Patients were grouped based on diabetic vs. nondiabetic ME. Masked graders analyzed the central 1,500- $\mu$ m macular region for changes, including cystoid abnormalities, length and extent of DRIL, and outer retinal layer disruption.

In both DME and nondiabetic ME groups, VA after resolution of edema correlated with baseline VA. In a DME model including baseline VA and DRIL, total length of the DRIL was associated with subsequent VA as determined by a parameter estimate

(PE) of 0.0003 (95% CI, 0-0.0006;  $p = .03$ ). The VA change during the 8-month period, after adjustment for baseline VA, was best associated with DRIL change (PE, 0.0002 [95% CI, 0-0.0003];  $p = .04$ ). DME participants whose DRIL resolved, whether early or late, showed improvement in their VA deficit at 8 months (least squares mean [SE], 41.3 [28.5] and 40.9 [37.5], respectively) compared with those who did not have resolution. After adjustment for baseline VA, the largest difference in VA in DME eyes was between those with persistent DRIL after ME resolution versus those with no DRIL at baseline (-89.6 [27.2] versus 49.7 [19.6], respectively;  $p = .006$ ). However, in nondiabetic ME, no association was found between DRIL and VA after resolution of edema.

Although the interpretation of the results might be limited by the small number of eyes evaluated at a single clinical site and by a retrospective study design, the authors concluded that the presence of DRIL at baseline and its resolution pattern may be associated with subsequent VA after resolution of center-involved DME.

#### **NAION and Obstructive Sleep Apnea Syndrome**

July *JAMA Ophthalmology*

Aptel et al. sought to evaluate the prevalence of obstructive sleep apnea syndrome (OSAS) in patients with nonarteritic anterior ischemic optic neuropathy (NAION) as well as the influence of OSAS on second-eye involvement. The researchers examined 118 patients with NAION referred to a tertiary care center from Jan. 1, 2003, through Dec. 31, 2010.

Patients underwent polysomnography to detect OSAS and were then followed prospectively to assess the risk of second-eye involvement. In 89 patients with NAION who underwent polysomnography, 67 (75%) had OSAS. Second-eye involvement was found in 10 of 73 patients (13.7%) at 3 years, occurring in 8 of 52 patients (15.4%) with OSAS and 2 of 21 patients (9.5%) without OSAS ( $p = .04$ ).

In multivariate analysis, the risk of second-eye involvement was increased by nonadherence to treatment with continuous positive airway pressure (CPAP) among patients with severe OSAS (hazard ratio, 5.54; 95% CI, 1.13-27.11;  $p = .04$ ).

The results suggest that OSAS is common in patients with NAION and that polysomnography should be considered in these patients. The findings also suggest that those with severe OSAS who are nonadherent to CPAP treatment have an increased risk of second-eye involvement.

#### **Clinically Meaningful Low Vision Rehabilitation Outcomes**

July *JAMA Ophthalmology*

Patient-centered measurements that reflect clinically meaningful changes in visual ability are necessary to facilitate comparative outcomes research in low vision rehabilitation (LVR). Goldstein et al. performed a prospective observational study to quantify the effects of currently provided LVR on patients in the United States.

This study enrolled 779 new patients seeking outpatient LVR services at 28 U.S. clinical centers from April 2008 through May 2011. The Activity Inventory (AI), a visual function questionnaire, was administered to measure overall visual ability and visual ability in 4 functional domains (reading, mobility, visual motor function, and visual information processing) at baseline and 6 to 9 months after usual LVR care. The Geriatric Depression Scale, Telephone Interview for Cognitive Status, and Medical Outcomes Study 36-Item Short-Form Health Survey physical functioning questionnaire were also administered, and clinical findings of patients were provided by study centers.

Of the original group of patients, baseline and postrehabilitation measures were available for 468. The main outcome measures were changes in the study population and minimum clinically important differences in the individual in overall visual ability and in

the 4 functional domains as measured by the AI. Minimum clinically important differences in overall visual ability were seen in 47% of participants. In addition, the percentages of patients who achieved minimum clinically important differences in the functional domains were as follows: 44% in reading, 38% in visual motor function, 33% in visual information processing, and 27% in mobility.

Age ( $p = .006$ ) was found to be an independent predictor of changes in overall visual ability, while logMAR visual acuity ( $p = .002$ ) was predictive of changes in visual information processing. The authors concluded that 44% to 50% of patients presenting for outpatient LVR show clinically meaningful differences in overall visual ability after LVR, and the average effect sizes in overall visual ability are large, close to 1 standard deviation.

## ROUNDUP OF OTHER JOURNALS

### Preserving MMC's Reliability

*Journal of Glaucoma*

Published online May 14, 2015

**K**inast et al. compared the effects of common preparation and storage conditions on the stability of mitomycin C (MMC) solutions. They found that the different MMC solutions showed similar stability as soon as they reached room temperature. However, further storage at room temperature led to mild degradation of some of the solutions.

For this study, 5 MMC solutions were freshly prepared according to manufacturers' standards. Two preparations were stored under refrigeration for 1 or 2 weeks; the third was frozen for 23 days, and the fourth was frozen for 32 days after compounding and then shipped on ice. The fifth preparation was generated using dry powder. The samples were then analyzed after they were warmed to room temperature. This was done at 4 time points: at the moment when they reached room temperature and after 1, 4, and 24 hours.

The researchers found similar high levels of stability when the solutions were analyzed immediately upon reaching room temperature. However, by the 24-hour point, 2 preparations—the solution that had been refrigerated for 2 weeks and the one shipped on ice—showed some degradation. All told, losses of up to 7% of MMC stability were noted.

Although this level of degradation is unlikely to significantly limit fibroblast inhibition, it could possibly affect the consistency of trabeculectomy results, the researchers said.

### Gene Therapy for Leber Congenital Amaurosis

*New England Journal of Medicine*  
2015;372(20):1887-1897

**B**ainbridge et al. set out to evaluate the safety and efficacy of gene therapy in a small group of patients with Leber congenital amaurosis (LCA). Although they found a modest level of improvement, it peaked at 6 to 12 months after treatment and then declined thereafter.

This phase 1/2 open-label trial involved 12 participants, aged 6 to 23 years at enrollment, and lasted 3 years. The gene therapy used—a recombinant adeno-associated virus 2/2 (rAAV2/2) vector that carried the RPE65 complementary DNA—was administered at 2 dose levels.

Improved retinal sensitivity was apparent in 5 of the 8 patients who received the higher dose, and in 1 of the 4 who received the lower dose. This was evident within 1 to 2 months after vector administration, and it continued to progress for 6 to 12 months. Although the improved sensitivity subsequently declined, it was still evident in 2 participants at the 3-year mark. Overall, the level of improvement varied widely among participants, and no improvement was of a magnitude that could be detected by electroretinography (ERG). In addition, no clear correlation emerged between participant age and degree of response.

A parallel study was also conducted in dogs, in which the researchers in-

vestigated the relationships among vector dose, visual function, and ERG findings. In this study, substantial improvements in retinal function could be measured by ERG and were highly dose dependent.

### Intraoperative Aberrometry and Toric IOLs

*Journal of Refractive Surgery*  
2015;31(4):237-242

**D**oes intraoperative aberrometry improve placement of toric intraocular lenses (IOLs)? Hatch et al. investigated this question and found that it does.

In this nonrandomized retrospective study, 64 eyes underwent cataract surgery with toric IOL implantation. In all eyes, IOL power and alignment were determined by means of automated keratometry, standard optical biometry, and an online calculator; this process was further refined with intraoperative aberrometry in 37 of the 64 eyes.

The mean postoperative residual refractive astigmatism (RRA) was  $0.46 \pm 0.42$  D and  $0.68 \pm 0.34$  D in the eyes evaluated with and without aberrometry, respectively. Further analysis indicated that intraoperative aberrometry yielded better results not only in postoperative RRA but also in manifest cylinder reduction and in manifest cylinder percentage change.

The authors acknowledged that intraoperative aberrometry has drawbacks, including cost, additional time in the operating room, and a learning curve for the surgeon.

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*Ophthalmology summaries are written by Jean Shaw and edited by Susan M. MacDonald, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. JAMA Ophthalmology summaries are based on authors' abstracts as edited by senior editor(s). Roundup of Other Journals is written by Jean Shaw and edited by Deepak P. Edward, MD.*

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